The Conceptual Design of

3D Miniaturised / Integrated Products

as Examined through the Development of a

Novel Red Blood Cell / Plasma Separation Device

A thesis submitted for the degree of Doctor of Philosophy

By

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I, David Topham, declare that this thesis titled The Conceptual Design of 3D Miniaturised / Integrated Products as Examined through the Development of a Novel Red Blood Cell / Plasma Separation Device and the work presented in it are my own. I confirm that:

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Abstract

The aim of this research is to examine the conceptual design issues concerned with integrating product capabilities that can only be generated at the micro- scale (through feature sizes generally of the order of 100nm to 100µm) directly into 3-dimensional products at the macro-scale.

Such macro-scale products could accordingly contain internal devices that are too small to be seen or touched by unaided human designers, which begs the question as to how to enable designers to work with objects which are beyond direct human experience, and how can the necessary collective discussion take place within teams of designers, and between these teams and those responsible for product manufacture?

This thesis examines and tests a concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures using procedures allied to those used by graphic designers to create solid objects from 2-dimensional prototype geometries through, for example, extrusion or rotation.

Applying such procedures to theoretical diagrams in order to transform them into scalable 3-dimensional devices is not yet in general use at the macro-scale, but with increasing recognition of the unique capabilities of the micro- scale the idea may grow in appeal to alleviate the difficulties of conceiving of functional structures that, when built, will be too small to experience directly.

Furthermore this design method, through its basis upon a common currency of functional diagrams, may overcome many of the problems of describing and discussing the design and manufacture of normally intangible objects in 3 dimensions.

Finally, it is shown through the example of a novel Red Blood Cell / Plasma Separation Device that the geometric transformation process can lead to the design of functional structures which would not readily be arrived at intuitively, and that may be effectively and efficiently integrated into host products.

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Preface

The research began in April 2007 as an activity within the 3D-MINTEGRATION [1] Grand Challenge project, an EPSRC-funded project, described in [2], which ran from September 2005 to March 2010.

3D-MINTEGRATION, which grew to encompass 8 universities and some 20 companies, was concerned with "The Design and Manufacture of 3D Miniaturised/Integrated Products." From the outset, even though "Design & Simulation" was the subject of one of the project's five work packages, this aspect of the project was restricted to focus upon assisting designers to chose and use the project's developing manufacturing processes, and to assess the benefits and risks of using these processes. A series of loosely-defined demonstrator products was incorporated within the project plan for the purpose of testing the new manufacturing processes being developed.

Unexpectedly, the manufacturing process developers found it difficult to conceive of demonstrator products, prompting the realisation that the actual conceiving of design had not been recognised as a necessary component of the Design & Simulation work package. To resolve that omission the School of Engineering Design at Brunel University was invited to join the project through a Doctoral Training Award disbursement which in part supported the work reported here.

Embarking upon the design of the demonstrators revealed that the activity of conceptual design itself would have to be extended to cope with the transformation of underlying product principles, typically in 2D diagrammatic form, into a 3D topology. As a result, a transformation routine was developed for the generation of a 3D product from a 2D example. This idea, and the notion that a 3D miniaturised/integrated approach should be beneficial, was examined through the design, prototyping and testing of the project's "Minifluidic" demonstrator, a novel Red Blood Cell / Plasma Separation Device.

The experiences and observations arising during the course of the conception and development of the red blood cell / plasma separation device form the backbone of this thesis.

Acknowledgements

Grateful thanks go to my supervisors, Professor David Harrison and Dr Peter Evans, both of whom impressed me when I met them originally as an external manager of an EPSRC programme. Now they have managed me. They have both displayed remarkable patience and delivered hugely important nudges in just the right places to keep this thesis on track. I have learned so much. I also wish to thank part-time co-workers Katy Jenkins and Odette Valentine, who brought very different and inspirational viewpoints, and some very good questions.

Other team members at Brunel University London have been at all times gracious and helpful to me, in both the laboratories and the library. A well-curated library, both electronic and shelved, is a vital resource when otherwise faced with information overload from the web at large.

This thesis has benefitted enormously from a broad spectrum of contributors: the sparky band of Principle Investigators, researchers and industrialists who made up the 3D-MINTEGRATION project community, which contributed problems and took up the solutions; the interviewees, survey correspondents, workshop volunteers and conference attendees drawn from the European smart systems community, who all freely donated not only their knowledge but their time too. Big thanks to you all.

I was very fortunate to be folded under the wing of the late Dr Albert Kempton (1911-2000) as my tutor and physics supervisor at Christ’s College Cambridge. I only became fully aware of his formative effect upon me when I read his obituary. It was an emotional moment.

Announcing an exam success, he wrote to me “I am pleasantly surprised to tell you...” In the tradition of surprises, this thesis has surprised me, and I hope it surprises its readers. I dedicate the work to his memory.

Chapter 1 Introduction

1.1 Objectives and background

The aim of this research is to examine and improve conceptual design processes concerned with integrating product capabilities that can only be generated at the micro- scale (through feature sizes generally of the order of 100nm to 100μm) directly into 3-dimensional products at the macro-scale, through:

- Studying the interpersonal difficulties of conversing about the intangible when product designers need to choose and use principles which are beyond everyday human experience, and the degree to which designers depend upon expert intermediaries.

- Examining, testing and assessing the interpersonal and engineering benefits that could arise from using the concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures, investigated through the practical evolution of a novel Red Blood Cell / Plasma Separation Device.

1.1.1 The problem of unobservable devices

In everyday life, the great majority of products and systems now contain internal devices based upon mechanical, thermal, chemical, fluidic/hydraulic/pneumatic, or electromagnetic principles, or combinations of principles, to enable the products or systems to perform the roles expected of them. If the incorporated devices are at the normal human scale of sight and touch they are easy to recognise and understand by appropriately skilled people, who may then communicate and discuss the working of the devices with other people, such as those in design teams, in order that products may be improved, or so that entirely new products can be conceived of based upon the experience gained in the design and operation of preceding products.

But what of designing products and systems containing devices that are too small to be seen or touched by unaided human designers? How can designers work with objects which are beyond direct human experience, and how can collective discussion take place within teams of designers, and between these teams and other teams responsible for product manufacture?

1.1.2 Functional building blocks

One approach to the above problem might be to treat products containing devices that are too small to understand directly as being assemblies of a range of standardised “functional building blocks”, each standard block having been originally crafted by experts, with well-defined attributes and interfaces to each other such that they may be selected, arranged and put together without in-depth knowledge of their “hidden” working principles.

The design of electronic integrated circuit “chips” is an example of such “high level design”, ie design at an abstract, functional, level that excludes involvement with the detailed constitution of the working parts. Although the following description of the issues around designing with functional building blocks focuses upon electronics, it should be understood that other systems, for instance cell-based plants and animals, are routinely depicted in much the same way.

The minute working parts of integrated circuits are devices, termed “junctions” or “gates”, which control the flow of electric current. They are constructed from contiguous conductor, semiconductor and dielectric materials, with geometries typically at the scale of tens of nanometres and hence outside the bounds of direct human observation. However, the high level design of integrated circuits only needs to concern itself with the configuration of connections between junctions or gates, based solely upon their functional attributes, not their internal composition.

The scheme of high level design using standardised functional blocks is all very well for electronic circuits, where there is a common factor of electrical current flow which makes for standard interfaces between the blocks, there being in principle no technology boundaries to cross. The approach fails however if it is necessary to interface differing technologies like, for example, mechanical functional blocks to fluidic blocks, which then entails a further layer of design to create bespoke interfaces.

From the preceding it will be appreciated that the use of pre-designed standardised functional blocks can be supremely efficient in the creation of complex systems within the single-technology continuum of electronics, as is evidenced by the relentless growth of the global semiconductor industry.

On the downside, the technique constrains designers to a single technology, to rely upon the expertise of a restricted elite of functional block “gurus”, and, as a high level designer, to be excluded from any opportunity to tailor the parameters of the blocks themselves to better fit them to the exact requirements of the final product.

Accordingly, although the building block approach can be very productive, the trade off is a degree of inflexibility leading to sub-optimal performance and a potential to stifle innovation through constraining the designer to the legacies of a single technology.

1.1.3 Beyond electronics and into 3 dimensions

The design of electronic chips is now in the main rooted upon building blocks that encapsulate specialised physics applied through esoteric materials at nano-scale geometries. But the precision micro-fabrication processes originally developed for chip manufacture are now finding application to create new, and bespoke, non-electronic structures providing, for example, miniaturised mechanical and fluidic functions which may with cost and performance advantages be integrated into products.

While there are many examples of non-electronic building blocks, spanning from bricks to genes, the building block approach cannot possibly be extended to the whole broad range of physical phenomena that may be employed in technology-based devices, and the further multiplicity of interface permutations between devices of differing technologies.

As a case in point, mechanical phenomena are underpinned by a plethora of scientific effects, including mass, force, acceleration, leverage, friction, inertia, potential and kinetic energy, angular momentum, elasticity and many more. By comparison, electronics is confined essentially to the interaction of electromagnetic energy with linear and non-linear resistance and reactance.

Moreover, the functional building block approach for electronic chips, constrained by the planar nature of chip manufacturing processes, always results in flat arrangements of interconnected devices which, under magnification, appear much like city plans, with buildings connected by roads.

This flat formation is often at odds with the 3-dimensional form of products which incorporate electronic chips, leading to design compromises such as wasted space and materials, and difficulties in connecting the electronic heart of the product to the outside world of the user or ultimate application. This is particularly true of biological implants, and health and usage monitoring systems to be embedded into airframes, automobiles and load-bearing structures.

1.1.4 Transforming 2-dimensional diagrams to 3-dimensional forms

The approach followed by this thesis firstly recognises that physical phenomena themselves may often be described theoretically in the form of 2-dimensional diagrams. Such 2-dimensional diagrams are a common currency understood by the design, engineering and manufacturing communities, and furthermore provide a secure and agreed basis for discussion.

Building upon that observation, the thesis examines and widens a concept that 2-dimensional diagrams of function may be transformed into 3-dimensional working structures, using procedures allied to those used by graphic designers to create solid objects by manipulating 2-dimensional prototype geometries through, for example, extrusion or rotation.

The procedures adopted by graphic designers to create 3-dimensional objects from prototype cross-sections are well known, and have become easily and widely used through the adoption of Computer Aided Design software and systems.

1.1.5 Usefulness and contribution to knowledge

Applying graphical procedures to theoretical diagrams in order to transform them into scalable 3-dimensional devices is not yet in general use at the macro-scale, but with increasing recognition of the unique capabilities of the micro- scale the idea may grow in appeal to alleviate the difficulties of conceiving of functional structures that, when built, will be too small to experience directly.

This design method, through its basis upon a common currency of functional diagrams, may overcome many of the problems of describing and discussing the design and manufacture of normally intangible objects.

Finally, it will be shown through the example of a novel Red Blood Cell / Plasma Separation Device that the geometric transformation process can lead to the design of functional structures which would not readily be arrived at intuitively, and that may be effectively and efficiently integrated into host products.

Figure 1: Concept model of Red Blood Cell / Plasma Separation Device

1.2 Scope, structure and approach of work

1.2.1 Scope

The primary thrust of the research is to examine the application of graphical procedures to transform theoretical diagrams into scalable 3-dimensional devices, with an emphasis upon the example of a novel Red Blood Cell / Plasma Separation Device. But in the wider sense the research is set in the context of how designers can work with micro- scale objects which are beyond direct human experience, and how in these circumstances discussion can take place within design teams, and consequently with other teams responsible for product manufacture.

Accordingly, the reach of the research can be visualised as in Figure 2, below:

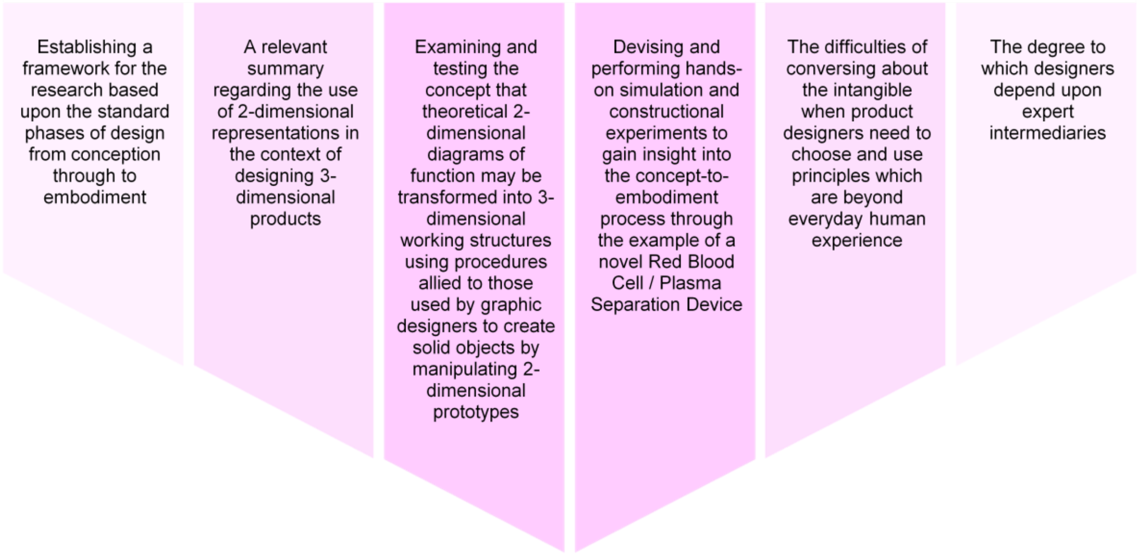


Figure 2: Research scope

1.2.2 Boundaries

Although the research used the development of a novel Red Blood Cell / Plasma Separation Device as an example of a product that may be conceived through the transformation of a theoretical diagram into a scalable 3-dimensional device, the research intentionally made no attempt to extend into the clinical domain, save for gathering typical “in-use” parameters and ascertaining that such a device could gain useful acceptance.

Similarly, although aspects of the research gained usefully from modelling and simulation procedures, and some cues from the concept of similitude, it was not the intention of the research to add significantly to the sum of knowledge in these topic areas. Nevertheless, the work provided examples and stimulation for workers researching in these fields, eg Xue, Bailey et al. [3], [4], [5], [6] and [7].

1.2.3 Structure

The elements depicted in the preceding Figure 2 are taken as six inter-related research topics, shown in Figure 3, below, along with a summary of the activities supporting the research.

Three distinct strands emerged: “Background Knowledge”; “Interpersonal” which focused upon the observations from, and of, people in the design regime; and “Practical” comprising work concerned with the in-practice design, construction and assessment of design-to-embodiment issues related to the exemplar Red Blood Cell / Plasma Separation Device.

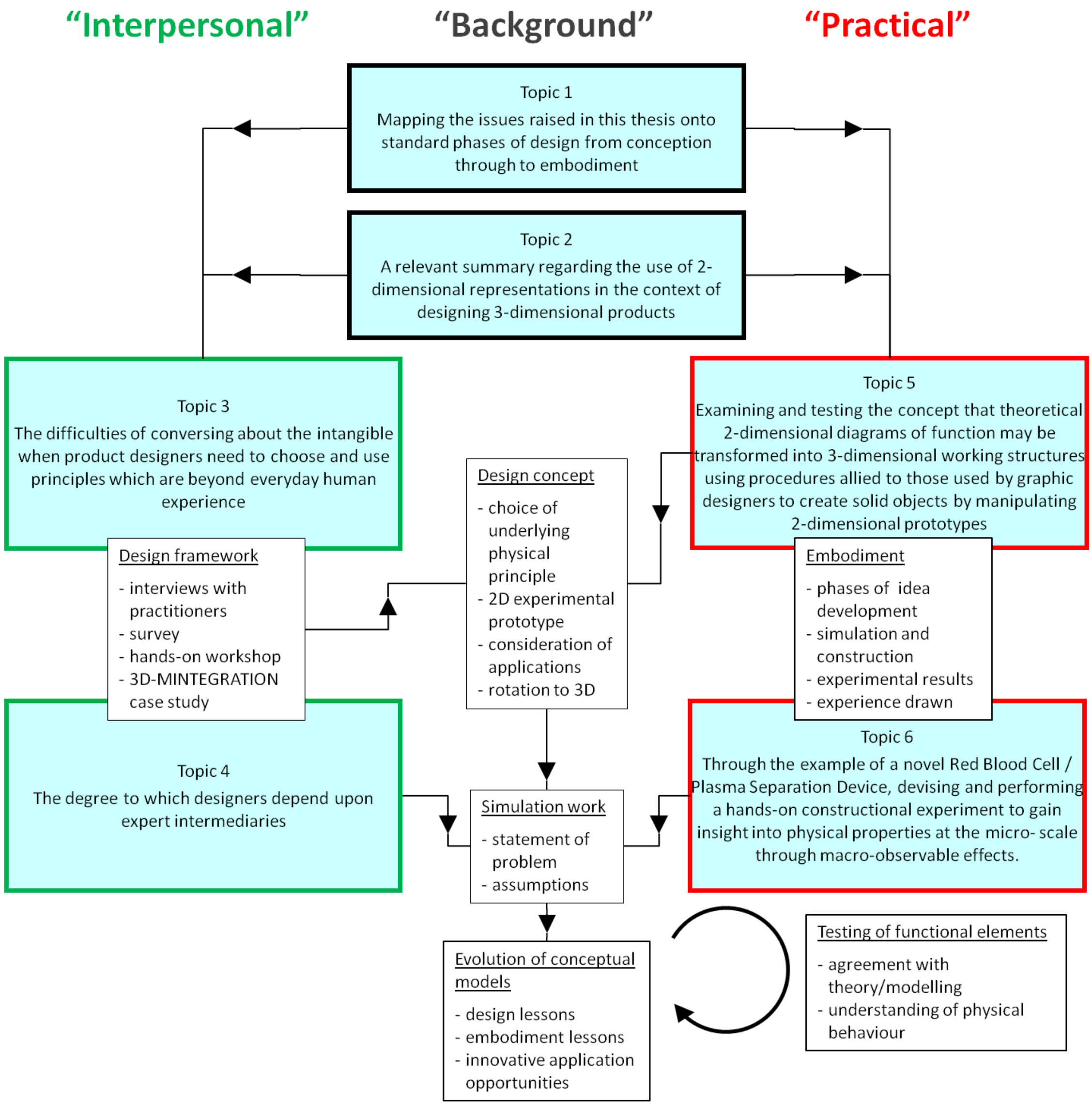


Figure 3: Topics and activities

1.2.4 Activity

The work revolved around six research topics as shown in Figure 3, above.

Topic 1 comprised a desk-researched assimilation of the phases of design from conception through to embodiment, as relevant to the focus of this thesis, resting largely upon a standard framework of design put forward by Pahl, Beitz, Feldhusen and Grote [8]. This framework (see 2.3 on page 27) was chosen because it is a disciplined approach to the design of engineered products.

Other descriptions, such as the “Double Diamond” design process model, a graphical way of describing the design process developed through in-house research at the Design Council in 2005 have more broad application from services to products and market/user research. Although echoing the work of Pahl, Beitz, Feldhusen and Grote, albeit with modified headings, the categories are not so specific to engineering design.

This thesis does not attempt to compare and contrast design process descriptions. References are made in [9], [10] and [11]. The choice of the framework derived by Pahl, Beitz, Feldhusen and Grote was on the basis of it being appropriately clear and consistent to structure the observation and analysis of design-team based actions, and their interactions, when faced with unfamiliar engineering concepts.

Topic 2 reviewed the use of 2-dimensional representations in the context of designing 3-dimensional products. The combined work of Topics 1 and 2 was necessary to provide a framework for the remaining four topic areas:

Topics 3 and 4 were examined through interviews, observation, discussion and workshops. Topic 3 concerned the issues of conversing about the intangible within design and manufacturing teams, where the use of diagrams is a common currency, and Topic 4, which extended the considerations of Topic 3, touched upon the degree of reliance designers might place upon expert intermediaries.

Topics 5 and 6 went hand-in-hand, as researching the concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures centred upon the practically-worked example of conceiving of, designing and developing conceptual models of a novel Red Blood Cell / Plasma Separation Device.

1.3 Research motivation and application

1.3.1 Primary stimulus

This research was prompted through participating in the 3D-MINTEGRATION [1] project, a four-year EPSRC-funded collaboration between eight universities and some 20 companies. The project was concerned with “The Design and Manufacture of 3D Miniaturised/Integrated Products.”

The “Design” aspect of the project was envisaged to focus upon assisting designers to chose and use the project’s developing manufacturing processes, and to assess the benefits and risks of using these processes. Accordingly a series of loosely-defined demonstrator products was incorporated within the project plan for the purpose of testing the new manufacturing processes being developed.

Unexpectedly, the manufacturing process developers found it difficult to conceive of demonstrator products, prompting the realisation that the actual conceiving of design had not been recognised as a necessary component of design.

In retrospect, one should not be surprised that a consortium of manufacturing process orientated researchers might lack design experience. Nevertheless, this lack of a specific skill set identified and amplified the need for better linkages between design and manufacturing particularly in respect of the exploitation of new technologies and new manufacturing methods.

Group discussions regarding the design of the demonstrators revealed that the activity of conceptual design would have to be extended to cope with the transformation of underlying product principles, typically in a 2-dimensional diagrammatic form, into a 3-dimensional topology. As a result of observing the group discussions, which rested strongly upon sketching and gesticulations, a transformation routine was developed for the generation of a 3-dimensional product from a 2-dimensional example.

This idea was consequently examined through the design, prototyping and testing of the project’s “Minifluidic” demonstrator, a novel Red Blood Cell / Plasma Separation Device.

The experiences and observations arising during the course of the conception and development of the red blood cell / plasma separation device form the backbone of this thesis.

1.3.2 Extended application

During the progressing of this research, the notion that product design teams might benefit from better connections to the underlying physical principles gained further topical relevance with the upsurge of the “maker” [12] community, whose members are wresting some elements of the design and manufacture of technology products from commerce to be applied on an individual or ad-hoc “cloud” basis.

Furthermore, the advent of personal manufacturing techniques, including for example "3D Printing" [13], brings an additional need to equip non-specialists with the wherewithal to connect with underlying physical principles to support their creation of useful and effective products.

These latter observations regarding the usefulness of the research were suggested by Odette Valentine [14] in the course of her own research at Brunel University London, and David Benqué during his time at the Royal College of Art, London.

1.3.3 Limits of application

The ideas and observations examined and developed in this thesis are not put forward as a general panacea for the difficulties of creating highly integrated technology products, but the outcomes should provide elements to build upon and apply across a broad family of products, notably in "Smart" products that incorporate sensors, actuators and local data processing into items that retain or mimic their previous, and possibly familiar, "traditional" form.

1.4 Overview of thesis

This chapter and the next provide the background to the research, with Chapter 2 providing a literature review gathering and assessing firstly definitions, then supporting information grouped around summaries of the six Topic areas of the research. This chapter forms the background to the research, includes the results of the desk studies comprising Topics 1 and 2 and documents the ongoing information gathered as needed during the course of the research.

Chapter 3 describes the Research Methodology applied to the six Topic areas.

Chapter 4 concerns research into interpersonal exchanges in the design arena as defined in Topic areas 3 and 4: The issues of conversing about the intangible when product designers need to use principles which are beyond everyday human experience, and the degree to which designers depend upon expert intermediaries.

Chapter 5 focuses upon Topic areas 5 and 6, which concern testing the concept that theoretical 2-dimensional diagrams may be transformed into functional 3-dimensional structures using procedures allied to those used by graphic designers, and the practical investigation of the concept through designing, simulating and prototyping a novel Red Blood Cell / Plasma Separation Device.

Chapter 6 comprises discussion and conclusions arising from the research as a whole.

Chapter 2 Literature Review

2.1 Approach

2.1.1 Perspective

In addition to a formal course of research, this thesis also calls upon personal observations drawn from a career spanning fundamental electronic circuit design, the design and construction of integrated electronic modules, the creation and marketing of technology-based products and, latterly, participation in, and management of, science and engineering research projects as collaborations between industry and the research community.

A common thread arose throughout the foregoing experiences: the often unsatisfactory position of designers at the fundamental technical level being effectively insulated from the objectives of end-product specifiers and users, and the dislocation of product designers concerned primarily with form, fashion and ergonomics who fail to trust in a safety net of design-for-manufacture activities to provide a somewhat compromised bridge between the advanced technologies within the product and the final form of a product to be made appealing and effective for the user.

These issues are to a degree being addressed by shared workspaces such as the WALL participatory design workspace [15], but these approaches only seek to streamline a traditional sequence of operations and the now widely-accepted iteration of potentially several rounds of conception, testing and embodiment.

Two emerging factors are largely neglected by this streamlining of traditional activities: The advent of truly integrated products wherein the technology content is inextricably formed as part and parcel of the structure of the product itself; and the emergence of sole or craft-scale designer/producers who are embarking upon highly localised or even desk-top manufacture akin to the introduction of desk-top publishing in the 1980s.

This work is not intended to study or extend the formalities of design and manufacture, for which there is already a formidable body of past and current research. Bayazit [16] provides a review of 40 years of design research in the broadest sense, as does Cross [17] on the evolution of design research, but gaining a framework for the current study has been aided strongly by the analyses of the “artificial intelligence” community eg “Knowledge aided design” [9], an introduction to the train of activities from thought to embodiment as described by Henry Petroski [10] and Baxter [11] and a rigidly thorough exposition of the framework of design according to Pahl, Beitz, Feldhusen and Grote [8].

2.1.2 Organisation

The course adopted for the literature review followed the six topics forming the structure of this thesis, but with emphasis shifting appropriately to the needs of each topic area. As a precursor, section 2.2 introduces definitions of terminology adopted during the course of research with a view to establishing consistency and reducing ambiguity.

The section 2.3 review concerning Topic 1, establishing a framework for the research based upon standard phases of design from conception through to embodiment, is pursued to a depth judged adequate to establish a structure for Topics 3, 4, 5 and 6, whilst avoiding being drawn into researching the huge body of work describing the design-to-embodiment field as a whole.

Section 2.4 provides the background for interpreting the research into Topics 3 and 4, which explore the difficulties of conversing about the intangible when product designers need to use principles which are beyond their everyday experience and the degree to which designers depend upon expert intermediaries.

Section 2.5, which supports Topic 2 in its summary of the use of 2-dimensional representations in the context of designing 3-dimensional products, is similarly constrained, rather than embarking upon an all embracing grand tour of visualisation and perception.

Topics 5 and 6 investigate, test and assess the concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures. Accordingly, section 2.6 surveys the matters of 3-dimensional transformations, embodiment design, simulation and modelling that are part-and-parcel of these topics.

Section 2.7 provides an overview of the need for and the approaches to Red Blood Cell / Plasma Separation, but it is important to note that although the design and prototyping of a separator device is used as a focus for Topics 5 and 6, any medical parameters collected are generalised; an in-depth exploration of medical practice is not attempted.

Section	Content
2.1	Approach to literature review: perspective and organisation
2.2	Definitions of terms used
2.3	Phases of design from conception through to embodiment
2.4	Communicating the intangible
2.5	The use of 2-dimensional representations in the designing of 3-dimensional products
2.6	Transforming theoretical 2-dimensional diagrams of function into 3-dimensional working structures: concept and practice
2.7	The need for and the approaches to Red Blood Cell / Plasma Separation
2.8	Summary discussion

Figure 4: Guide to literature review

2.2 Definitions of terms used

The following terms have more general meanings in other settings, but their definitions are tightened for their very specific and consistent use in this thesis:

2-Dimensional, Planar, 3-Dimensional

All physical objects in the real world have length, breadth and thickness (height). Except in the form of concepts, there are no 1-dimensional or 2-dimensional things. Consequently this thesis defines items whose thickness is very much less than either of the other two dimensions as "planar", and notes that planar items may be bent or folded to become recognisably 3-dimensional objects. The use of the term "2-dimensional" in this thesis is confined to describing the solely informational, conceptual content of diagrams, maps and sketches (qv below), disregarding any thickness of the substrate (often paper or a screen) upon which they may be drawn, printed or displayed, and disregarding also any unintended folds or bends in that substrate.

Picture, Photograph, Print

Pictures, photographs and prints intended to be formed into, or conformed onto, models are considered as "planar" physical objects in this thesis.

Diagram, Map, Sketch

Diagrams, drawings, maps and sketches are considered to be purely "2-dimensional" in this thesis, recognising solely their informational content and ignoring their physical manifestation.

Functional Diagram

A functional diagram is regarded as symbolic of the function of a device rather than representing the actualities of its construction. Electrical circuit diagrams and certain classes of map (for example journey planners) are examples of representations that largely diverge from the geometry of the object they describe, whilst functional diagrams of certain mechanical systems, for example the pendulum, and fluidic systems, for example pipes and channels, are stylised versions of the physical embodiment of objects based upon the depicted principles.

Integration

As used in this thesis "integration" implies an irreversible and intimate fusion of structures, potentially formed in a single process, as opposed to "assemblies", which are structures of parts that are joinable and separable, each potentially the result of individual design and manufacture.

2.3 Phases of design from conception through to embodiment

This work is not intended to extend the formalities of design, for which there is already a formidable body of past and current research. A Brunel library search for publications containing “Conceptual Design of Products” yielded 90 results, headed interestingly by “The conceptual design of products benefiting from integrated micro-features” for which this researcher is the principal author [18]. The majority of these results were concerned with either CAD systems, or business or reliability issues. In view of this, the gaining of formal background knowledge for the current study was aided strongly by the analyses of the “artificial intelligence” community eg “Knowledge aided design” [9], and introductions to the train of activities from thought to embodiment as described by Henry Petroski [10] and Baxter [11] . The artificial intelligence community was careful to delineate and categorise human activities in its attempt to automate the processes from design to manufacture.

Following the preceding familiarization a rigid framework of design according to Pahl, Beitz, Feldhusen and Grote in their thorough and specific exposition “Engineering Design, a systematic approach” [8] was adopted. On pages 131 to 134 the authors define four stages of design, recorded here in brief:

Planning and task clarification

- Generates a requirements list

Conceptual design

- Abstracts the essential problems
- Seeks and proposes candidate principles for their solution
- Specifies a front-running solution or set of solutions that show promise against the outline criteria. (Could be a sketch of building blocks, layouts of technological possibilities, etc)

Embodiment design

- Drafting of layouts to critique according to the constraints of potential manufacturing processes, including financial viability
- The assessing of any compromises that may arise against the original requirements list

Detail design

- Production documentation

Models and prototypes happen at every stage, possibly iterating several times.

2.3.1 Conceptual Design

Matters of conceptual design are central to this thesis, as reflected in its title: “The Conceptual Design of 3D Miniaturised / Integrated Products as Examined through the Development of a Novel Red Blood Cell / Plasma Separation Device.”

The core of the work concerns the difficulties of conversing about the intangible when product designers need to use principles which are beyond everyday human experience, and the potentially alleviating concept that theoretical 2-dimensional diagrams may be transformed into 3-dimensional structures, tested through designing the blood separation device.

Accordingly, the background study supporting the research has an emphasis upon the conceptual design process. This, as mentioned in the previous section, firstly abstracts the essential problems that the product or system seeks to address, then identifies underlying principles for their solution. From these candidate principles a principal solution or solutions may then be selected according to criteria which best fit the constraints of manufacturing and use.

The above description depicts a logical train of activity which draws a veil over real-life obstacles including those examined in this thesis:

- In defining the essential problems the differing perspectives of users, makers, marketers and the cultural demands of fashion and aesthetics almost certainly demand the application of teams of people rather than a single individual.

- Gaining access to underlying principles requires sources of those principles, abilities to associate them to the essential problems and to assess their capability to solve those problems.

- Communicating and discussing candidate solutions across a team of differing disciplines.

- Marrying the chosen principal solution or solutions with optimal efficiency to a manufacturable product, the available processes for its production and the demands and desires of users and their wider culture.

- The situation where the principles driving the product are beyond normal human experience, either through matters of scale or shrouding through their intimate integration with the product itself, is an exacerbating matter affecting all the above.

In addition to the above impediments, the “spark” or “idea” that sets off the process of conception and subsequent inventive problem solving needs to be acknowledged. Pahl, Beitz, Feldhusen and Grote [8] in describing the problem solving process introduce intuitive thinking on page 47, drawing upon the works of Abeln [19] and Müller [20] in terms of “flashes of inspiration” caused by some trigger or association, also folding in background “silent” knowledge, episodic memories, vague concepts, and imprecise definitions.

Regarding the last notions of “vague concepts and imprecise definitions”, which may lose some meaning in translation from the original German, it is often observed that superficial or imprecise knowledge of a subject may indeed lead to inventive breakthroughs. However, this “kick from uncertainty”, if not properly considered in the light of safer information, can lead to dangerous errors, not only of detail, but of approach, as will be seen in the thesis sections 4.3.3 “Pitfalls of analogues and assumptions of authority”.

2.3.2 Problem solving aspects of conceptual design

The review of literature providing background to this thesis revealed that, if one excludes purely cerebral subjects such as the design of software code, the overwhelming body of design-related texts relies heavily on anecdote to illustrate statements and arguments.

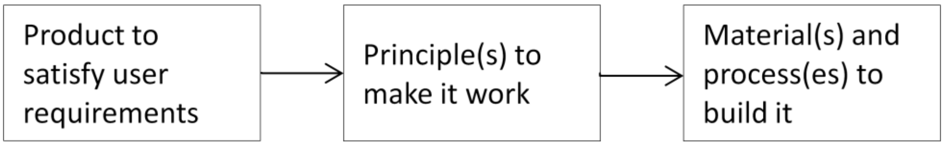
Design across all aspects of even a simple product is complex, for example a spherical ball: its dimensions and to what tolerance?; weight, colour, texture, taste, smell, “feel”?; elasticity and aerodynamics?; solid, layered, filled or hollow?; how does it appeal to and interact with different classes of user?; manufacturability, cost, environmental matters? safety, flammability, toxicity?; longevity in use, end of life disposal? And probably more, including matters such as the work of Dan Lockton on “Design with Intent” - how users’ behaviour is influenced by design [21].

Brown and Chandrasekaran [22] see design as a search through a large and complex set of alternatives. French [23] suggests a “repertoire of known means” as identifying a smaller subset of principles to follow, but only provides narrative illustrations in the form of case histories.

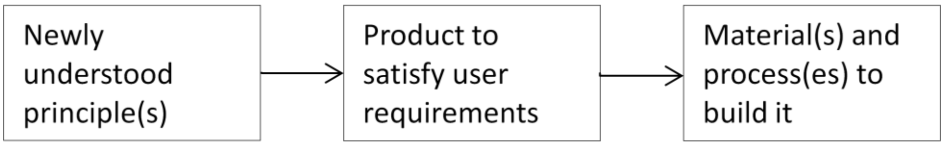
The subject of “decomposition”, ie breaking the problem into understandable parts, is described succinctly by Poli [24] where, in the introduction he cites the simple decomposition of a wheelbarrow into “wheel” and “barrow”, and then goes on to use the example of pumps, where a type may be selected according to circumstances, which is subsequently scaled, then specified in suitable materials and manufacturing tolerances.

Such a decomposition is only useful when the elementary parts are well-known and tangible. Nevertheless, a more general approach to narrow down a field so immense that it requires description by richly complex examples might be to concentrate on just three questions regarding the design of a product: What is it for, how will it work, how will it be made?

Figure 5 (below) presents alternative highly simplified sequences for product conception based upon the application of these questions.



1. Product driven by user needs



2. Product driven by exploiting new knowledge

Figure 5: Alternative sequences of product conception

The first sequence, that generally put forward in product design and business development literature, sees the design-to-manufacture process serving requirements defined by the user (or on behalf of the user by another authority or marketeer). The requirements then drive a selection process regarding choosing then ranking the physical principles that will provide the functionality expected of the product, and then the development of embodiment options regarding the materials and processes that will allow its manufacture. In reality iterations occur at every stage to refine the answers to the 3 basic questions.

The second sequence is prevalent in the progressing of innovation. New understanding of a physical phenomenon often raises, in addition to the value of building new knowledge, an opportunity, and in some cases an obligation, to exploit the new knowledge by applying it usefully. In this sequence there may be a very strong emphasis upon developing production methods, and a concomitant effort in generating user interest and appetite for the new product capabilities that have been enabled, where previously there was either no demand at all, or purely speculative wishes.

In this second sequence the technical principle to be used is a given, in that it is the new invention or understanding that is to be exploited. But in the first sequence the technical principle has to be identified and chosen. Section 2.3.4 “Overcoming the barriers: existing approaches, tools” provides insight into the approaches that can assist.

Whichever sequence applies, particular aspects of the question “How will it work?” and its relationship to “How will it be made?” are central to this thesis, along with the inevitable need to communicate and discuss concepts and requirements across the team or teams involved in the product generation process.

“How will it work?” and its relationship to “How will it be made?” was revolutionised in electronics when integrated circuit building blocks became widely available in the late 1960s, triggering seismic changes in the design process in terms of centralisation of the fundamental design of building blocks, the unleashing of complexity by downstream designers stringing together the building blocks in innovative ways, and a concomitant explosion in the capabilities and feature sets of end products.

However, as reported in [18], the design and manufacture of 3D miniaturised / integrated products, although apparently akin to the design and manufacture of integrated semiconductors, differs in *one momentous respect*: whereas, through design and manufacturing formality, electronics designers do not need to know the intimate physics of electron flow within a chip, integrated product designers need to know precisely the mechanical, optical, magnetic, thermal, fluidic, biological or chemical processes which underlie the operation of the microstructures that they intend to craft.

2.3.3 Drivers and obstacles for this topic area

Microengineering, through the continuous development and proliferation of the semiconductor chip, has been a dominant driver for technological products and systems over the past 50 years. Latterly, the manufacturing and ancillary processes associated with semiconductor chip production have been applied to non-electronic devices, “MEMS – Micro-Electro-Mechanical-Systems” - providing access to mechanical, fluidic and thermal physical effects which take upon different and useful attributes to those which they display at macro dimensions. Chapter 4, “Microscale Physics”, of An Introduction to Surface-Micromachining [25] provides a useful introductory review.

Micromachined mechanical devices, such as strain gauges, accelerometers, pressure sensors, switches and valves provide typically higher speed, lower power use and more sensitivity in operation than their macro- scale equivalents, due primarily to their lower mass.

Microfluidic devices exploit highly laminar flow to enable very precise manipulation of liquids and particle suspensions due to their narrow channel width. They are also able to process minute quantities of material, which may be important to work with a limited availability of samples.

Micro- optical devices may contain structures commensurate in size with the wavelength of light, or highly responsive moveable low-mass mirrors or prisms to steer light beams to enable, for example, displays, spectroscopy, or quantum encryption.

The application of microengineering techniques promises the above benefits and more, but has generally fallen short of optimal exploitation in mainstream products due to difficulties of integrating micro- and nano- scale processes into conventional product structures. Although it is relatively easy to microengineer gyroscopes, temperature sensors, accelerometers and microphones in component form – all used in “smartphone” products – they remain as stand-alone components to be fixed individually onto supporting and interconnecting substrates.

The planar form of the iPhone 5 is determined largely by the display, and the need for pocketability. Planar construction of the working parts is compatible with this form, although the assembly of a great number of small parts is undesirable.

Products such as Baidu’s “Smart Chopsticks” which are conceived to detect food temperature, sweetness, acidity and impurities, do not favour planar construction as their form and use is strongly constrained to the expectations of a traditional product. Such products beg for 3D Miniaturised / Integrated approaches in design and manufacturing.

A further driver for the adoption of 3D Miniaturised / Integrated approaches is the increased recognition of “bio-inspiration” - examining the approaches evolved by nature and adopting like strategies for the creation of functional products. Like nature, which typically builds its functions on a cellular scale, the advent of microengineering techniques allows the exploitation of mechanisms - chemical, mechanical, fluidic and optical – which can perform functions analogous to those observed in living organisms. A good introduction is provided by Jenkins [26], who cites an early example of bio-inspiration in the development of Velcro® fasteners following the observation of the burrs upon burdock seeds by De Mestral in the 1940s.

The drivers for 3D Miniaturised / Integrated approaches in design and manufacture may be summarised as follows:

- The ability to introduce technology-based functionality into the physical form of traditional products, or into new products, such as medical implants, that need to fit efficiently into 3-Dimensional spaces.

- The ability to integrate microengineered functions without the constraint of using planar interconnecting structures.

- The opportunity to introduce capabilities inspired by biology.

- Improved functionality whilst reducing mass and the use of materials.

The barriers impeding the adoption of 3D Miniaturised / Integrated approaches include:

- The capability to design within the form of a product without recourse to a catalogue of building blocks.
- A lack of familiarity with the workings of elements at micro- scale, which are intangible to normal human senses.
- The difficulty of designing and manufacturing integrated solutions depending upon bespoke non-standard interfaces between functional elements.
- The need to be able to transform physical principles, typically understood in planar form, into more effective 3D structures that may be incorporated directly into macro-products.
- The need for an environment for whole design teams to experience and debate the behaviour of micro- features, and thereby to capitalise upon the strength of teams, not individuals, to solve "large" design problems at product and system level.

2.3.4 Overcoming the barriers: existing approaches, tools and resources

Figure 6 sets out the main avenues to address the design-related barriers shown in 2.3.3 to impede the conceiving of 3D Miniaturised / Integrated products.

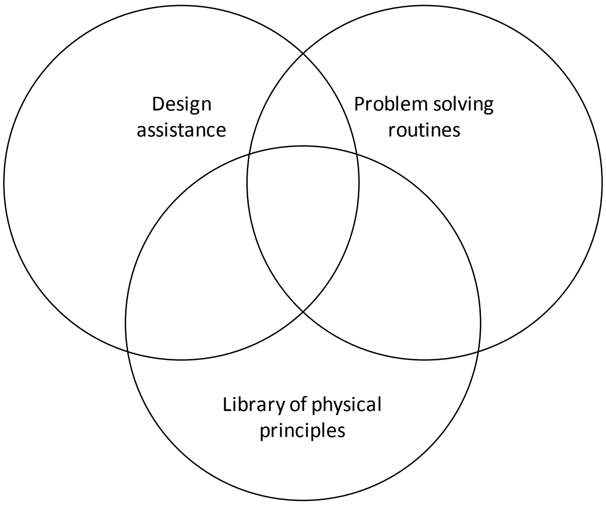


Figure 6: Current means to address barriers in design

Ideally, the tools and resources shown in Figure 6 should be interlinked, but during the annual international Smart Systems Integration conference, held in March 2015 this topic was discussed with fervour in a panel discussion: "Design of Smart Systems". The gathered experts considered that as of 2015 no viable integrated approach was available. Accordingly, examples of each of the three individual approaches are as follows, with comments:

2.3.4.1 Design assistance: Computer aids

Marc Green in his 1997 compilation Knowledge Aided Design [9] lists and defines the following:

Design aide	suggests alternatives
Design informer	a memory aide of easy-to-find possibilities
Design demon	warns of violations
Design strategist	ranks decision ordering
Design secretary	shares status of design and knowledge base
Design translator	shows the design in different lights of functionality, manufacturability
Design documenter	records and classifies decisions, successes and failures for future use
Design simulator	first principles representation of the design

The foregoing list is typical of the directions being addressed by the AI community in the late 20th Century, with Green suggesting that “The next generation of tools should provide knowledge aided design (KAD), where computers supply the knowledge necessary to help engineers in the earlier stages of design”.

As will be put forward in section 2.4.1.2, there needs to be a clear distinction between explicit, or factual, easily codified *data and information* as opposed to the tacit, entwined and difficult to codify *knowledge (awareness of facts in context), understanding and experience*.

Accordingly, computer aids nearly 20 years later remain as aids, often also automating mundane tasks, and not the “expert systems” that they may be billed as by their purveyors.

2.3.4.2 Problem solving routines: TRIZ

“TRIZ” is the (Russian) acronym for the “Theory of Inventive Problem Solving.” The methodology was created and developed by G.S. Altshuller and his colleagues in the former Soviet Union between 1946 and 1985, and since then has been further extended and refined to reflect the needs of the design community and the discovery of new technologies.

The original work arose from the analysis of patents to reveal a backbone of 40 “Inventive Principles” which can be used to resolve conflicts between pairs drawn from a collation of 39 “Engineering Parameters.”

In themselves the indications provided are not useful unless linked to identifiable, employable physical principles. TRIZ is therefore not a substitute for properly educated and experienced individuals, inquisitive enough to appraise developments in the solution space they work within.

Access to lists of physical principles, and explanations of their bases, is available variously as described below in 2.3.4.3. It should be mentioned here that theoretical descriptions of physical principles are unlikely to provide instruction regarding the practicalities of their embodiment in end products, save through case histories.

2.3.4.3 Library of physical principles

TRIZ is almost always presented with some form of access to examples of physical principles that can be selected as solutions to product design problems.

Many other libraries exist, ranging from web sites such as the free resource “How stuff Works” to the blue chip “Goldfire Invention Machine” platform, which aims to provide a complete solution, with powerful semantic searches across engineering texts, patents and a Scientific Effects Knowledge Base containing more than 8,000 animated effects and examples.

It is not clear how the above libraries keep abreast of the breadth of scientific discovery that impact product design, and no evidence was found of ability to deal with conflicts and synergies arising from the juxtaposition of technologies resulting through intimate integration.

As with the comment made about computer aids in 2.3.4.1, the searchable libraries of physical principles focus upon easily codified data and information as opposed to the tacit, difficult to classify combination of knowledge, understanding and experience.

2.4 Communicating the intangible

Conventionally, design offices comprise multi-disciplinary teams with a store of experiences. In the macro- world experiences are easy to appreciate and share as they stem from either a familiar world view or are explicable and debateable in familiar terms.

The progress of electronics has been remarkable when it is considered that electron flow, fields and waves themselves (rather than their effects) are largely imperceptible to the unaided observer, but in the case of electronic design, the selection of characterised components with known high-level functions permits the design process to proceed largely without intimate knowledge of the underlying physical principles of electron flow, fields and waves.

Outside the province of electronics, physical principles at the macro- scale are well-known, and often related easily to every-day experience: heat, light, weight, tension, leverage, vibration, wind and water flow are all examples of shared experiences that design teams can communicate, discuss and relate to the special case of the product or system that they are designing.

At the micro- scale the situation is radically different. Components with characterised high-level functionality are not generally available, *and an extensive literature research found no comprehensive lists of components, nor, consequently, any routines for choosing between them*. Furthermore, cross-disciplinary connections, as for example fluidic/optical interfaces, need to be considered on a case-by-case basis at the level of underlying physical principles.

The behaviour of the micro- world, where for example gravity may be inconsequential compared with electrostatic forces, is outside the every-day experience of designers. Discussing these matters within a team requires a deeper understanding of physical principles normally reserved for specialists. Real-life analogues are fraught with pitfalls and misunderstanding.

To compound this difficulty, expert knowledge of the micro- world is fragmented, residing within relatively small groups, distributed sparsely across the world, and more often than not highly specialised according to narrow applications and rigidly-defined manufacturing processes optimised solely for those applications.

Examining the communication of the intangible means understanding the breadth, content and modes of communication, and also the methods available for engaging with “inaccessible” technologies. These are examined in 2.4.1 and 2.4.2.

2.4.1 Communicating across and beyond the design team

The preceding sections introduced the need for the design process to respond to technology and market drives, to solve problems and to overcome barriers, perhaps aided by specialist tools. Satisfying this need almost certainly demands the application of teams of people as referred to above rather than a single individual.

2.4.1.1 What is needed to be communicated?

In their 1998 article concerned with the knowledge needs of designers in SMEs [27] Rodgers and Clarkson carefully define the terminology of Data, Information, Knowledge, Understanding and Experience drawing upon the 1997 PhD thesis of Marsh [28]. Mapping their definitions onto the topic of the current section 2.4.1 “Communicating across and beyond the design team” results in the following:

Data reduces to facts and quantities, such as dimensions, material properties and parameters. Throughout design teams these may be conveyed in plain language, spoken, written and tabulated.

Information, described in [27] as “structured data [including] what is said or recorded”, again presents no significant impediments to normal communications, as long as any specialist terms are universally understood.

Knowledge, Understanding and *Experience* are delineated in [27] as follows:

- knowledge being “awareness of facts [comprising] an assimilation of related information ... in the context of a frame of reference”
- “The term understanding is used to imply human cognitive processes through which associations and inferences can be used to apply knowledge appropriately”
- a definition of experience as “knowledge and understanding generated from exposure to events and artefacts.”

Rodgers and Clarkson do describe the listed definitions as “inadequate as they stand” suggesting that “A further distinction between the terms knowledge and information is required in the context of design”.

Skyrme in his 1997 publication regarding knowledge management [29] recognises two distinct types of knowledge - explicit and tacit. He defines “explicit knowledge” as essentially being the data and information, which, as has been noted above, may be conveyed in plain language, spoken, written and tabulated, presenting no significant impediments to normal communication, as long as any specialist terms are universally understood.

He goes on to describe the remaining “tacit knowledge”, as that which Nonaka and Takeuchi define in [30] as “highly personal and hard to formalise. Subjective insights, intuitions and hunches fall into this category of knowledge."

Skyrme cautions against the loose use of “information” and “knowledge” interchangeably. He then recognises that information itself is easily communicable, and that the tacit “knowledge that is in people's heads” is not easy to codify.

This remaining difficulty is compounded by Skyrme, Nonaka and Takeuchi referring to “knowledge” itself as a subset of “tacit knowledge.”

To resolve this, at least for this thesis and the purposes of the topic of this section “Communicating across and beyond the design team”, *knowledge, understanding and experience* can together be considered as corresponding to the “tacit” category: tightly interwoven awareness of facts and their application in context guided by appropriate prior experience, together providing an integrated stream of *conceptual communication* which runs alongside the more straightforward communication of the items categorised as “explicit” - data and information.

Accordingly the following elements of communication are adopted for this thesis:

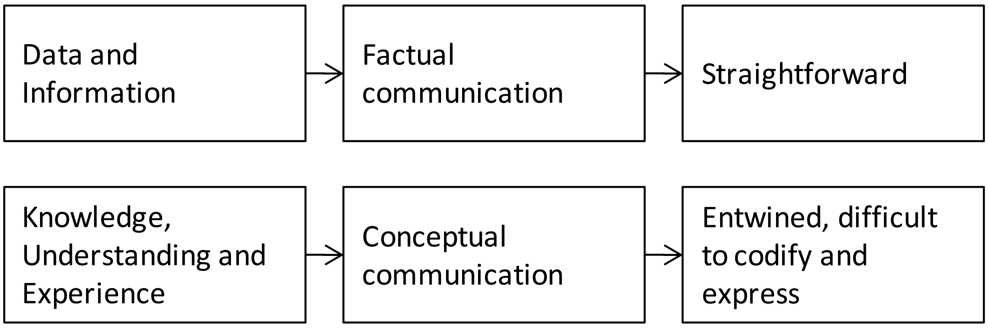


Figure 7: Parallel streams of design communication

2.4.1.2 Modes of inter-personal communication in design

The problem of communicating concepts between individuals and teams of widely differing experience and outlook has been a contention of the HCI (Human Computer Interaction) community, where notably there is a chasm between programmers, computer hardware designers, applications designers, interface designers and users.

Michael J. Muller surveys methods, techniques, and practices in Participatory Design (PD) in the paper “Participatory design: the third space in HCI”, a chapter within The Human-Computer Interaction Handbook [31].

He cites PD as stemming from a movement of politically-motivated workplace democratisation (Involving the workforce) in Scandinavia as depicted by Ehn and Kyng [32], and goes on to introduce a “Third Space” or “In-between” region as an environment for debate, like a territory “invaded” by the various tribes of participants, who hammer out common understandings and languages. The creation of a “hybrid” culture in this territory is argued by Bhabha [33].

In terms of potential modes of communication within this third space, the following from Muller's list are apposite for this thesis:

Settings
For example "Bring the designers to the workplace" or "Bring the workers to the design room" suggested by Robins, J [34], and as witnessed in practice by the author at Renishaw Plc, UK, February 2008, when it was observed that the company had intentionally constrained its designers to traverse the prototyping area on the way to their own workplace.

Workshops
Often providing an environment intentionally unfamiliar to the participants, as exemplified by the workshop recorded in section 4.2 of this document

Stories
Including perhaps discussion of popular shared media such as the cinema film "The Fantastic Voyage", in which fictional characters are shrunk in size to explore the inner workings of the human body.

Photographs
Curiously Muller's survey only mentions photographs and does not include diagrams and sketches in the shared experience of grouping artefacts, which again was central to the workshop recorded in section 4.2 of this document. Section 2.5 of this thesis "2D representations used in the design of 3D objects" considers the topic of diagrams, how they can be a common currency for communication and how they may assist in the conceiving and embodiment of products.

Constructions and the making of descriptive artefacts
Making physical objects is a strong "draw" for collaborative discussion, and was the subject for workshop activity that took place in the 3D-MINTEGRATION [1] project recorded as a Case Study in section 4.3 of this document.

Evolutionary Prototyping and Cooperative Prototyping
For example the creation of prototype models of the Novel Red Blood Cell / Plasma Separation Device to focus public and private debate as recorded in Chapter 5 of this document.

The survey by Muller does not mention shared cyberspaces, possibly as the internet was nascent at the time of its publication. In the course of the research supporting this thesis no web-based real-time forum applications dedicated to interdisciplinary design discussion were found, moreover design practitioners reported low use of virtual reality systems in the survey recorded in sections 4.1.2 and 4.1.3 of this document.

Neither does the survey mention *Dance* (or other forms of gesture) as a method of expression to transcend verbal language and static diagrams. Section 4.3.5 of this thesis records a pirouette performed by Professor W O'Neill, of the University of Cambridge, as being the starting demonstration for the concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures.

2.4.1.4 Round up of section 2.4.1 Communicating across and beyond the design team

This section has:

- Explored in 2.4.1.1 the nature of the elements to be communicated and introduced the concept of two distinct parallel streams.
- In 2.4.1.2 examined approaches to address communications difficulties within the HCI community that may be applied to resolve shortcomings arising in the *conceptual communication* stream between players involved in the conceptual design of products.

Chapters 4 and 5 of this thesis probe further into the difficulties of communicating across and beyond the design team.

2.4.2 Engagement with "inaccessible" technologies

Conventionally, design groups comprise multi-disciplinary teams with a store of experiences that are easy to share, aided perhaps with some shorthand "jargon" to encapsulate more complex concepts.

In the case of electronics design, the fundamentals of resistance and reactance, plus the application of the equations of Ohm, Thevenin/Norton and Maxwell are sufficient bases to work from, as long as the "parasitic" or "stray" components arising from the practicalities of physical embodiment are also recognised and accounted for.

Four strategies to enhance engagement with "inaccessible" technologies are as follows:

2.4.2.1 Learn from preceding products using the technology

Outside the province of electronics, "Bio-inspired-Engineering" presents an interesting example, as modern instrumentation such as spectrometry and electron microscopy has revealed some of the inner workings of nature that, although imperfectly understood and largely beyond direct human experience, may be employed in new products.

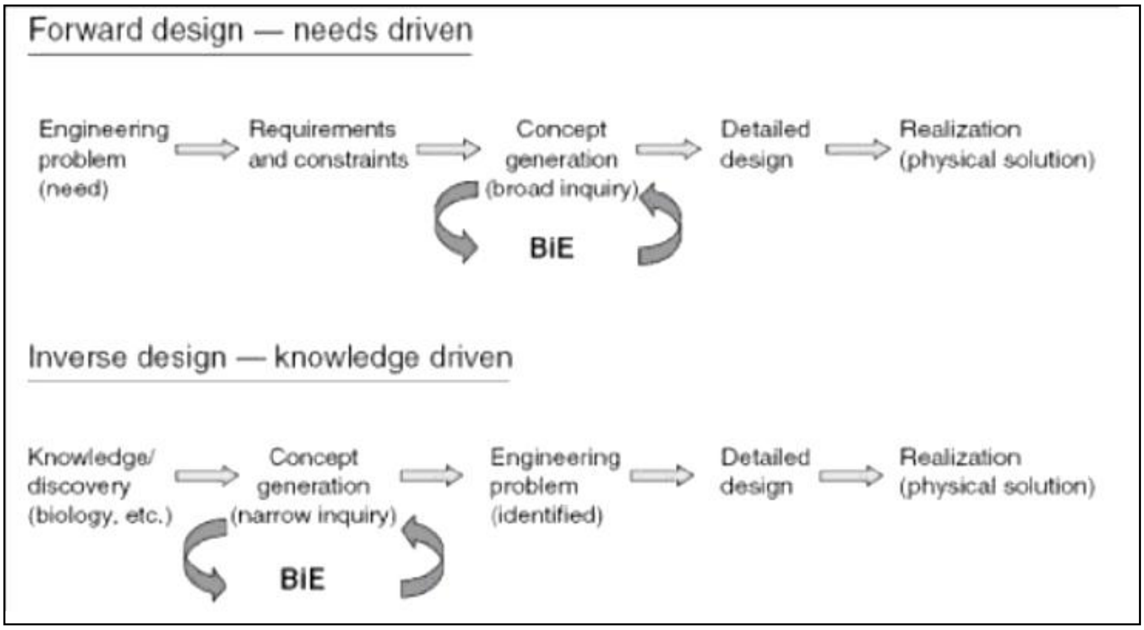


Figure 8: Forward vs inverse design
(Adapted from Jenkins H M, Bio-Inspired Engineering)

Jenkins [26] amplifies the simplified sequences for product conception introduced in Figure 5 of section 2.3.2, this time in terms of "Forward" and "Inverse" design (Figure 8).

Illustrating his point with particular respect to Bio-inspired Engineering (BiE) he observes that when a design responds purely to needs, the field in which to search for solutions is broad, whereas when a product is to be designed to exploit a new discovery the field of solutions to search is narrow - presumably focused around the new discovery.

Like the unfamiliarity of the underlying workings of biology, the behaviour of the micro- world, where for example gravity may be inconsequential compared with electrostatic forces, is outside the everyday experience of designers. To make teamwork meaningful, designers need to be able to identify appropriate physical principles and engage with, for example, the different emphases of forces, intense heat gradients, strongly laminar flow, stiction, electrostatics and magnetics, in a totally alien world.

Building upon the observations of Jenkins, design teams interested in adopting micro- properties could with strong advantage study prior product developments that have been driven by the exploitation of micro- discoveries. This leads to the idea that the whole team, and possibly users, can enhance understanding by discussion based around tangible preceding products.

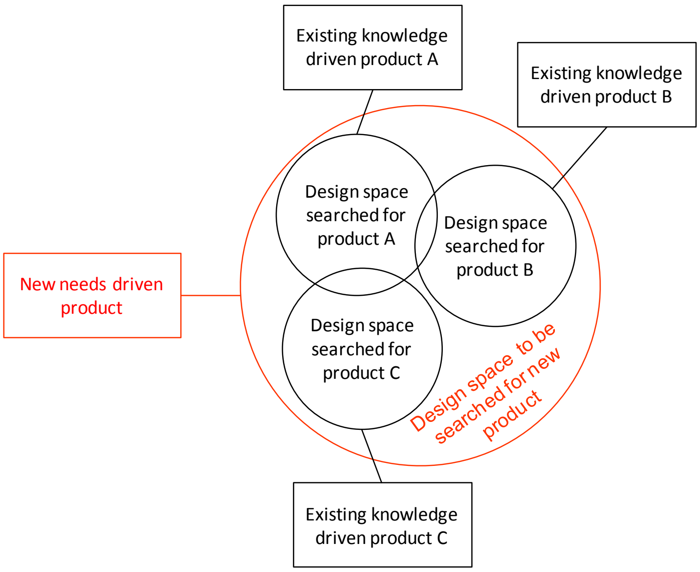


Figure 9: Knowledge-driven products contribute to more general solutions

Some computer design system providers publish case histories from users which can also be useful in this respect. COMSOL featured in 2015 a searchable gallery of 90 examples.

2.4.2.2 Virtual reality

Another approach available is the immersion of designers into a room-sized virtual environment constructed to mimic the behaviour of the micro- world, through 3D-visualisation and/or haptic feedback as provided by systems such as the CAVE Cave Automatic Virtual Environment [35], which creates a space large enough for a whole design team, and possibly potential product users, to observe and experience the principles and effects of interest.

The shared experience of the CAVE should transcend the alternative use of goggles, where other users can only be represented rather than interacted with directly

2.4.2.3 Macro- models based upon similitude

A further approach to sharing and discussing the intangible is the application of “Similitude”. Similitude is a concept used in the testing of engineering models. A model is said to have similitude with the real application if the two share geometric similarity, kinematic similarity and dynamic similarity. Similitude's main application is in hydraulic and aerospace engineering to test fluid flow conditions with scaled models. It is also the primary theory behind many textbook formulae in fluid mechanics.

Its use to support micro- discussions within design teams need not be restricted to computer models. Real, physical scale-up models, constructed from materials to mimic micro- behaviour yet at macro- scale can be constructed.

Kaneko, Watanabe & Nishihara of the University of Tokyo and the Central Research Institute of Electric Power Industry have studied disk drive behaviour using ten times enlarged models of drive elements operating in water, which, beyond facilitating easier observation, allows the time scale of the phenomena of interest to be about 1,300 times slower than that of the actual components operating in air [36].

Such macro-scale models allow teams, and users, to gain literally "hands-on" experience, and strong common grounds for debate.

2.4.2.4 Use of symbolic artefacts

Sketches and diagrams are considered in the following section 2.5 of this thesis. A development upon such illustrations is to use artefacts – printed or representative models – to illustrate the functional attributes of elements within potential products or systems to focus and weld together design-to-manufacture teams in their consideration of the features, problems and management concerns around a development. This approach was examined in the workshop activity reported in section 4.2 of this thesis.

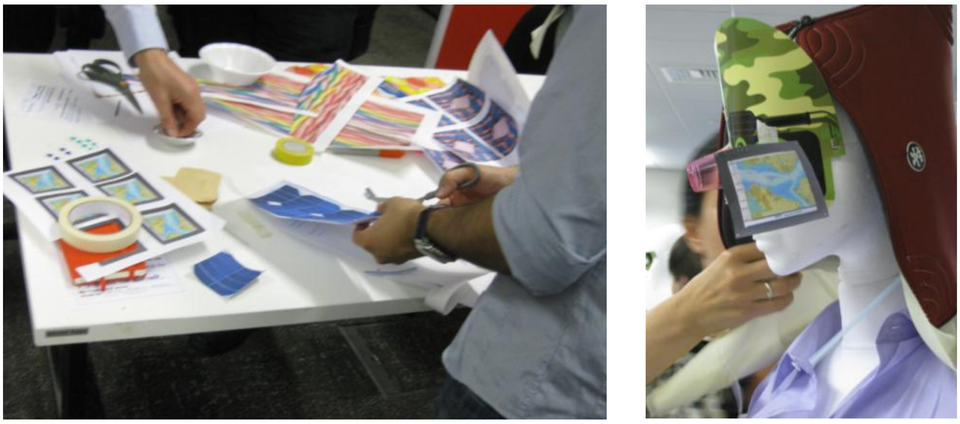


Figure 10: Symbolic artefacts used to enhance design teamwork

2.4.2.5 Round up of section 2.4.2: *Engagement with "inaccessible" technologies*

This section has:

- Shown in 2.4.2.1 that the pathfinding development of knowledge-driven products can contribute to more general solutions.
- Indicated the benefit of shared experience that may be achieved through virtual reality, macro- scale models based upon similitude, and the use of symbolic artefacts.

2.5 2D representations used in the design of 3D objects

French in his 1994 “Invention and Evolution: Design in Nature and Engineering” [23] observes on p12 that “Design and drawing are very close – indeed the word ‘dessin’ means ‘drawing’ in French”, and goes on to suggest that “most designers, most of the time, will think in images rather than words.” He then explains that although sketching is a fluid medium for the development ideas, scaled drawings, such as orthographic projections, are more suitable for “precise thinking”, being presumably the more detailed consideration that is needed as a design becomes firmer.

On p13 of his 1998 Conceptual Design for Engineers [37] French classifies both sketches and scaled drawings solely as “documentation” punctuating the culmination of, respectively, the conceptual and embodiment phases of design.

There is a very large body of work considering the use of drawings and diagrams in the design process. Many authors, like French, chart the evolution of sketched ideas into manufacturing drawings. A 1998 review of the field “Drawings and the design process” by Purcell and Gero [38] makes a distinction between research into “the sketch and its role in design”, and research into the “cognitive psychology and cognitive science” around the process of creating and using both sketches and diagrams.

In their review Purcell and Gero tend to roll “sketch” and “diagram” together, which is vague. The more specific convention adopted in this thesis is that:

- A *sketch* is an imprecise drawing intended to give an impression of an object, concept or function. It may be prepared quickly and regarded as a draft in a sequence of such renderings that evolves through further thought, the ongoing realisation of constraints and potential improvements, and may often serve as an important focus for group discussion and the collection of ideas.

  Some regard sketches as ephemeral, to be discarded once superseded, but in many cases a sequence of sketches can record a process of revision and provide a “snapshot” to revert to perhaps to explore another avenue of ideas.

- A *drawing* has more precision than a sketch, and ultimately an *engineering drawing* can be used to identify conflicts and may be scaled to provide manufacturing dimensions.

- A *diagram* may itself be the result of sketching or more precise drawing. A diagram may represent the way that parts are to be assembled (an *exploded diagram*); it may be simply a series of text blocks indicating the individual functions of a system and how they are connected; it may be a series of items depicting a sequence of events or steps in a process; it may be a stylised map showing geographic connectivity or, in the case of a *circuit diagram* the connections between symbols representing electrical components; it may be a *plan* or *section* which depicts a cross-section of a 3D object; a *projection* depicting the face of an object; or, as a *functional diagram*, it may indicate a physical principle using stylised representations for components such as fulcrums, coiled springs, masses, pipes and valves.

Lopes suggests, concerning Pictorial Realism [39], that most pictures do not represent all aspects of their subject matter: most pictures remain non-committal about some properties of their subject.

With a field so broad, this thesis necessarily needs to limit its own analysis, and accordingly focuses upon:

- The role of sketches and diagrams in the conception of new products enabled by the selection and integration of micro- scale technologies.
- The role of sketches and diagrams in communication across design teams involved in the creation of products enabled by the selection and integration of micro- scale technologies.
- The potential for diagrams of function to be transformed spatially as a basis for the embodiment of a product.

This thesis will suggest in section 2.6 “Transforming 2D functional diagrams into 3D functional objects” that sketches and drawings resulting in *functional diagrams* may become, in appropriate circumstances, tools in the generation of physical models, but first it is as well to examine the relationship between 2-dimensional representations and the 3-dimensional objects that they represent as an adjunct to communication between and beyond design teams working in technology fields with which they are as yet unfamiliar due to (1) the technology being at a scale too small to be experienced directly and (2) the technology being at an early phase of exploitation.

2.5.1 Sketches

There is universal consensus in the literature that designers almost always use sketches in the early stages of the conceptual design process. So what are the particular attributes of sketching that progress the conceiving of products enabled by the selection and integration of micro- scale technologies?

2.5.1.1 Concepts and images

Fischbein [40] makes a clear distinction between the *figural concept* portraying a class of things and the *mental image* of an imagined object. Nevertheless, both occur in the mind, and both may be externalised in sketches, possibly even jointly as in, for example, the inclusion of streamlines sketched in upon a representation of a liquid-carrying channel at the micro- scale to indicate the characteristics of flow which are hidden from the unaided eye.

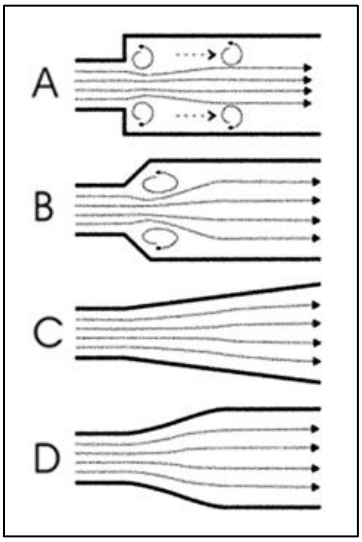


Figure 11: Sketch of physical channel geometries with notional flowlines
(Adapted from Hawkes and Radel, [41])

Figure 11 externalises and combines a *mental image* of a structure, in this case a channel at the micro- scale, with a *figural concept* depicting the behaviour of a fluid flowing through it. In the form of a sketch both the structure and the portrayal of flow can be modified easily to postulate different geometries and to converse and debate the design with co-workers. It is notable that the precise theory behind the modification of the flowlines does not have to be stated, indeed as a set of equations its communication would be incomprehensible.

2.5.1.2 Depicting the invisible

Sketching is not, however, always the externalisation of a purely mental image. Once the use of a microscope became relatively commonplace, biologists and particularly botanists sketched what they saw in the miniature world (sometimes fancifully) for the interest, information and entertainment of a wide audience.

Figure 12: A Victorian microbial fantasy
(From a set of trade cards “In the Year 2000” sold at the 1900 Paris Exposition)

The very publication of these images sparked speculation as to what was happening at the microscopic scale, and conjectures that resulted in a new branch of science beyond the “naming of parts” focus of classification that had previously characterised the study of the living world.

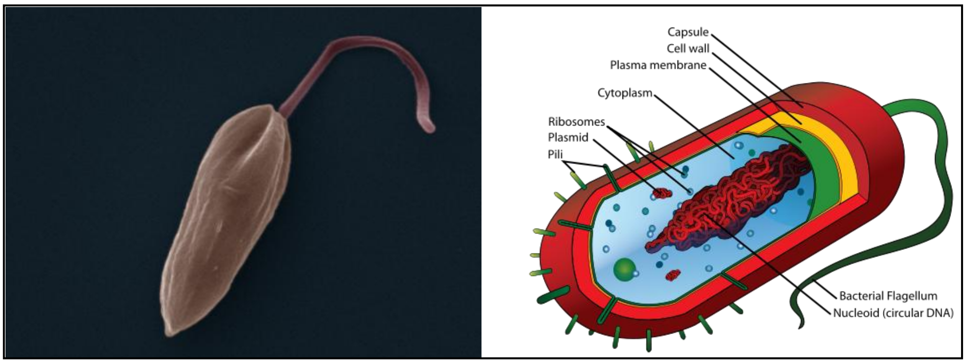


Figure 13: SEM micrograph of bacterium ↔ sketch of components
(Wikimedia commons)

The ability to image objects with features at or below the wavelength of light has revealed, for example, the internal structures of bacteria. Figure 13 shows in its left panel an image obtained through scanning electron microscopy, while the sketch on the right delineates the features in a way that enhances understanding and discussion.

Ferguson [42] suggests that a sketch is likely to be made for one of three reasons and from one of three sources (1) to communicate the physical nature of an entity conceived in the imagination; (2) to visually recall the physical nature of objects or environments from memory; and (3) to make a quick visual representation of entities or environments exposed to the *naked eye*. This suggestion omits the representation of entities that are *not* visible to the naked eye, a fundamental use of sketching when considering and conveying the attributes of items existing at the micro- scale. This is critical for the consideration of precident “case history” structures as put forward in 2.4.2.1 and Figure 9.

2.5.1.3 Computers as a tool

McGown, Green and Rodgers for their paper “Visible ideas: information patterns of conceptual sketch activity” [43] devised a 5-level “scale of complexity” to classify sketches during their described research project, including also text annotations as part of the measure. Although the authors acknowledge the use of computer technology in sketching, perhaps because of the 1996 date of the experiment in the paper they, and the other authors they cite, see sketching as primarily a paper-based activity.

Accordingly the research they report is based upon observations of paper-based activity. They do not foresee today’s adeptness of generating shapes on snap-to-grid touchscreens, transforming them and joining them to create images which, although they appear more “finished”, are nevertheless sketches akin to the right-hand panel of Figure 13. It would be interesting to repeat the experiments of McGown, Green and Rodgers, this time allowing the subjects to use tablet computers or similar.

2.5.1.4 Round up of section 2.5.1: Sketches

A summary of the roles of sketches *special* to the conceptual design of products enabled by integrated micro- scale technologies, and to communicating the issues across the design teams involved is as follows:

- The externalisation and progressing, at a workable scale, of mental images of structures to be constructed on the micro- scale
- The externalisation and progressing, at a workable scale, of concepts regarding normally unobservable physical processes (pressures, velocities, fields etc) acting on the micro- scale
- The superposition, at a workable scale, of the actions of theoretical physical processes upon images of structures at the micro- scale
- The representation and annotation at a workable scale of precident “case history” examples drawn from existing objects with structures too small to observe directly
- The techniques used to investigate, identify, characterise, visualise and debate biology at the cellular scale have relevance to the techniques used to generate and evolve technology-based designs enabled by functions at the micro- scale

2.5.2 Diagrams

Section 2.7, which examines the needs for red blood cell / plasma separation and the approaches to satisfy those needs, contains 57 images, of which 29 are diagrams, the remainder being 28 photographs including microphotographs.

As indicated in the introduction to section 2.5 (see page 44), a *diagram* may depict, clarify or represent facets of objects, actions and concepts using a plethora of graphic approaches. Just as pictures do not represent all aspects of their subject matter (see Lopes [39]), diagrams expressly select aspects to consider and communicate.

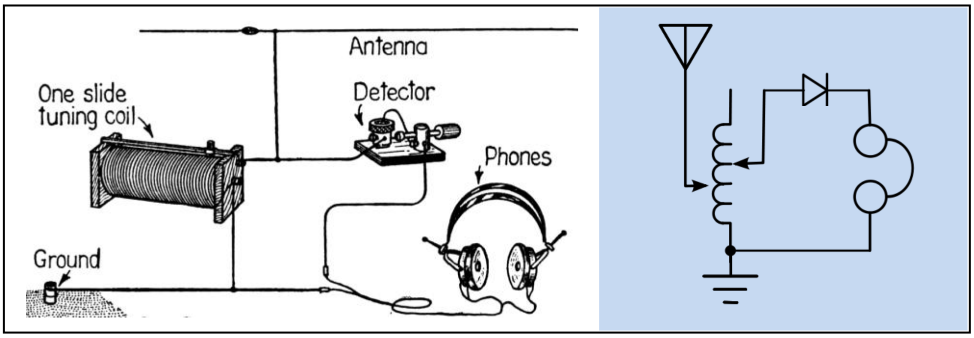


Figure 14: Pictorial diagram compared with schematic diagram
(Wikimedia commons)

In Figure 14 the pictorial diagram to the left shows how to connect the component parts of a crystal radio set, whilst the equivalent schematic diagram to the right uses stylised symbols adhering to conventions understood by those conversant with electronic technology.

The pictorial diagram could certainly be used by a non-expert provided with the components and connecting wire. The constructor would be able to recognise the parts, as sketched, even though no dimensions are included.

The schematic diagram is more generalised. It would enable an expert constructor to substitute different kinds of parts whilst maintaining the same connectivity and circuit operation.

A useful overview “What is a diagram?” is provided by Fathula and Basden [44] in which they stress and record the variety of diagrams, which may often be of mixed types. The authors put forward a framework for understanding diagrams and consider the activities of their creators and onlookers.

The analyses of Fathula and Basden are too deep for this thesis, save to say that diagrams stylise, simplify and generalise in many ways, depicting objects, space, sequence, concepts, physical relationships and more - so what are the particular attributes of diagrams that progress the conceiving of products enabled by micro- scale technologies?

Perini, in her paper regarding the use of diagrams in biology [45], argues that in stylising, simplification and generalisation, the crucial utility of diagrams might be generated by the elements that they leave out.

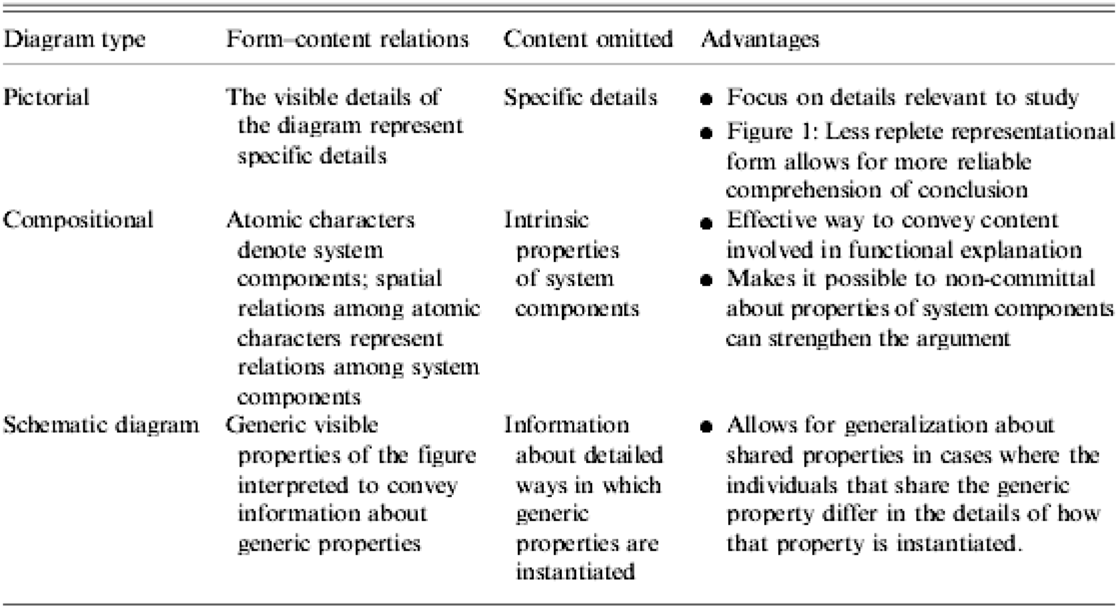


Diagram type	Form–content relations	Content omitted	Advantages
Pictorial	The visible details of the diagram represent specific details	Specific details	● Focus on details relevant to study ● Figure 1: Less replete representational form allows for more reliable comprehension of conclusion
Compositional	Atomic characters denote system components; spatial relations among atomic characters represent relations among system components	Intrinsic properties of system components	● Effective way to convey content involved in functional explanation ● Makes it possible to non-committal about properties of system components can strengthen the argument
Schematic diagram	Generic visible properties of the figure interpreted to convey information about generic properties	Information about detailed ways in which generic properties are instantiated	● Allows for generalization about shared properties in cases where the individuals that share the generic property differ in the details of how that property is instantiated.

Figure 15: Table of biological diagrams after Perini
(Adapted from Perini [45])

As mentioned in respect of sketching, the needs of investigating, understanding and discussing cellular biology do have parallels to the issues in generating and evolving technology-based designs enabled by functions at the micro- scale.

An examination of Figure 15 suggests that “pictorial” and “schematic” diagrams allow clarity of comprehension with respect to particular biological specimens and insight into generalised properties. This suggests a good starting point in the quest to focus *solely* upon the role of diagrams in micro- scale developments, but first it is essential to consider how diagrams may have hindered the evolution of microminiaturised technology products.

2.5.2.1 “The map is not the thing” - the need to escape from Flatland

In the mathematically-inspired 1884 novel Flatland [46] A Square, a two-dimensional being inhabiting a two-dimensional world, travels to The Land of Three Dimensions, an experience that forever changes his perspective.

The physical principles that underly the working of a product are predominantly represented in diagrammatic form, and as a result of this there is a very real danger that the physical embodiment of these principles will be influenced by the flat two-dimensional form of diagrams.

In the case of electronics this is clear. It is no surprise that the innovative representation of the London Underground system, providing route-planning functionality for the traveller rather than geographic accuracy today was penned by an electrical engineer [47]. In Beck's days, flat circuit diagrams represented the contemporary bulky constructions of components wired together in 3D space, as illustrated in Figure 14.

It is interesting to reflect that the flattened circuit diagram may perhaps also have influenced inventive thinking, resulting in the innovative leap to the flat printed circuit boards that have replaced free-form wiring, and the ultimate progression to the planar construction of semiconductor chips.

A geographer may infer general relationships and connectivities between places on the London Underground map, but even with its stylised symbols, no insight is gained into the mechanism of trains and signalling that makes the system fulfil its people-carrying purpose. Similarly, a conversant chip designer may look at a chip diagram and gain a generalised view of its complexity and its architecture in terms of interconnected functional blocks, but not a hint of the underlying principles of electron flow, field effects and circuit elements that make it work.

Although it is generally evident that “the map is not the thing” (drawing from Korzybski's ideas of the distinction between words and objects [48]), the diagrammatic tools for each layer in the semiconductor photolithography process certainly look like maps, and “the thing” produced very much takes on the planar nature of these maps.

As a result, problems are starting to occur in the form of time delays between signals disposed around the area of planar chips. Semiconductor integration has forced itself into this layer-by-layer state of affairs through its original adoption of planar manufacturing processes, which now represent a huge, and global, capital base.

For benefits of scale, semiconductor manufacturers regularly move to higher resolutions and larger diameter wafers, leaving the equipment for processing the preceding generation of wafers under-utilised. The older equipment then becomes attractive for the manufacture of micro-enabled components.

In this way a focus on planarity stemming from circuit diagrams, continuing through the development of circuit boards and on to integrated semiconductors has now impacted upon the embodiment of micro- enabled products, perhaps to an extent where – through habit or engineering culture – the benefits of design and manufacture using truly 3D techniques are being passed over by design teams.

2.5.2.2 Pictorial diagrams: Reality vs theory

Figure 15 (page 50) suggests the usefulness of pictorial diagrams in biology.

Perini [45] builds upon the idea of clarity-through-omission by introducing the work of Lynch [49] who contends that the diagram does not merely leave out some information conveyed by the micrograph, rather, the diagram enhances aspects of theory, but at the expense of the reality captured by the micrograph.

2.5.2.3 Schematic diagrams: The gateway to analogues

Perini in [45] provides a usefully clear definition that "The schematic drawing provides a way to communicate about generic properties while not asserting that those properties are instantiated in a particular way" but unfortunately is unable to provide a convincing example in the biological field.

The fundamental elements of schematic diagrams are (1) lines to depict boundaries and connectivity, and (2) symbols to represent, in a generic form, constituent parts that exhibit known characteristics.

Symbols, unless obvious from shared experience, for instance  (sunrise), in reality provide a form of shorthand - a shorthand that may only be decoded by those conversant with the relevant topic.

Liikkanen and Perttula describe lack of domain knowledge as a significant barrier in their paper "Exploring problem decomposition in conceptual design among novice designers" [50]. Schematic diagrams provide one approach to resolving this difficulty, if the designers can map a familiar domain onto the unfamiliar territory.

Schematic analogies are powerful aids to understanding behaviour at the micro- scale, but dangers lurk as high-level schematics skip over the realities of practical cases. For example, the equations of electrical analogues ignore the flow conditions occurring in fluid vessels at the boundaries of the channels, which may become dominant as geometry shrinks.

2.5.2.4 Functional diagrams

The review by Purcell and Gero [38] notes that "The process of learning how to draw and use diagrams could be at the heart of physics expertise, not only for novice learners but also for expert physicists", referring to Anzai who on page 64 of the collection "Toward a General Theory of Expertise: Prospects and Limits" [51] observes that physicists "develop new theories to explain the physical world from novel points of view". Working up new theories through discussion with peers undoubtedly requires the portrayal of a point of view, implying the use of diagrams that illustrate function in progress.

Anzai does caution that physicists tend to represent problems in the abstract, with for example point masses, inextensible strings and frictionless surfaces.

Figure 16: Galileo observing a swinging lamp at Pisa Cathedral
(Fresco by Luigi Sabatelli 1772-1850)

The famous observation of a swinging lamp by Galileo Galilei, in which, using his steady pulse as a clock, he noticed that the period of the swing was sensibly independent of is amplitude, has been encapsulated as a primary functional diagram taught both in mathematics and physics.

Stylised, as in Figure 17, the functional diagram provides a generalised statement of the principle, which may be extended to calculate the period of varying lengths of the suspending material, whilst suggesting that the mass, although not contributing to the calculation of period, should be concentrated at the end of the suspension.

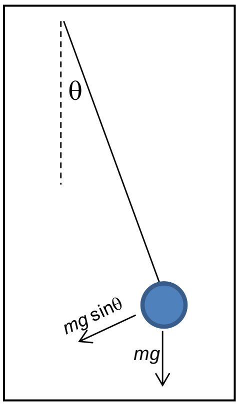


Figure 17: Functional diagram of simple pendulum

Functional diagrams are useful because they explain the operation of physical principles, generalised so that practical embodiments are not constrained by particular applications.

Users of functional diagrams need to be very aware that they reflect “pure” physics with its, for example, point masses, inextensible strings and frictionless surfaces. Practical embodiments need to take account of effects that may not be at all “secondary” at the micro- scale, such as Van der Waal forces, stiction and surface roughness as a greater proportion of working dimensions.

Although there is a large body of research and measurement regarding specific cases, there does not as yet (2015) appear to be a publicly-available consolidated review or repository of knowledge regarding physics at the micro- scale and the properties of materials at the small dimensions involved, but proprietary resources such as Comsol’s MEMS Module Software for Microelectromechanical Systems (MEMS) Simulations are available for licensees.

2.5.2.5 Round up of section 2.5.2: Diagrams

A summary of the uses of diagrams *special* to the conceptual design of products enabled by integrated micro- scale technologies, and to communicating the issues across the design teams involved is as follows:

- Diagrams expressly select aspects to consider and communicate. “Pictorial” and “schematic” diagrams allow clarity of comprehension with respect to particular objects and functions, and promote insight into generalised properties.

- The physical principles that underly the working of a product are predominantly represented in diagrammatic form, and as a result of this there is a very real danger that the physical embodiment of these principles will be influenced by the flat two-dimensional form of diagrams.

- In tackling new technologies, schematic diagrams can allow designers to map a familiar domain onto unfamiliar territory.

- Functional diagrams are useful because they explain the operation of physical principles, generalised so that practical embodiments are not constrained by particular applications.

- Users of functional diagrams need to be very aware that they reflect “pure” physics, whereas practical embodiments need to take account of effects that may not be at all “secondary” at the micro- scale.

2.6 Transforming 2D functional diagrams into 3D functional objects

As summarised above, functional diagrams are useful because they explain the operation of physical principles, generalised so that practical embodiments are not constrained by particular applications, but on the other hand there is a danger that the form of a product design based upon these principles will be influenced by the flat two-dimensional geometry of diagrams.

Section 2.3.3 “Drivers and obstacles for this topic area” introduced as an example products such as Baidu’s “Smart Chopsticks”, which do not favour planar construction as their form and use is strongly constrained by the expectation of the user.

This thesis examines and tests a concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures using procedures allied to those used by graphic designers to create solid objects from 2-dimensional prototype geometries through, for example, extrusion or rotation.

This design method, through its basis upon a common currency of functional diagrams, may overcome many of the problems of describing and discussing the design and manufacture of normally intangible objects in 3 dimensions.

Furthermore it will be shown the geometric transformation process can lead to the design of functional structures with improved performance that would not readily be arrived at intuitively, and that may be effectively and efficiently integrated into host products.

2.6.1 Geometric transformations

The procedures adopted by graphic designers to create 3-dimensional objects from prototype cross-sections are well known, and have become easily and widely used through the adoption of Computer Aided Design software and systems.

The particular transforms of interest are a subset “Solid Modelling”, in which computers are used to automate and accelerate complex mathematical equations to calculate the position of many points in space, and to render the results both as a visual display and as co-ordinates to produce either virtual or physical models.

Three common transforms are:

- *Sweep*	Extends a 2D object along a path.
- *Extrusion*	Extends the shape of a 2D object in a perpendicular direction into 3D space.

- *Revolve* Sweeps a 2D object around an axis.

Other transforms are possible, but the three above are the simplest to contemplate. It is worth considering that the path that *sweep* operates along may itself be in 3D space. A circle can, for example be swept along a helix to form a coiled tube.

2.6.2 Application of transforms to functional diagrams

Figure 18 is a simplified example showing the transform of a 2D functional diagram "A" to become a 3D functional object by extrusion along the length "Z", which is perpendicular to the plane of "A".

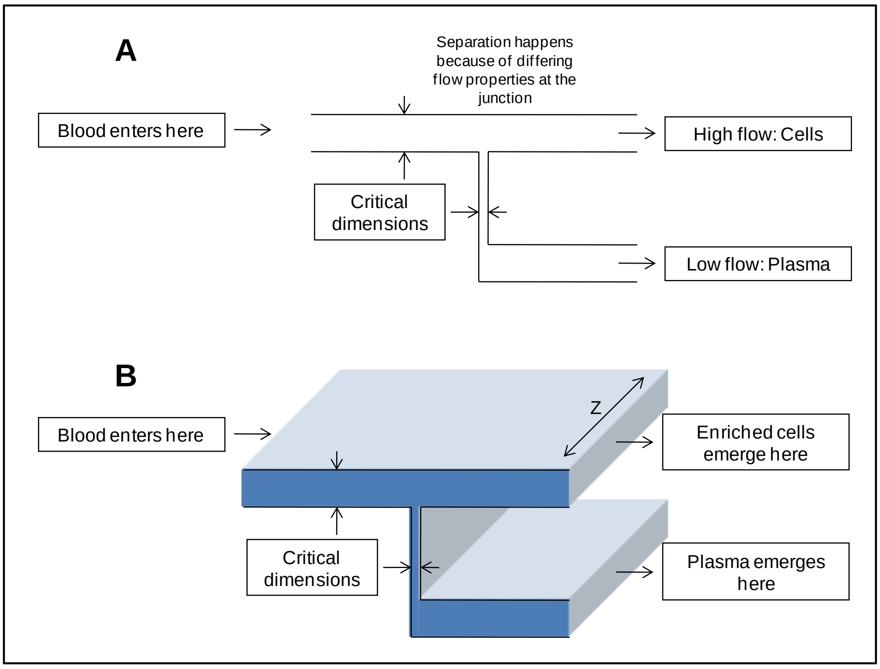


Figure 18: (A) Functional diagram (B) Extruded 3D functional object

Microscale approaches for red blood cell / plasma separation are reviewed in section 2.7.3 of this thesis. Figure 18 "A" represents a candidate separation method, reported by Yang, Undar and Zahn [52] concerning the behaviour of particles at a bifurcation in fluidic channels having dimensions small enough to guarantee highly laminar flow.

The diagrammatic form of Figure 18 "A" lends the designer towards a picture of planar canals in the micro domain. This is reinforced by a persuasion to use readily available planar lithography as a manufacturing process. Figure 19 shows a test implementation cited in [18] generated by Kersaudy-Kerhoas and Desmulliez during the 3D-MINTEGRATION [1] project.

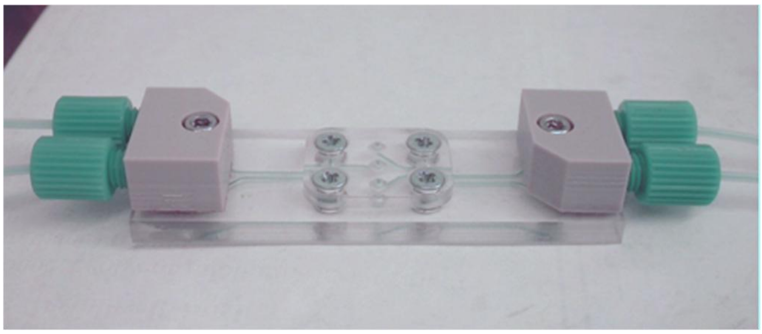


Figure 19: Experimental microfluidic blood separator
(After Kersaudy-Kerhoas and Desmulliez, 3D-MINTEGRATION)

With channel depth also typically 50 microns, and a blood flow rate of some 10mm per second in order that excessive pressures do not damage the red blood cells, the blood throughput is of the order of 90 microlitres per hour, which may be sufficient for some sensitive analytical procedures.

Should flows of 90 microlitres per hour not be sufficient, then the cell of Figure 19 needs to be scaled up. However, the blood separation process depends upon laminar flow arising from the critical dimensions indicated in Figure 18 “A”, so the wholesale scaling up of dimensions is not possible.

To increase the throughput by a factor of 1000, to achieve a target flow rate of 90 ml per hour - a perhaps convenient 5 ml within around 3 minutes - one approach might be to parallel 1,000 of the Figure 19 devices. This inconveniently would result in a matrix approximately 30 cm square and some severe difficulties to arrange parallel fluid feeds to each device.

A more elegant approach has been suggested by Jaggi et al. [53]. This approach, illustrated in Figure 18 “B”, extrudes the diagram of Figure 18 “A” in the Z direction such that the critical dimensions that maintain laminar flow are retained, but rather between parallel plates rather than channel walls. In this case an implementation to secure a 1,000-fold increase in flow rate would entail a Z dimension of around 5 cm, and with none of the difficult manifold problems that would arise in feeding a flat matrix of planar elements.

Further transformations and an examination of their benefits will be discussed in the practical design study of Chapter 5, which concerns the practical investigation of the concept through designing, simulating and evolving a novel Red Blood Cell / Plasma Separation Device.

2.7 Red blood cell / plasma separation: Needs & Approaches

This section provides an overview of the need for Red Blood Cell / Plasma Separation, and the approaches that may be applied to create devices to perform this role. It is important to note that although the design and prototyping of a separator device is used as a focus for Topics 5 and 6 of this thesis, only the most general medical parameters have been sought in support of this focus, accordingly *an in-depth exploration of medical practice was judged as not warranted and has not been attempted*.

2.7.1 Needs for red blood cell / plasma separation

Human blood is composed of about 55% by volume liquid “Plasma”, 1~2% white blood cells and platelets, and a remaining ~45% of “Red Blood Cells” which are essentially flexible, deformable oval disks, responsible for the distribution of oxygen within the circulatory system, the removal of some of the waste carbon dioxide and various secondary functions which aid the flow of blood under abnormal circumstances.

Figure 20 illustrates the constituents of blood in a graphical form depicting the results of separation through centrifugation, a laboratory method for the preparation of batches of blood for subsequent analysis.

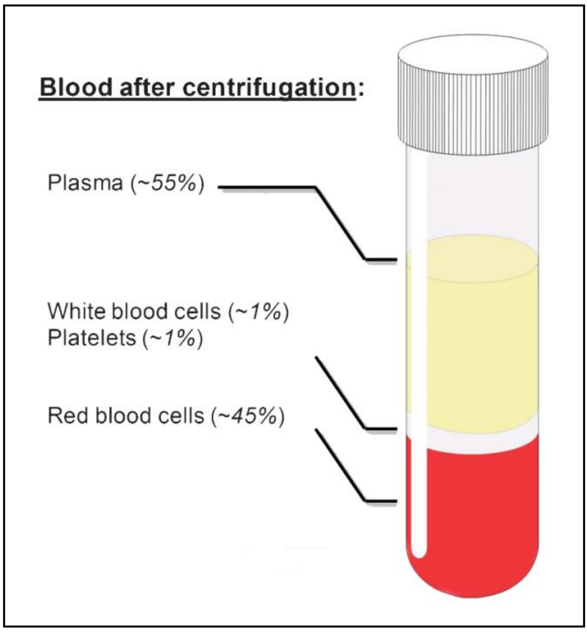


Figure 20: Constituents of human blood
(After Kersaudy-Kerhoas and Sollier [55])

The medical needs for the separation of blood into its constituent parts (apart from scientific investigation) are primarily:

- The small volume batch preparation of samples for diagnostic purposes
- The continuous separation of blood to allow real-time monitoring of patient health during surgery
- The high volume separation of blood may be needed (1) to correct imbalances in its constituents, or (2) to provide bulk plasma for the treatment of sick and wounded patients without reference to blood type, or as a source for further fractionating into plasma-derived healthcare products.

2.7.1.1 Small volume batch separation is a common clinical procedure, typically following the routine extraction of a blood sample (typically 1 to 5 mL) by syringe for subsequent testing. Whilst some tests can be performed upon whole blood, such as for the measurement of glucose content or for “cell counting” to determine the normality or otherwise of cell concentration, some sensitive tests for genetic markers, proteins, enzymes and antigens use processes and/or reagents which would be upset by the presence of red blood cells. Conversely, some tests, for example to analyse the DNA of foetal red blood cells found in maternal blood as shown in Figure 59, require the selection of red blood cells alone, free of the blood plasma and other constituents.

2.7.1.2 Continuous separation is mentioned by Yang, Undar and Zahn [52] in the context of a need to detect inflammatory responses in real time during the progress of cardiopulmonary bypass surgery in order that surgical or anaesthetic procedures may be modified to reduce the inflammation. The inflammation may be detected through a rise in the levels of clinically relevant proteins, changes which are difficult to detect in the presence of red blood cells, hence the need for separation. Yang et al report flow rates of the order of 3-4 $\mu L\ min^{-1}$ through an experimental separator integrated with a cardiopulmonary bypass pump.

2.7.1.3 High volume separation. The preceding categories of separation are concerned with blood volumes ranging from microlitres to a few millilitres, as needed for analysis. Higher volume separation is necessary when blood needs to be processed either to have its composition modified before re-introduction into the patient, or for its constituents to be made available and safe for other patients (as in donation) or for subsequent processing to yield, for example, therapeutic proteins. Regarding the latter processing, Curling reported in 2002 [54] that in the US more than 500 tonnes of human serum albumin and more than 40 tonnes of intravenous immunoglobulins were produced annually from more than 22 million litres of source plasma. Donors of source plasma actually donate whole blood. After the plasma is separated, the red blood cells may be returned to the donor, stimulating the generation of replacement plasma.

As opposed to the above processing aspects of high volume separation the removal, treatment, and return to the patient of components of blood, plasmapheresis, may be applied to a broad range of therapies that re-introduce the patient’s own treated blood, with the advantage of avoiding incompatibilities or other risks associated with the use of donor blood.

2.7.2 Traditional approaches for red blood cell / plasma separation

Satisfying the diverse medical needs outlined in 2.7.1 attracts solutions based upon a broad range of functional principles and engineering approaches.

2.7.2.1 High volume separation typically collects whole blood from a donor or patient through a needle inserted into the arm. To optimize flow and to minimize shearing force damage to the red blood cells the needle has an internal diameter of 1~1.2 mm, and the flow rate is of the order of 1 mL sec^{-1} as reported by van der Meer and de Korte in their 2009 paper [55] concerned with the resistance induced by the needle and associated tubing during collection.

Following collection, the separation of red blood cells from plasma has to date been accomplished through the use of centrifuges with varying degrees of automation, software controls and safety systems. Anticoagulant and preservative solutions may also be introduced if the blood components are not to be used immediately. Such centrifuges are typically operated to provide accelerations of about 1000g, the blood being under rotation for around 10 minutes.

Despite the considerable installed base of centrifuge equipments, alternative high volume separation methods are in development, with a view to simplifying the equipment, making it cheaper, more portable and less dependent upon a developed infrastructure of power, maintenance skills and operating environment. One such development “A Highly Portable Continuous Plasma Separator for Whole Blood” was disclosed by Takayasu and Ash in 2011, based upon gravitational sedimentation. It is difficult to see how sedimentation under normal gravity could compete with the 1000g of a centrifuge.

2.7.2.2 Small volume separation typically commences through the collection of batch samples of the order of 3~10 mL by syringe or a similar device, each sample being obtained in a matter of seconds, indicating a flow rate very similar to the 1 mL sec^{-1} reported by van der Meer and de Korte for high volume collection [55], as mentioned in 2.7.2.1 above.

The collecting of blood by the conventional syringe relies upon the skill of the medical practitioner to draw back a plunger at a suitable rate, and furthermore the sample must generally be transferred from the syringe to a sealable container for transport to the place of analysis.

Brunel’s Katy Jenkins, a part time contributor to this research, describes the use of an alternative, the Vacutainer®, in her 2008 “Blood Separation Syringe: DM3306 Major Project Report” as follows:

“The Vacutainer is an evacuated tube into which blood is collected. There is no need to use a plunger to draw blood into the container. This means that the container is simple and inexpensive to produce. There are several strengths of vacuum available for use with different vein sizes.

“Some of the Vacutainers contain coagulants, anticoagulants, or other additives for blood processing, as is the case with the S-Monovette products.

“The needle is inserted into the patient’s vein. It is connected to a plastic holder. The Vacutainer test tube is pressed onto the plastic holder and a small needle pierces the rubber cap. This allows the vacuum in the tube to be filled with blood.”

Clearly collection systems such as the Vacutainer reduce the chance of inconsistency in the sampling process by reducing reliance on practitioner skills and by eliminating the step of transferring from the syringe to a sealed container.

Jenkins continued in her report to describe the next step of sample separation:

“The typical existing system for separating blood prior to diagnostic tests requires blood to be sent to a laboratory where it is centrifuged. The centrifuge separates blood using centrifugal force, generated by the rotating action of the device containing on its outer edge a holder for the sample, to push large blood cells to the base of the sample tube, leaving the plasma and smaller constituents at the top. This method is bulky, costly and time consuming.

“From discussions with biochemists working in these labs, I found that the turnaround time is one hour for urgent results, or 2-3 hours in non-urgent situations.”

The drawbacks of the widely used sequence and methods of low volume blood sample collection and preparation are:

- Withdrawing the blood and transferring to the laboratory carries risks of inconsistent handling, a transit environment that requires control, loss in transit, and the possibility of miss-identifying patient details.

- The use of equipment at the laboratory, which is typically remote from the point of care, can engender queuing and bottlenecks, an undesirable administrative overhead and delays in transmitting the results of tests to the healthcare practitioner and patient.

2.7.3 Microscale approaches for red blood cell / plasma separation

The drawbacks of the conventional collection and separation methods recorded in 2.7.2.2 have encouraged the research and development of alternative approaches based upon microengineering, firstly applying to the separation process the behaviour of particle-carrying fluids at the microscale, then performing analysis by sensors also based upon microengineering techniques.

Such miniaturisation promises the following advantages:

- The potential to perform analysis at the point of care, eliminating the delays and uncertainties of sending specimens to a laboratory.
- The possibility of manufacturing cost-effective "use-once" systems that can be disposed of safely, avoiding the need to decontaminate/sterilize shared equipment.
- The prospect of developing fully integrated collection/preparation/analysis systems that eliminate steps between processes where contamination can occur.
- In the case of a fully integrated collection/preparation/analysis system working directly from the patient, the extracted blood may remain at body temperature, allowing analysis results to be more representative of the blood remaining in the patient.

2.7.3.1 Candidate microengineered approaches. The immensely detailed and valuable Critical Review by Kersaudy-Kerhoas and Sollier [56] compiled in 2013 provides a comprehensive review of available techniques. Another useful resource is the 2010 review provided by Bhagat et al. [57].

These two sources complement each other in the provision of background information about the medical needs for cell-separation, and also give some historical perspective. In particular the Kersaudy-Kerhoas and Sollier review provides an analysis of the upsurge of research papers compiled using Thomson Reuters citation database on the ''Web of Science'' website using the key words ''blood'', ''plasma'', ''separation'' and ''microfluidic''.

There is an interesting acceleration in publication marked by the progress of cell-based research, potentially stimulating cell-based medical diagnosis.

Of the two reviews, that of Kersaudy-Kerhoas and Sollier [56] examines the greater number and variety of techniques. The principal methods discussed in the reference are collated in Figure 21, which is compiled from Figures 5, 6, 7 and 8 in the referenced document. The authors' tabling of dilution, flow rate, purity and yield is of particular note.

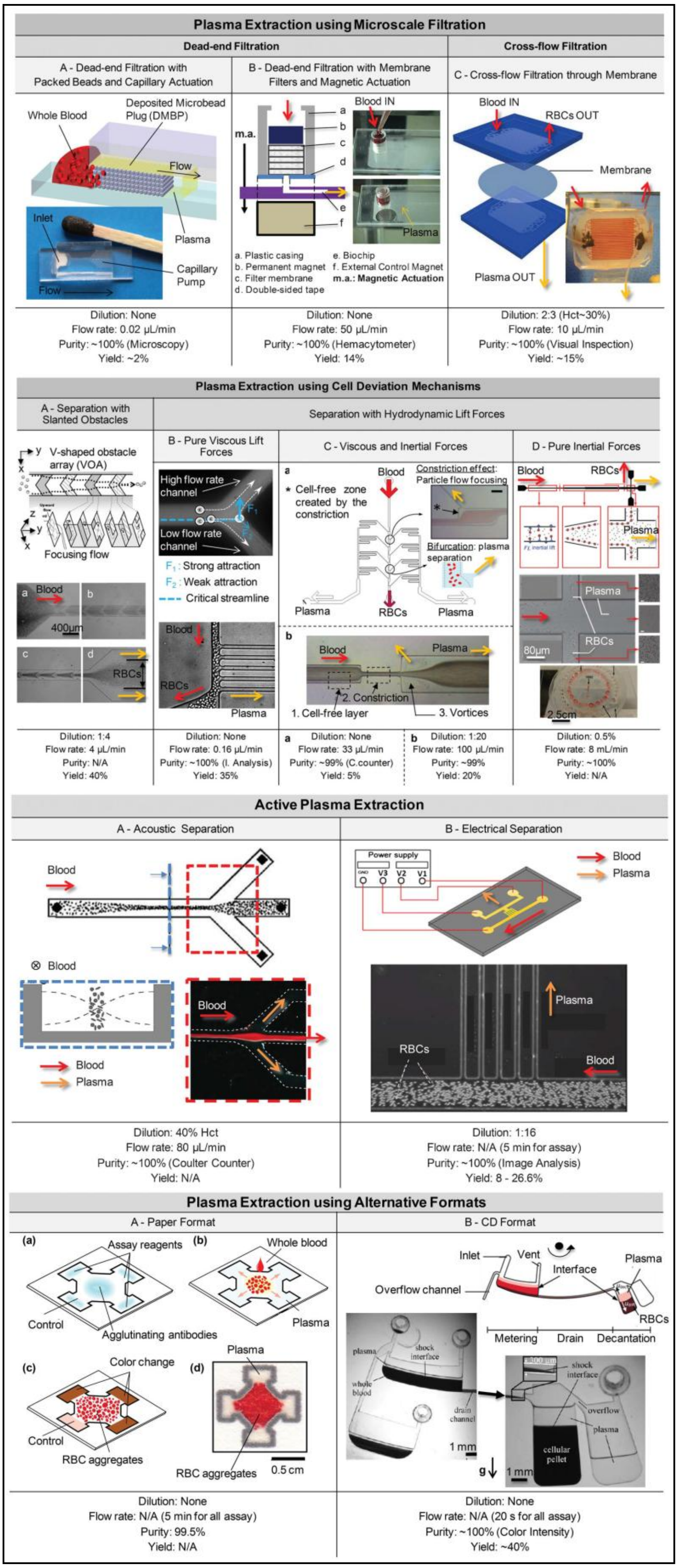


Figure 21: Examples of microscale cell separation techniques
(After Kersaudy-Kerhoas and Sollier [56])

Kersaudy-Kerhoas and Sollier usefully include a lexicon of terms used in their review [56] page 3324. Those of principal interest to this thesis are:

Dilution ratio: $^{\text{(undiluted volume of blood)}}/_{\text{(total volume of sample after dilution)}}$

Purity: Purity relates to the number of Red Blood Cells remaining in the plasma extracted. In the review it is defined as a percentage derived from:

$1 - {}^{\text{(cell count in plasma output)}}/_{\text{(cell count in input sample)}}$

Yield: "The percentage of extracted plasma volume over the total volume of blood injected"

The question of "Yield" in the above quoted definition is vexed. Looking at the examples in the text of the Critical Review, and also through inspecting a number of the source referenced documents, "Yield" seems to be actually the volume of essentially Red-Blood-Cell-free liquid extracted by a separator expressed as a percentage of the total volume of liquid introduced into the separator. This departure from the stated definition is important as, in the case of diluted blood, the make-up of the extracted – yielded – liquid is not pure plasma, it is in fact plasma plus the diluting agent.

This matters when considering the sample size of whole blood that is required from the patient to provide a given quantity of plasma for analysis. Figure 22 tables the volume of blood required before dilution to produce 1 unit of plasma within the extracted liquid.

	Volume of blood required before dilution to produce 1 unit of plasma within the extracted liquid			
Dilution Ratio / Separation Yield % *	Undiluted	1:5	1:10	1:20
55% (the maximum for undiluted blood) **	1.8 units	9 units	18 units	36 units
25%	4 units	20 units	40 units	80 units
10%	10 units	50 units	100 units	200 units
5%	20 units	100 units	200 units	400 units
2.5%	40 units	200 units	400 units	800 units

Figure 22: Whole blood sample size required to yield 1 unit of plasma

* Defined as the ratio of the volume of Red-Blood-Cell-free liquid extracted by a separator expressed as a percentage of the total volume of liquid introduced into the separator

** Whole blood is typically 45% Red Blood Cells by volume, hence the separation yield limit for undiluted blood

The volume of plasma required for analysis will depend upon the nature and sensitivity of the analysis, but from Figure 22 one can see that, for example, a separation method that requires a 1:10 dilution ratio to allow it to attain a separation yield of 25% will produce only the same volume of plasma as a process that, although it achieves a separation yield of 2.5%, will work on undiluted blood.

The great majority of microscale separation techniques require the sample blood to be diluted at ratios greater than 1:5 and provide at most a separation yield of 25%. This dilution, often employed to enhance fluid flow and to avoid clogging, may be perfectly acceptable if the blood requires to be diluted by a liquid that also preserves cell integrity or performs an anticoagulant role, or if the separation objective is cell-based, perhaps to classify a range of different cells or particles as, for example, reported in the work of Kuntaegowdanahalli et al. [58].

Dilution is clearly a disadvantage for integrated diagnosis at the point of care, for continuous monitoring, as cited by Yang, Undar and Zahn [52] in the context of cardiopulmonary bypass surgery, and also for requirements for the recovery of pure plasma from whole blood, either for donation or further processing or for treatment and re-introduction into the patient.

2.7.3.2 The fundamentals of junction-based separators

The following examples have instructive features.

The 2009 work of Kuntaegowdanahalli et al. “Inertial microfluidics for continuous particle separation in spiral microchannels” [58] has already been mentioned in the context of the collection and classification of a range of different cells or particles, commonly referred to as “cell sorting”.

Their use of a spiral is instructive in that the fluid physics in a spiral microchannel are more complex than the physics of a mechanical centrifuge. As the authors explain: (1) *“The curvilinear geometry of a spiral microchannel introduces a centrifugal acceleration component directed radially outward resulting in the formation of two symmetric-counter rotating vortices known as the Dean vortices in the top and bottom halves of the microchannel.”* (2) *“inertial lift forces result in particle equilibration at the inner microchannel wall. The position at which the particles equilibrate is dependent on the ratio of these two forces.”* (3) *“Particle equilibration in rectangular microchannel cross-section... ...rather depends on the shortest channel dimension (microchannel height, H) due to varying shear rates across the channel cross-section.... ...We use this result to design low aspect ratio spiral microchannels to enhance the separation between individual particle streams over a wide range of particle sizes.”*

Describing a prototype device the authors give the following dimensions: *"The spiral designs had an initial radius of curvature of 1 cm, with spacing between the successive spiral loops fixed at 500 µm. Width of microchannels was fixed at 500 µm, while microchannel height was varied from 90 µm to 140 µm. At the outlet, the 500 µm wide channel opened into a 1 mm wide segment to increase spacing between particle streams before splitting into eight 100 µm wide outlets".*

The application of a similar device to the separation of plasma from red blood cells rather than cell sorting was presented by Jumpei Morikawa at the 16th International Conference on Miniaturized Systems for Chemistry and Life Sciences in 2012. In this case a separation yield was not reported, save that a sample with a dilution ratio of more than 1:10 yielded a "plasma" stream of unspecified volume from which 90% of red blood cells had been removed. The flow rate through the device was reported as 5 mL per minute through a 7.5 turn spiral with channels recorded as having a cross section of "50000 μm^2", with aspect ratio (width:height) 10:1.

Burke et al. reported a similar cell separator in 2004 [59] that features fluid removal from the circumference of the outer spiral in a bid to increase the concentration of rare cells for cancer metastasis diagnosis and prognosis.

Tripathi et al. collated useful background material, as also used by a broad community of workers in the field, to support their 2013 paper "Blood plasma separation in elevated dimension T-shaped microchannel" [60]. Like many groups, Tripathi et al. reference Fahraeus, who provided an early description of the behaviour of blood flowing through narrow channels in his 1929 paper "The Suspension Stability of the Blood" [61].

Following an enlightening review of the speed of sedimentation of red blood cells under gravity and its relevance to health diagnosis, Fahraeus on page 262 of his paper commences a discussion on the flow of suspensions through narrow tubes which is devoid of mathematics and so commendably clear that it requires no diagrams.

In the words of Fahraeus:

"In the case of a fluid flowing through a tube, we know well that the speed of the current is greatest in the centre, gradually diminishing toward its wall. A reverse condition prevails as regards the pressure within different parts of the fluid, that is to say, it is least in the centre of the tube, from where it gradually increases toward the wall. A particle situated in the moving fluid somewhere between the axis and the wall of the tube will be exposed to a greater pressure on the side facing the wall, than on the side facing the axis. Therefore the particle will be subjected to a force striving to carry it in a direction toward the axis... ... A fluid containing a

considerable quantity of suspended particles will, therefore, be divided, the particles moving along the axis of the tube, i.e., in the so-called axial current, while the fluid will be more or less completely relegated to the wall of the tube, constituting the so called peripheral current."

He goes on to say:

"Since the speed of the current increases with the distance from the wall of the tube, the particles will attain a greater average speed than the fluid, and among particles of different sizes those of larger size will move along quicker than the smaller ones. This difference in speed of the different constituents of a suspension is of great consequence for understanding the distribution of the blood-cells within different areas of the vascular system."

Figure 23, adapted from that in the paper by Tripathi et al. [60], illustrates the scenario put forward and observed by Farhaeus.

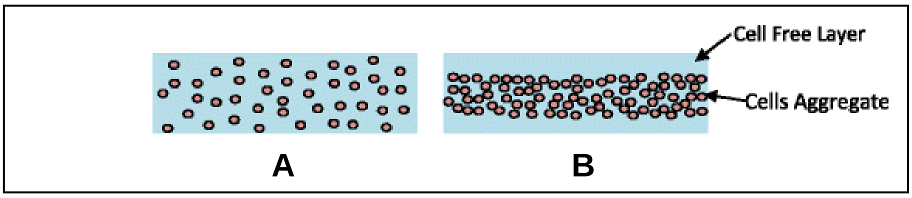


Figure 23: (A) red blood cells in static blood (B) in fluid flow
(Adapted from Tripathi et al. [60])

Tripathi et al. go on to depict the extraction of liquid from the cell-free layer through a side channel:

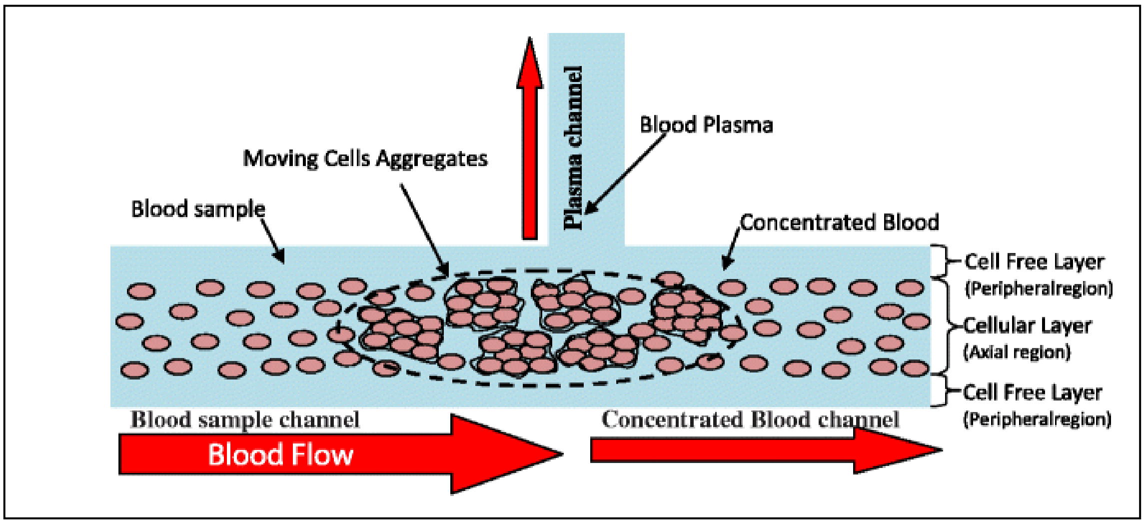


Figure 24: Plasma extraction via a side channel and aggregate formation
(Adapted from Tripathi et al. [60])

Figure 24 illustrates that the removal of liquid from the side channel can result in aggregated "clumps" of red blood cells in the resulting more concentrated stream. Tripathi et al. suggest that in the case of the separation device they discuss *"such aggregation is expected to be temporary or reversible because of the negatively charge surface of blood cells, which will cause partial repulsion between the cells."* On the other hand Fahraeus mentions on page 261 of his 1929 paper [61] that *"The blood of the horse in the finer vessels is really not at all a suspension, the erythrocytes running along as a compact coherent string in the middle of the vessel; only when the stream is slowed by pressure on the supplying arteries does the string show granulated outlines and finally break to pieces."*

The temporary formation of aggregates and the effect of electrical charge on the surface of the cells are just two examples of how the make-up and behaviour of blood is far more complex than might be expected by engineers and researchers more familiar with inanimate systems. In his 2007 work [62] Bagchi considers that *"Computational modeling of blood flow in microvessels with internal diameter 20–500 μm is a major challenge... ... because blood in such vessels behaves as a multiphase suspension of deformable particles."*

Despite the misgivings arising from the difficulties of simulation, the broad physical principles of the Fahraeus effect have been validated by the practical construction of plasma/particle separators based upon microscale junctions.

Figure 25, adapted from Table 4 in the Tripathi et al. paper [60], provides a comparison of the performance of three practical approaches to T-channel separators using the principle illustrated in Figure 24.

	Jaggi et al. (2007) [53]		**Yang et al. (2006)** [52]		**Tripathi et al. (2013)** [60]						
Design	**High Aspect ratio T-channel, Width 14 mm, Thickness 50 µm**		**Main channel 15 µm, 5 plasma channels 9.6 µm**		**Main channel 400 µm, plasma channel 100 µm, flow ratio 54:1**						
Hematocrit %	4.5	15	45	39	2	3	5	10	16	22	45
*Dilution Ratio	1:10	1:3	1	1	1:22	1:15	1:9	1:4·5	1:3	1:2	1
Separation Efficiency %	92	42	30	100	99	97	97	72	65	61	42
Yield %	2.5		25		1.81						
**Flow rate	5 mL min^{-1}		10 µL hour^{-1}		0.1472 mL min^{-1}						
*Volume of blood required before dilution to produce 1 unit of plasma in the extracted liquid	400 units	120 units	4 units	4 units	1215 units	828 units	497 units	249 units	166 units	110 units	55 units

Figure 25: Comparison of T-channel separators in practice
* Calculated using the principles of Figure 22
** As recorded in the referenced papers

The Jaggi et al. [53] design is based upon a 3-Dimensional “extrusion” of the basic principle that will be discussed further in section 2.7.4. The high throughput rate compared with the other designs is of note, and is due to the highly parallel nature of the design.

The Yang et al. [52] design achieves its high claimed yield through the use of 5 sequential junctions.

Figure 26 shows the blood plasma separation region after infusing defibrinated sheep blood (39% Hematocrit – the red blood cell content) through the whole blood inlet at a flow rate of 10 μL hour^{-1}.

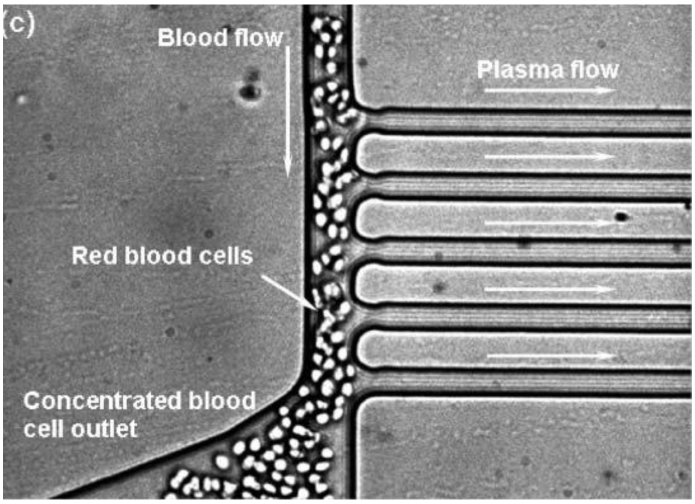


Figure 26: 5 section separator
(Adapted from Yang et al. [53])

Although a separation efficiency of 100% for a hematocrit level of 39% is recorded for this design in Figure 25, it is important to note the very low flow rate, and that the sample was sheep blood, not human blood, also stated to be “defibrinated”, which would reduce clotting.

The Tripathi et al. study revealed a severe compromise of separation performance due to the relatively wide 400 μm main channel, which will exhibit only a limited “Fahraeus Effect” cell-free region. Nevertheless, the effect on separation efficiency of changing the dilution ratio is demonstrated ably and usefully, and a relatively high throughput rate is achieved as a result of adopting the 400 μm wide main channel.

2.7.3.3 Improvements upon junction-based separators

Increased yield and separation efficiencies through detailed modifications to the T-channel geometry are reported by Kersaudy-Kerhoas et al. [63] and similarly by Rodriguez-Villarreal et al. [64], [65].

The root of these modifications can be found in the work of Faivre et al. [66] which introduces a concept of “geometrical focusing of cells” to enhance the thickness of the cell-free layer as a result of blood flowing through a constriction in a microchannel.

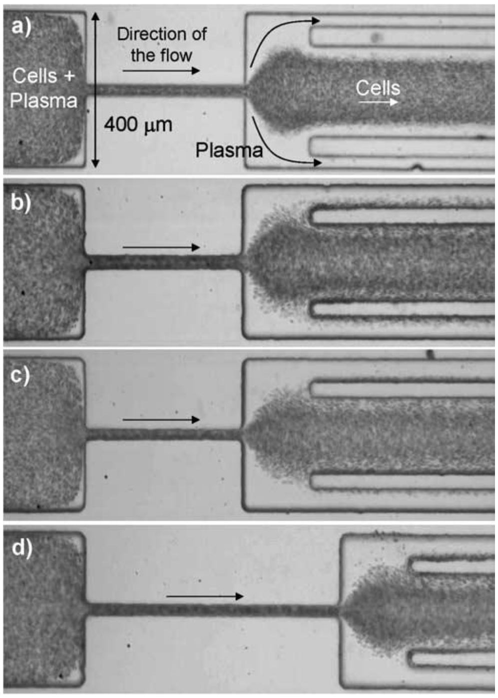


Figure 27: Geometric focusing

From Faivre et al. [66] "*A microfluidic design for separating plasma from blood. (a) w = 25 µm, L = 500 µm, Q = 200 µl/hr, width of the outermost channel is 30 µm. (b) Increase of the width of the outermost channel to 50 µm, with w = 25 µm, L = 500 µm, Q = 200 µl/hr. (c) Decrease of the constriction width to w = 15 µm with L = 500 µm, Q = 200 µl/hr and the width of the outermost channel is 50 µm. (d) Increase the length of the construction to L = 800 µm with w = 25 µm, Q = 200 µl/hr, and the width of the outermost channel is 50 µm.*"

Describing the geometry of Figure 27 Faivre et al. record in [66] the "focusing" of cells following flow through a constriction and demonstrate the extraction of plasma from the enhanced cell-free regions.

The use of the word "focusing", although properly descriptive of the observed effect, is potentially misleading as it may introduce the idea of "jetting" into the minds of designers, who may as a result assume that the construction requires symmetry.

Kersaudy-Kerhoas et al. [63] and Rodriguez-Villarreal et al. [64], [65] both similarly describe the formation of a cell-free zone following a step in the microchannel.

In their 2009 "Validation of a blood plasma separation system by biomarker detection" Kersaudy-Kerhoas et al. [63] declare the geometry shown below in Figure 28:

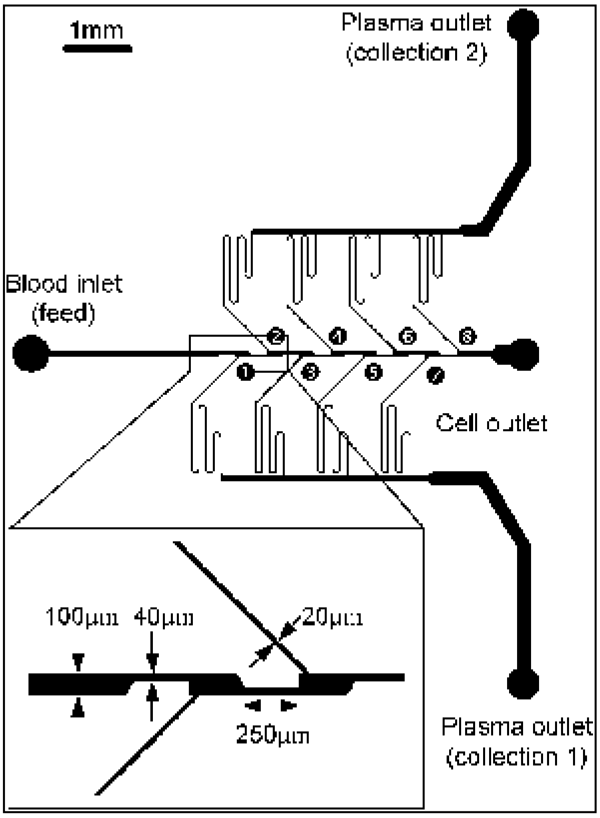


Figure 28: Plasma separation following a constriction (step?)
(From Kersaudy-Kerhoas et al. [63])

Although the 250 μm long 40 μm wide lengths of channel are described in the Kersaudy-Kerhoas et al. paper as "constrictions" the geometry could equally well be described as a 40 μm wide channel with T-junctions modified by the inclusion of a "step", and indeed the photographs of the device in operation, concentrate upon the step feature:

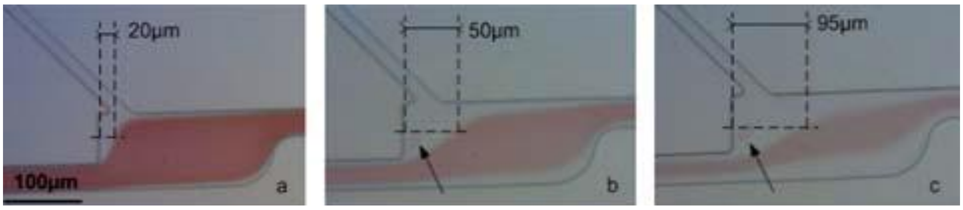


Figure 29: Cell-free zones formed following a step in the channel wall
(From Kersaudy-Kerhoas et al. [63])

Rodriguez-Villarreal et al. in their 2009 "High flow rate microfluidic device for blood plasma separation using a range of temperatures" [64] and associated US Patent Application [65] propose and demonstrate a very similar geometry:

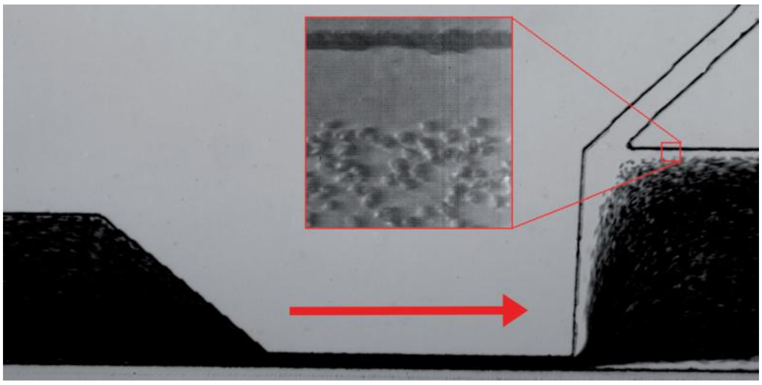


Figure 30: Cell free zone after a step according to Rodriguez-Villarreal et al.
(Rodriguez-Villarreal et al. [64])

Their paper usefully records a temperature dependence for the flow behaviour at the step:

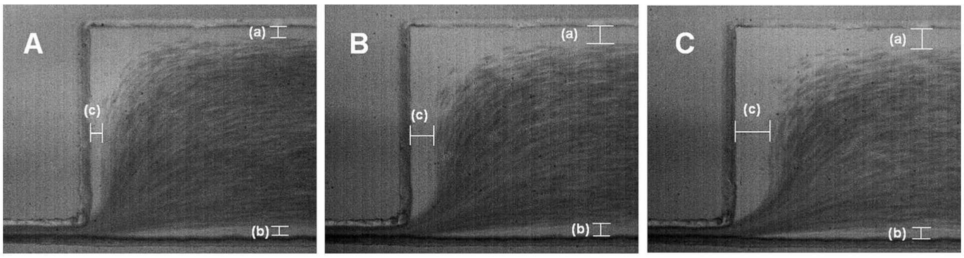


Figure 31: Temperature effects upon the cell-free zone

From Rodriguez-Villarreal et al. [64]: “*Flow behaviour while increasing temperature: (A) 25 °C, (B) 40 °C and (C) 50 °C. The cell-free areas are a, b & c.”*

The dimensions of the device used for the experiments were:

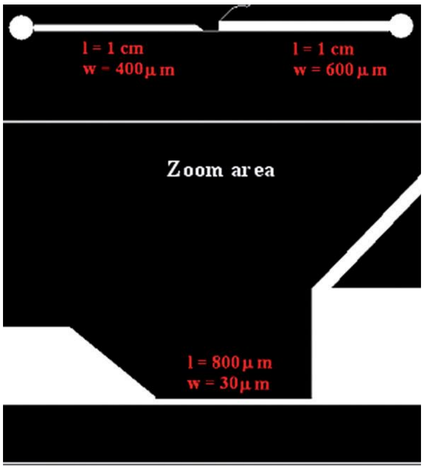


Figure 32: Dimensions of junction/ “step” used by Rodriguez-Villarreal et al.
(Rodriguez-Villarreal et al. [64])

This “step” modification to the simple T-junction originally introduced in Figure 24 clearly provides an extended cell-free area from which to extract plasma.

2.7.3.4 Integrating sample collection with separation and analysis

In a research letter to Nature Biotechnology [67] Fan et al. describe an integrated “card” for blood analysis:

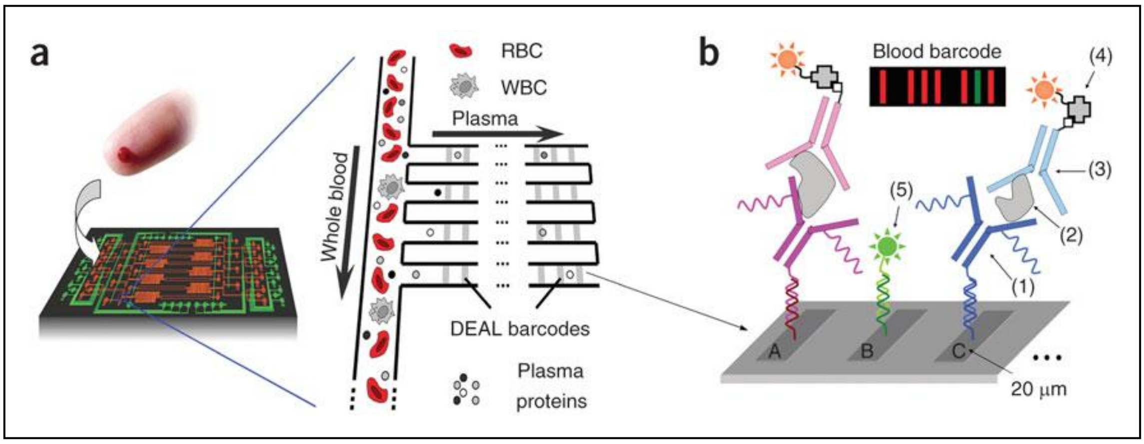


Figure 33: Card-based integrated analysis system proposed by Fan et al.

From Fan et al. [67]: “*(a) Scheme depicting plasma separation from a finger prick of blood by harnessing the Zweifach-Fung effect. Multiple DNA-encoded antibody barcode arrays are patterned within the plasma-skimming channels for in situ protein measurements. (b) DEAL barcode arrays patterned in plasma channels for in situ protein measurement. A, B, C indicate different DNA codes. (1)–(5) denote DNA-antibody conjugate, plasma protein, biotin-labelled detection antibody streptavidin-Cy5 fluorescence probe and complementary DNA-Cy3 reference probe, respectively. The inset represents a barcode of protein biomarkers, which is read out using fluorescence detection. The green bar represents an alignment marker”*

The outline depicted in Figure 33, which is devoid of the practicality of pumps etc, is indicative of a broad swathe of proposals based on planar manufacturing approaches. The very title of the research journal “Lab on a Chip” does draw the mind of the researcher and designer to emulate the planar approach to semiconductor design and manufacture, along with hopes of “building block” elements as introduced in section 1.1.2 of this thesis.

True integration does however beg the question of how to integrate microscale functions into more “odd-form” products.

As a step towards this, the next section examines two examples of taking microscale Red Blood Cell / Plasma Separation into truly 3D geometries, with potentially beneficial results in terms of performance and product integration.

2.7.4 Taking microscale separation into 3 dimensions

Jaggi et al. in 2007 [53] proposed and demonstrated a 3D separator, the performance of which is recorded in the leftmost column of Figure 25.

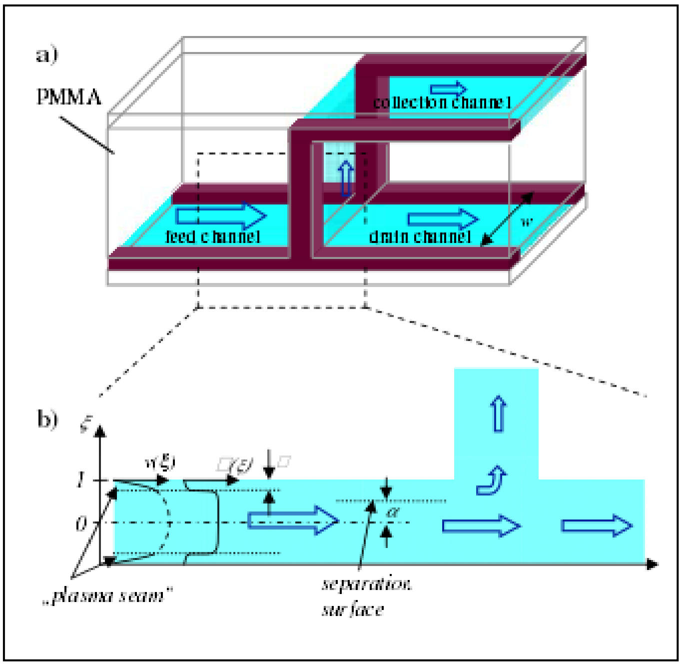


Figure 34: (a) Extrusion of (b) Diagrammatic T-Junction
(Jaggi et al. [53])

The geometric transition from 2D diagram to a 3D representation is shown in Figure 34, whilst a photograph of the resulting separator is shown in Figure 35.

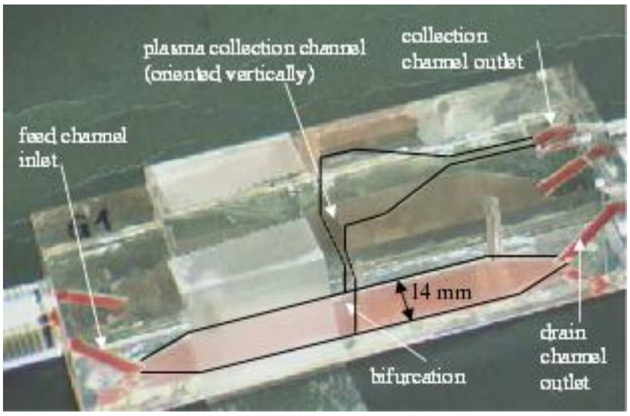


Figure 35: 3D separation device with high-aspect ratio channels

From Jaggi et al. [53]: *"Channel boundaries are outlined with black lines for clarity (optical refraction gives rise to multiple images of the feed and the drain channel)"*

Although the device depicted shows relatively poor separation efficiency on whole blood, an evident path for improvement would be to incorporate the "step" modification of Figure 29, which might promote higher separation efficiency whilst retaining the high throughput arising from the 3D geometry, whose 14mm channel width effectively “parallels” 140 separators 100 μm wide.

The Jaggi et al. device will be revisited and considered further in Chapter 5 of this thesis.

2.8 Pertinent findings and their influences on the subsequent research

The overall thrust of the research is to examine the application of graphical procedures to transform theoretical diagrams into scalable 3-dimensional devices, with an emphasis upon the example of a novel Red Blood Cell / Plasma Separation Device. But in the wider sense the research is set in the context of how designers can work with objects which are beyond direct human experience, and how in these circumstances discussion can take place within teams of designers, and consequently with other teams responsible for product manufacture.

The objectives for the literature review were to seek supporting information and previous research results to gain:

1. A framework for the research based upon standard phases of design from conception through to embodiment, focused where possible upon the issues of the micro- scale.
2. Approaches to overcome the difficulties of conversing about the intangible when product designers need to use principles which are beyond everyday human experience.
3. Insight into how the necessary collective discussion can take place within teams of designers, and between these teams and those responsible for product manufacture.
4. Views concerning the degree to which designers depend upon expert intermediaries.
5. Background regarding the concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures using procedures allied to those used by graphic designers.
6. A review of the need for, and the approaches to, Red Blood Cell / Plasma Separation as an aid to devising and performing an in-practice study into the concept-to-embodiment process based upon a conceptual product for this field.

2.8.1 Novelty of the central premise

The central concept of this thesis is that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures using procedures allied to those used by graphic designers to create solid objects from 2-dimensional prototype geometries. This is introduced in section 2.6, commencing on page 55, its genesis is recorded in Figure 63 on page 119, and its further development is described in Chapter 5.

- No evidence was found for prior art regarding the geometric conversion of *functional diagrams* into functioning products. However, the reverse process, of deconstructing 3D drawings of functioning objects to reveal 2D diagrams from which function may be ascertained was found in the CAD system SolidWorks, and also the routine of converting 3D objects to 2D “slices” is used frequently in computer modelling, when symmetry allows, to reduce the computation load, as demonstrated in Chapter 5.

- The nearest example found is the extruded separator system described by Jaggi et al. [53] as examined in section 2.7.4 on page 74. They do not explicitly claim to have transformed directly from a diagram of physical principle.

2.8.2 New perspectives from the literature review

The review was of necessity wide ranging. Apart from the gathering and collating of essential underpinning information, new perspectives were generated during the process when typically broader topics from the literature were evaluated solely from the point of view of their relevance at the micro- scale. The chief insights and observations were as follows:

- Superficial or imprecise knowledge of a subject may indeed lead to inventive breakthroughs. However, this “kick from uncertainty”, if not properly considered in the light of safer information, can lead to dangerous errors, not only of detail, but of approach

- A parallel was found between needs for explanatory diagrams in cellular biology and similar needs in the discussing, understanding and communication of micro- scale technologies (see Figure 55: i-ball internal workings mimic the organs of a mollusc on page 110).

- Like biology, which typically builds its functions on a cellular scale, the micron scales of microengineering allows the exploitation of mechanisms - chemical, mechanical, fluidic and optical – which can perform functions analogous to those observed in living organisms.

- The design and manufacture of 3D miniaturised / integrated products, although apparently akin to the design and manufacture of integrated semiconductors, differs in one momentous respect: whereas, through design and manufacturing formality, electronics designers do not need to know the intimate physics of electron flow within a chip, integrated product designers need to know precisely the mechanical, optical, magnetic, thermal, fluidic, biological or chemical processes which underlie the operation of the microstructures that they intend to craft.

- Searchable libraries of physical principles focus upon easily codified data and information as opposed to the tacit, difficult to classify combination of knowledge, understanding and experience.

- The design literature is generally lax in its definitions of “information” and “knowledge”, often using them interchangeably (resolved in 2.4.1.3 and Figure 7 on page 38), and behaving likewise with “sketch” and diagram”, which were explored carefully in sections 2.5.1 and 2.5.2 commencing on page 45.

- In 2.4.1.3 approaches to address communications difficulties within the HCI community showed potential to resolve shortcomings arising in the *conceptual communication* stream between players involved in the conceptual design of products.

- Like the approach reported by the “Bio-inspired-Engineering” community, design teams interested in adopting micro- properties could with strong advantage study prior product developments that have been driven by the exploitation of micro- discoveries. Some computer design system providers publish case histories from users which can also be useful in this respect. COMSOL features a searchable gallery of 90 examples.

- Sharing of experience may be achieved through virtual reality, macro- scale models based upon similitude, and the use of symbolic artefacts

- The physical principles that underly the working of a product are predominantly represented in diagrammatic form, and as a result of this there is a very real danger that the physical embodiment of these principles will be influenced by the flat two-dimensional form of diagrams.

- In tackling new technologies, schematic diagrams can allow designers to map a familiar domain onto unfamiliar territory.

- Functional diagrams are useful because they explain the operation of physical principles, generalised so that practical embodiments are not constrained by particular applications.

- Users of functional diagrams need to be very aware that they reflect “pure” physics, whereas practical embodiments need to take account of effects that may not be at all “secondary” at the micro- scale.

2.8.3 Influences on the subsequent research

The literature review as a whole formed a sound basis for the investigative research by *interview*, *survey, workshop, case study* and a practical concept-to-embodiment *design study*.

Further to the basic framework, some of the perspectives listed above were tested, or changed the emphasis of observation as follows:

- Aspects of the 3D-MINTEGRATION project *case study* were reported in the light of “Superficial or imprecise knowledge of a subject may indeed lead to inventive breakthroughs. However, this “kick from uncertainty”, if not properly considered in the light of safer information, can lead to dangerous errors, not only of detail, but of approach”.

- Attention was given to the use of diagrams in the *case study* and the *in-practice design study.*

- The *survey* examined the statement “Sharing of experience may be achieved through virtual reality, macro- scale models based upon similitude, and the use of symbolic artefacts” by asking respondents to rank their use of each item.

- The *workshop* was focused around the use of symbolic artefacts.

- The caveats around the abstractions of functional diagrams were a helpful notion during the *design study*, in both the simulation and construction activities.

- The review of the need for, and the approaches to, Red Blood Cell / Plasma Separation was central to the *in-practice design study.*

2.8.4 Influences upon the wider community

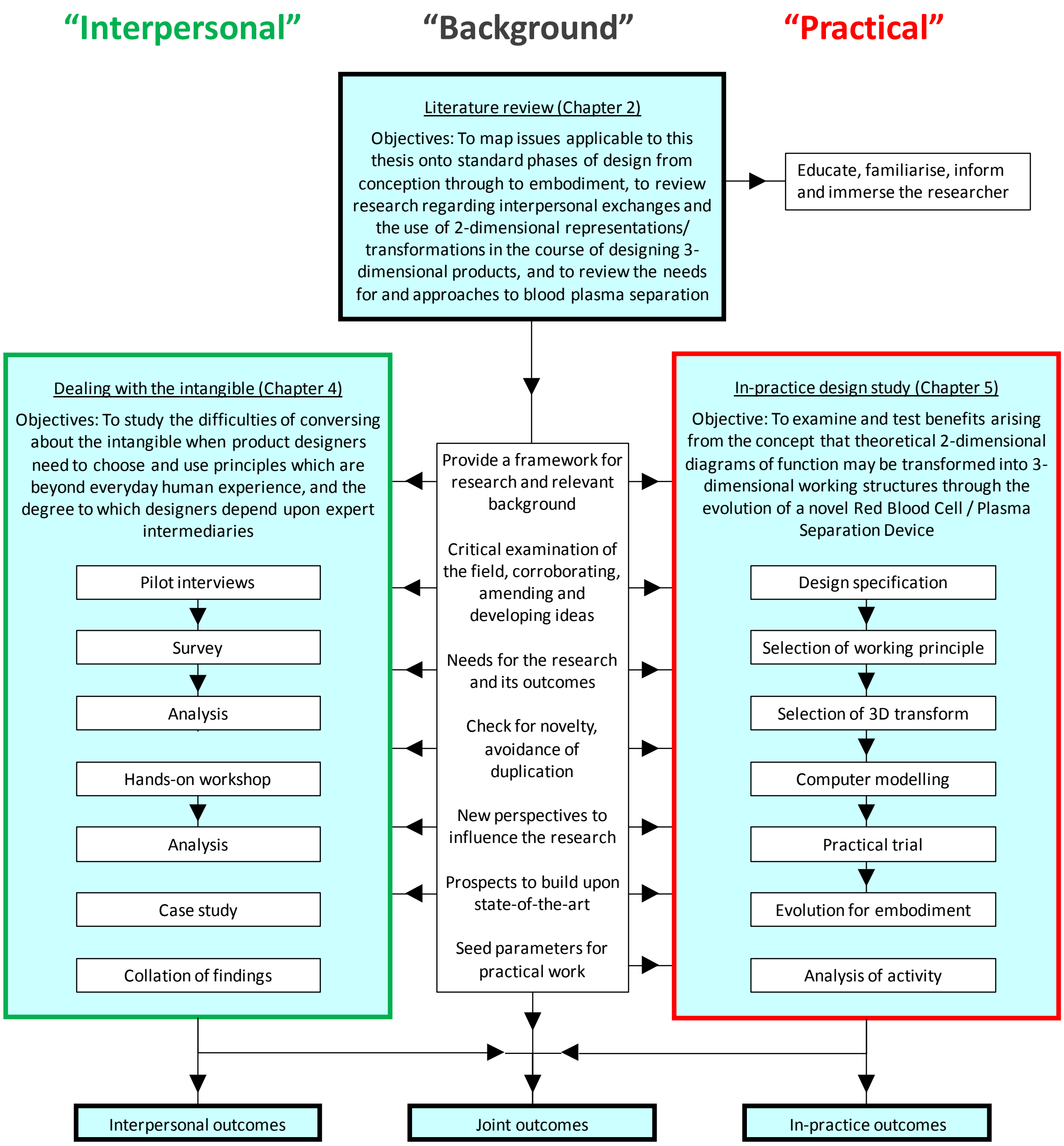
Elements uncovered during the literature review contributed towards a series of presentations to the “smart systems” community. Based on this exposure, design was finally adopted as a session topic at the community’s annual international conference held on 11-12 March 2015.

Chapter 3 Research methodology

Whilst chapter 1 section 1.2 describes the overall scope, structure and activities of the research, this chapter concentrates upon the methodology behind the research in terms of:

- The structure of the research activity from objectives to outcomes
- An assessment of the quality of the methodology

3.1 Structured methodology from objectives to outcomes



Objectives: To map issues applicable to this thesis onto standard phases of design from conception through to embodiment, to review research regarding interpersonal exchanges and the use of 2-dimensional representations/ transformations in the course of designing 3-dimensional products, and to review the needs for and approaches to blood plasma separation

Objectives: To study the difficulties of conversing about the intangible when product designers need to choose and use principles which are beyond everyday human experience, and the degree to which designers depend upon expert intermediaries

Objective: To examine and test benefits arising from the concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures through the evolution of a novel Red Blood Cell / Plasma Separation Device

Figure 36: The structured approach adopted

Figure 36 corresponds to and builds upon the project framework illustrated in Figure 3 on page 20 to reveal the three research activities, “Literature review”, “Debating the intangible” and “In-practice design study” along with their individual objectives, their linkages, and their activities culminating in individual and joint outcomes.

Within the overall methodology, the workings of the three research activities are described in more detail as follows:

3.1.1 Dealing with the intangible

3.1.1.1 Objectives

1. To study the difficulties of conversing about the intangible when product designers need to use principles which are beyond everyday human experience.

2. To determine the degree to which designers depend upon expert intermediaries.

3.1.1.2 Approaches

The introduction to chapter 4, commencing on page 90, further describes the activities shown within the “Dealing with the intangible” research strand depicted in Figure 36. The following descriptions are provided to clarify the reasoning behind these approaches:

3.1.1.2a Pilot interviews (recorded in section 4.1.1) were conducted with three interviewees selected for their competence and breadth of outlook in the topic area of integrated micro- scale technologies. Each face-to-face interview comprised the same three questions, which were compiled to spark discussion from which the following could be ascertained:

- In this topic area where do candidate design solutions stem from?

- Is there an interpersonal idea exchange problem at all in this topic area, and is it worthwhile to work towards its solution?

- If there are such issues, how are they addressed currently?

The answers secured from the interviewees were compared and contrasted, resulting in appropriate input to seed the paper survey of 3.1.1.2b.

3.1.1.2b Survey (recorded in section 4.1.2). The survey, comprising three questions with graded multiple-choice answers, was prepared in a form that would be easy to distribute and simple for respondents to complete, would cover the main points arising from the pilot study, and would lend itself to dispassionate analysis. All aspects of the survey were planned, sanctioned and undertaken within the ethical framework adopted by Brunel University London.

The questions were devised to rank contributors' responses with respect to:

- In this topic area, where do candidate design solutions stem from?
- In the case of product design issues beyond normal human experience, how are interpersonal idea exchange problems approached?
- What form of expert or leadership is employed?

The survey gained contributions from 22 respondents, which was judged sufficient for meaningful analysis of the four grades within each answer without undue granularity caused by the integer nature of 22 votes cast across 4 categories.

The respondents were engaged in the researching and designing of systems containing micro-enabled functionality. 12 were from the public research base, the remaining 10 from industry.

3.1.1.2c Hands-on workshop The workshop, as recorded in section 4.2, was designed and implemented to study the engagement of industry players when tasked with considering product design in an unfamiliar context. All aspects of the workshop were planned, sanctioned and undertaken within the ethical framework adopted by Brunel University London.

The format comprised:

- After a briefing, teams selected to include diverse abilities were tasked with describing new products, enabled by integrated micro- scale technologies.
- They were instructed to express their ideas in the form of dressed mannequins, using a diversity of objects and materials provided for the workshop.
- Whilst immersed in the activity, participants were requested to answer a set of eight questions related to their tasks and their confidence in the outcomes of each phase. The structure of the questions was devised to facilitate later analysis.

The 17 participants, invited from industrial partners within the EU Seventh Framework Programme Coordination Action IRISS (Implementation of Research and Innovation on Smart Systems Technologies), were divided into teams of 4 or 5, with each team comprising representatives from Design, Engineering and Marketing.

In a similar vein to the survey of 3.1.1.2b, the 17 workshop questionnaire returns, recorded in section 4.2.3, were judged sufficiently numerous for meaningful analysis without undue granularity caused by the integer nature of 17 votes cast across 3 categories.

3.1.1.2d Case study The study, as recorded in section 4.3, concerned observations and scrutiny of the discussions and interactions that took place during the course of the EPSRC-funded 3D-MINTEGRATION [1] Grand Challenge project, which was concerned with “The Design and Manufacture of 3D Miniaturised/Integrated Products.”

The observations were made over a 4-year period and were categorised and examined as follows:

- Effects of lack of experience
- Communal idea generation
- Pitfalls of analogues and assumptions of authority
- Formalising a design approach
- The introduction of 2D to 3D transformations

The 3D-MINTEGRATION project grew during its term to encompass 8 universities and some 20 companies. It comprised a community of some 70 researchers and industrialists. The project was essentially multi-disciplinary, with a structured matrix of research topics and demonstrator activities.

3.1.1.3 Outcomes

The outcomes of the research strand “Debating the intangible” included survey and questionnaire analyses in graphical form, and a collation of findings, recorded in section 4.4 under the headings:

- Conversing about the intangible
- Dependence upon expert intermediaries
- The use of diagrams
- Format of design related workshops
- Novelty and acceptance

In addition to satisfying Objectives 1 and 2 of 3.1.1.1, the activities of this research strand also responded to observations summarised in section 2.8.3 of the literature review in that:

- The *survey* examined the statement "Sharing of experience may be achieved through virtual reality, macro- scale models based upon similitude, and the use of symbolic artefacts" by asking respondents to rank their use of each item, amongst others.
- The *workshop* was focused around the use of symbolic artefacts
- The *case study* examined how superficial or imprecise knowledge of a subject may indeed lead to inventive breakthroughs and the caveats around the abstractions of functional diagrams

3.1.2 In-practice design study

3.1.2.1 Objectives

1. To examine, test and assess the benefits of the concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures using procedures allied to those used by graphic designers to create solid objects by manipulating 2-dimensional prototypes.

2. Through the example of a novel Red Blood Cell / Plasma Separation Device, devising and performing a hands-on simulation and constructional trial to gain insight into the concept-to-embodiment process when including a geometric transformation step.

3.1.2.2 Approach

The introduction to chapter 5, commencing on page 123, details the concept-to-embodiment sequence within the "In-practice design study" research strand, as depicted in Figure 36.

The notion of "In-practice research", "Action research" or "Reflective practice", in which the researcher engaged in an activity also reflects upon that activity, has attracted controversy for several decades, as reported by Mäkelä and Nimkulrat in their 2011 conference paper "Reflection and documentation in practice-led design research" [68]. Their paper concentrates on the role of documentation in respect of self- reflection, but a further question is whether the observer and the observed can be properly detached in a research sense when both are one and the same person. The pros and cons of the in-practice approach, and the measures taken by the researcher to maintain rigour, are discussed further in section 3.2.

As a reflective practitioner, the researcher was careful to follow the disciplined path laid down by Pahl, Beitz, Feldhusen and Grote [8] in order to avoid introducing variables other than the 2-dimension to 3-dimension geometric transformation. The path followed was:

- Generating a product concept based upon the needs and traditional approaches researched in sections 2.7.1 and 2.7.2 of the Literature Review, observing the formal disciplines of generating a requirements list and extracting the essential problems.
- Selecting and refining a working principle from those found in section 2.7.3 of the Literature Review.
- Generating and developing a conceptual design based upon a geometric transformation of the working principle, selected from the exploration of three options and the alternative of no transformation.
- Performing computer simulations of aspects of the potential embodiment.
- Performing a practical trial to test the veracity of the concept.
- Evolving proposals for embodiment.

Drawings, diagrams, text and calculations recorded the above activity. The textual records were then analysed using a count of word frequency and also a categorisation of the mental/communication exchanges that occurred during the activity, using categories developed in section 2.4.1.2 of this thesis, as illustrated in Figure 7 and seen in context on page 38.

The text analysis was supplemented by an appraisal of the proposed product embodiment, and contrasts between a planar approach and the 3D-transformed approach.

3.1.2.3 Outcomes

The outcomes of the research strand “In-practice design study” included:

- Computer models
- A successful test result
- A progression of evolving drawings and diagrams
- Text analyses and their discussion
- A comparison between planar and 3D transformed approaches

The outcomes are recorded in more detail in section 5.8, commencing on page 172. In particular section 5.8.1 of the summary describes the satisfying of Objective 1 of 3.1.2.1, whilst section 5.8.4 responds to Objective 2.

In addition, the outcomes provided further insight into *Communicating the intangible* and *Experiences from modelling.*

3.2 Assessing the quality of the methodology

A notable and unusual feature of the research supporting this thesis is its two parallel strands. Whilst engineering design research may often work towards and culminate in the construction of a demonstrator device, in this thesis one strand, the "In-practice design study", does indeed move in that direction, but focusing upon *researching the design processes* resulting in the demonstrator, whilst a second strand, "Dealing with the intangible", concerns the interpersonal communication issues affecting designer teamwork when faced with nascent and intangible technology.

The research approaches adopted to cover these twin fields included:

1. Desk research providing points of reference, critical reviews and new insights.
2. Three field interviews as a pilot for the generation and deployment of a survey.
3. A multiple-choice survey gaining 22 responses.
4. A hands-on workshop involving 17 participants.
5. A case study observing and drawing conclusions during a 4-year research project.
6. An in-practice design study.

Each of the above naturally possesses different characteristics, requiring different measures of their effectiveness. Furthermore, the research work as a whole needs to demonstrate an adequate degree of reliability if its outcomes are to be of value.

3.2.1 Relationship to DRM, Design Research Methodology

Blessing and Chakrabarti in their 2009 book "DRM, a Design Research Methodology" [69] and their summary conference paper [70] propose the adoption of a commonly accepted research methodology in the face of, as they put it, "increasing concerns about the efficiency of design research and the effectiveness of its outcomes."

It has to be said that despite the apparently all-embracing title of both the book and the conference paper the proposed methodology is canted towards research into improving the design process leading specifically to products, allowing the long-term success criteria for the research improvement to be couched in terms of, for example, “cost reduction”, “improved profitability” or “reduced time to market.” This is slightly at odds with the objectives of the research behind this thesis, which aims to improve the efficiency of the design process itself, the effectiveness of design-to-manufacture teams and the stimulation of conceptual design and its transition to embodiment.

Nevertheless, the authors’ developed frameworks provide a discipline, commencing with their carefully-stated objectives for design research, quoted verbatim here:

1. The formulation and validation of models and theories about the phenomenon of design with all its facets (people, product, knowledge/methods/tools, organisation, micro- economy and macro- economy, and

2. The development and validation of support founded on these models and theories, in order to improve design practice, including education, and its outcomes.

The “fit” of the above to the topic of this thesis may be judged from section 1.1.5 “Usefulness and contribution to knowledge” on page 18:

“Applying graphical procedures to theoretical diagrams in order to transform them into scalable 3-dimensional devices is not yet in general use at the macro-scale, but with increasing recognition of the unique capabilities of the micro- scale the idea may grow in appeal to alleviate the difficulties of conceiving of functional structures that, when built, will be too small to experience directly” corresponds to the DRM objective (1) above.

“This design method, through its basis upon a common currency of functional diagrams, may overcome many of the problems of describing and discussing the design and manufacture of normally intangible objects” corresponds to the DRM objective (2) above.

Figure 37 maps the research elements of Figure 36 (page 79) on to the DRM stages proposed by Blessing and Chakrabarti, along with a simplified “focus” for each stage derived from their fuller descriptions.

The correspondence of the current work with the DRM objectives 1 and 2, and its fit with the DRM stages as defined in [69] demonstrates that the chosen methodology is in keeping with the DRM philosophy.

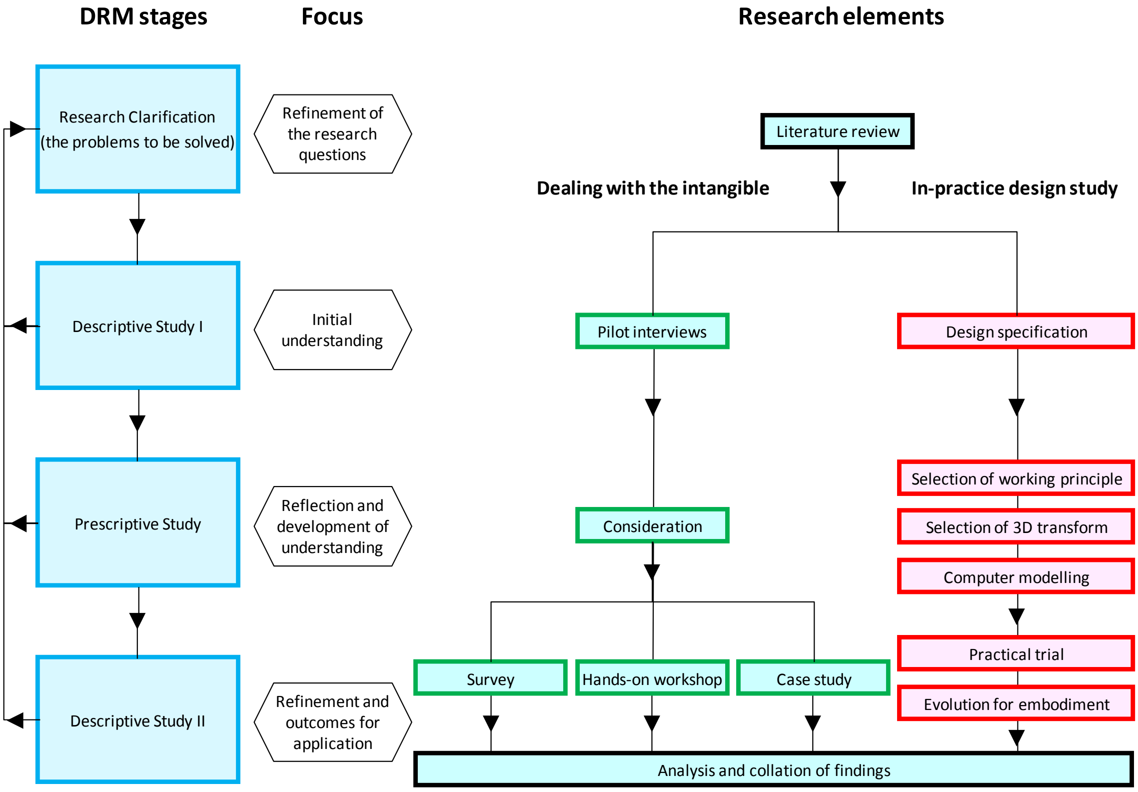


Figure 37: DRM stages after Blessing and Chakrabarti vs Research elements

3.2.2 Survey and questionnaire validity

Confidence in the results of surveys and questionnaires increases with the number of respondents. The following present considerations upholding the validity of the results obtained:

3.2.2.1 Survey

The survey recorded in section 4.1.2 comprised three questions with graded multiple-choice answers. For each answer there were only four options: “Never”, “Sometimes”, “Often” or “Always”.

All of the 22 respondents answered every question. If they had answered randomly each option would receive on average 5.1 responses, but adding the quantization that the number of responses can only be an integer, plus some randomization would result in each option receiving 4, 5 or 6 responses.

In practice the results were as shown in Figure 38, confirming a useful level of variability.

Never	Sometimes	Often	Always
3	12	6	1
0	4	12	6
3	8	4	7
4	12	5	1
0	2	10	10
0	5	15	2
0	4	10	8
3	6	9	4
2	8	8	4
2	9	9	2
4	8	6	4
10	11	1	0
1	4	12	5
6	4	9	3
1	7	7	7
7	9	3	3

Figure 38: Distribution of answers to survey question options

3.2.2.2 Workshop questionnaire

The workshop questionnaire recorded in section 4.2.3 comprised seven questions with graded multiple-choice answers. For each answer there were only three options: “Very confident”, “Not quite sure” or “Needing expert advice”.

All of the 17 respondents answered every question. If they had answered randomly each option would receive on average 5.67 responses, but adding the quantization that the number of responses can only be an integer, plus some randomization would result in each option receiving 4, 5 or 6 responses.

In practice the results were as shown in Figure 39, confirming a useful level of variability.

Very confident	Not quite sure	Needing expert advice
15	1	1
11	2	4
9	6	2
11	5	1
11	6	0
15	2	0
13	4	0

Figure 39: Distribution of answers to workshop questionnaire options

3.2.3 In-practice design study

As mentioned in 3.1.2.2, the notion of in-practice research, and its allied variations, has attracted controversy. As a demerit, objectivity might suffer when the observer and the observed are one and the same person. Conversely, there is merit in that a practitioner can bring explicit experience and tacit knowledge (Skyrme [29]) to bear upon the research. Römer et al. say that it is not sufficient just to observe practitioners, it is necessary to find out what they are thinking, hence their 2001 a postal survey [71] examining practitioners' own views of their use of external representations to supplement the limited ability of the brain to encompass all design aspects and all possible solutions at one time.

In-practice research can with safeguards have an important and unique contribution to make, but, as put forward by Mäkelä and Nimkulrat in [68], it only has value if the outcomes are documented effectively.

In their doctoral dissertations Mäkelä and Nimkulrat used sketches and text records in the form of diaries. They report that looking back at the diaries revealed not only thoughts, but also emotions.

For the in-practice research upholding this thesis the activity was recorded by drawings, diagrams, text and calculations throughout sections 5.1 to 5.6. In contrast to the work of Mäkelä and Nimkulrat the textual records were then analysed *dispassionately* using a count of word frequency and a classification of the "thinking" exchanges that occurred during the activity, using the categories newly-developed in section 2.4.1.2.

Chapter 4 Dealing with the intangible

This chapter concerns research into knowledge transfer in the design arena as defined in Topic areas 3 and 4 of this thesis. The topics are principally:

- The issues of conversing about the intangible when product designers need to use physical principles which are beyond everyday human experience
- The degree to which designers depend upon expert intermediaries

As reported in this chapter, the above matters were examined through:

- Pilot interviews with three respondents, their answers seeding the questions within a ***survey*** of 22 further respondents. This activity is recorded in 4.1 "Selecting principles to generate functional objects"
- A dedicated hands-on practical ***workshop*** including a set of questions related to and focused by the workshop activities. This activity is recorded in 4.2 "Collaboration and reliance upon expert intermediaries"
- A ***case study*** concerning the 3D-MINTEGRATION project [1], with observations concerning the discussions and interactions that took place during the course of the project. This is recorded in 4.3 "Case study: 3D-MINTEGRATION research project"

In respect of observations summarised in section 2.8.3 of the literature review, the activities of Chapter 4 also responded to:

- The ***survey*** examined the statement "Sharing of experience may be achieved through virtual reality, macro- scale models based upon similitude, and the use of symbolic artefacts" by asking respondents to rank their use of each item, amongst others.
- The ***workshop*** was focused around the use of symbolic artefacts
- The ***case study*** examined how superficial or imprecise knowledge of a subject may indeed lead to inventive breakthroughs and the caveats around the abstractions of functional diagrams

4.1 Selecting principles to generate functional objects

As introduced in 2.3.1 "Conceptual Design", the core of this thesis concerns the difficulties of conversing about the intangible when product designers need to use principles which are beyond everyday human experience.

Conceptual Design firstly abstracts the essential problems that the product or system seeks to address, then identifies underlying principles for their solution. From these candidate principles a principal solution or solutions may then be selected according to criteria which best fit the constraints of manufacturing and use.

Section 1.1.1 “The problem of unobservable devices” points out that the great majority of products and systems now contain internal devices based upon mechanical, thermal, chemical, fluidic/hydraulic/pneumatic, or electromagnetic principles, or combinations of principles, to enable the products or systems to perform the roles expected of them, and that if the incorporated devices are at the normal human scale of sight and touch their principles of operation are easy to recognise and understand by appropriately skilled people..

Accordingly, designing products and systems containing devices that are too small to be seen or touched by unaided human designers means selecting principles typically from categorised descriptions and/or representative diagrams.

The resources and tools currently available to support the selection of physical principles are reviewed in 2.3.4 regarding “Existing approaches, resources and tools”, whilst 2.4.1 “Communicating across and beyond the design team” introduces, amongst other observations, the idea that the problems of communicating concepts between individuals and teams of widely differing experience and outlook in the conceptual design of functioning objects might mirror the contentions of the HCI (Human Computer Interaction) community.

To test the real-life mapping of the above ideas on to the topic area of this thesis pilot interviews and a subsequent survey were conducted as follows:

4.1.1 Pilot interviews

Pilot interviews were conducted with three respondents. Their answers provided the insight to pose pertinent questions within the subsequent survey of 22 further respondents recorded in 4.1.2 below. The pilot interviews were conducted individually in person at the workplaces of design and development practitioners.

Interviewee 1 headed the Microsystems research activity at a University, with a particular emphasis upon design for manufacture using standardised “foundry” production processes

Interviewee 2 was engaged in the public/private development of integrated microsystems

Interviewee 3 was the Head of an application centre for smart system integration within a research institute

The interviews are recorded and commented upon as follows:

<table>
<tr><th colspan="3">Question 1: What are the purely micro-related problems of identifying candidate design solutions, and how are they approached?</th></tr>
<tr><th>Interviewee 1</th><th>Interviewee 2</th><th>Interviewee 3</th></tr>
<tr>
<td>- “Candidate physical principles are selected from diagrams in A-level physics text books. Their transformation to the micro-scale is aided by making physical prototypes and testing for deviations from the ideal case”
“The deviations noted either (1) enable designs to be modified so that their performance conforms more closely to the required specification, or (2) are investigated further to form the basis for entirely new designs. One instance of the latter is the use of stiction, an effect which is` enhanced at the microscale, to fabricate miniaturised stepper motors depending upon the enhanced effect combined with the relative strength of electrostatic fields at the micro-scale. In this way something regarded as an obstacle has become an enabling technique”</td>
<td>- “Many years ago my PhD researched scalability in Microsystems, particularly focusing upon the mechanical behaviour of cantilevered beams fabricated at the micro-scale. Through very delicate experiments using tiny weights to load the beams I was able to demonstrate that in this case behaviour corresponded exactly with that at the macro scale. Nevertheless, one needs to be careful not to make general assumptions, and to back up theory with practical experiments”
- “Currently I am involved in the fabrication of micro-scale electrical switches. The problems of contact performance are surprisingly formidable. These problems are not a feature of the micro-scale, it is simply that they become obvious at the micro-scale. I have discovered that the whole topic of interfaces is very poorly understood, because they are not significant at the macro-scale. It is not that they are outside everyday experience, it is just that they have not been a serious issue. Now we are forced to come to grips with them”</td>
<td>- “First we need to recognise three classes of design problem that attract new approaches such as microsystem technology:
(1) Problems that are traditionally unsolved, and are likely to stay that way
(2) Problems that require an improvement over previous solutions
(3) Entirely new activities enabled by harnessing effects at the micro-scale
“The Improvement problems of (2) and the enabling activities of (3) above are solved at IZM through a range of functional modules that may be further tailored to optimise performance for specific applications. These are macro- scale modules within which the micro-scale techniques are essentially hidden. This might be compared with electronic integrated circuits which package micro- scale electronics in handleable macro- scale packages with specified functionality and performance”</td>
</tr>
</table>

Observation:

- Primary approaches appear to be from texts, models, and experience gained from previous designs

Question 2: How does discussion of micro-related design proceed, when the issues lay outside everyday experience at the macro scale?

Interviewee 1	Interviewee 2	Interviewee 3
- “It depends very much upon which level of the design hierarchy is involved. Between experts in allied fields there is common experience so discussion is easy” - “Moving up the hierarchy towards whole product embodiment brings problems. We show micrographs and video clips of real prototypes to base discussions upon. Beyond embodiment, further up the pyramid towards system level project leaders, there are strong barriers - related to issues of visualisation but characterised possibly as fear of the unknown” - “Some companies have a culture of innovation which makes them more amenable or receptive to discussion outside the bounds of everyday experience. One such company being Oxley Developments. Conversely, a visualisation breakdown within the highly systematic company Thales meant that enthusiasm and dialogue at the engineering level could not progress to product level” - “In my view debate is aided strongly by microscope and video enlargement of real prototypes. This does however fail to cross wider boundaries of discipline or hierarchy”	- “At ST Microelectronics they employ 200 designers in Microsystems. They do not attempt to reach beyond the component level. They have a very pragmatic approach, designing microsystem components so that they can make them in their chip factory. Then they connect them to their electronic chips on PC boards. They admit it is hopelessly non-optimal from a technical point of view, but they can turn round product very quickly for mass markets which in themselves turn on very quickly.” - “There may not be time to integrate microstructures directly into macro products. The versatility and adaptability of component-level building blocks provides a vital agility, even though costs or performance are not optimum, customers have to be satisfied before they go elsewhere”	- “I was trained in precision mechanical design, which is highly disciplined. When we formed the Micro Electro-Mechanical Systems group we had to enable electronics engineers to work with mechanical engineers. The electronics engineers worked (and still work) at a high level of abstraction, using high level design blocks, and furthermore they do not have the strict framework of mechanical design. There is a vacuum between the disciplines, and no shared background. We solved our initial problems by making a range of demonstrator products.” - “Now, with system-level integration spanning even more disciplines, the problem returns. Currently we solve it with a hierarchy of individual solutions, again a building block approach.” - “We would really like to see co-design as a method of creating truly integrated systems, not just assemblies of blocks.” - *“The problem that you have identified is real and important. It needs to be recognised by industry and the research programme process. Its resolution is fundamental for EU industry to maintain an industrial lead.”*

Observation:

- Project leadership and “culture” are strong enablers of collaboration, along with a hope for progress in co-design capability. Customer urgency and a vacuum between disciplines are recognized as inhibiting the effectiveness of design

Question 3: Can you comment upon the notion of embedding microstructures directly into the macro fabric of products, which are typically 3-dimensional?		
Interviewee 1	Interviewee 2	Interviewee 3
- "As before, moving up the hierarchy towards product embodiment brings problems. We would need to somehow move beyond the use of the microscope to show whole-product issues and benefits" - "We are already working upon the direct integration of micro-structures into the cavities of CW lasers. It is a very hostile environment from which much will be learned beyond the micro-system itself" - "We are also embarking upon collaborative research into large-area systems, which is a move towards whole-product integration"	- *"You propose to completely revise industry. It is very ambitious"* - *"However, the difficulties you have identified of communicating outside everyday experience will become unavoidably challenging when the nano-scale needs to be integrated with the micro-scale"*	- "It is important to identify candidate areas for this notion. One such area is large area smart textiles, with embedded sensors, processors, actuators and power sources introduced through processes compatible with and inspired by textile manufacturing processes"

Observation:

- The notion of integrating micro-enabled functionality directly into macro products is seen to be novel, yet worthy of development

Two of the interviewees provided early stage confirmation of the usefulness of this research through their comments:

"The problem that you have identified is real and important. It needs to be recognised by industry and the research programme process. Its resolution is fundamental for EU industry to maintain an industrial lead."

"You propose to completely revise industry. It is very ambitious. However, the difficulties you have identified of communicating outside everyday experience will become unavoidably challenging when the nano- scale needs to be integrated with the micro-scale"

4.1.2 Survey

Following the pilot interviews, and based upon the experience gained from them, a survey was prepared in a form that (1) would be easy to distribute and simple for respondents to complete, (2) would cover the main points arising during the pilot study and (3) would lend itself to dispassionate analysis.

The respondents to the survey were provided with a Participant Information Sheet outlining the aims of the research, confidentiality and freedom to decline. They were also provided with a consent form, which all respondents signed and returned.

The questions and reply options were as follows:

Question 1: In the design of a new product using devices based on micro- or nano- effects, how would you choose the best physical principle to use?				
	Never	Sometimes	Often	Always
From a book?				
From a scientific journal?				
From the internet?				
From patents?				
By discussion with colleagues?				
From your own experience?				
Other (specify)				

Question 2: How does discussion of micro-related design proceed, when the issues lay outside everyday experience at the macro scale? (eg no gravity, high friction, weird fluid behaviour etc...)				
	Never	Sometimes	Often	Always
By drawing diagrams?				
Using equations?				
Making models?				
Comparing with macro- behaviour?				
Hand waving and gestures?				
Virtual reality?				
Computer simulation?				
Other (specify)				

Question 3: If, instead of using components, the design approach is to embed microstructures directly into the macro fabric of a 3-dimensional product – how then does discussion of the design proceed?				
	Never	Sometimes	Often	Always
Using an expert "Architect", with total product responsibility, to drive the whole design-to-manufacture team?				
Using an expert "Project Manager" to act as a joint resource between the team members?				
Using an IT-based "co-design" system				
Other (specify)				

The survey was completed by 22 respondents engaged in the researching and designing of systems containing micro-enabled functionality. 12 of these respondents were from the public research base, the remaining 10 from industry.

4.1.3 Analysis of survey

The survey results are summarised and analysed as follows:

Question 1: In the design of a new product using devices based on micro- or nano- effects, how would you choose the best physical principle to use?

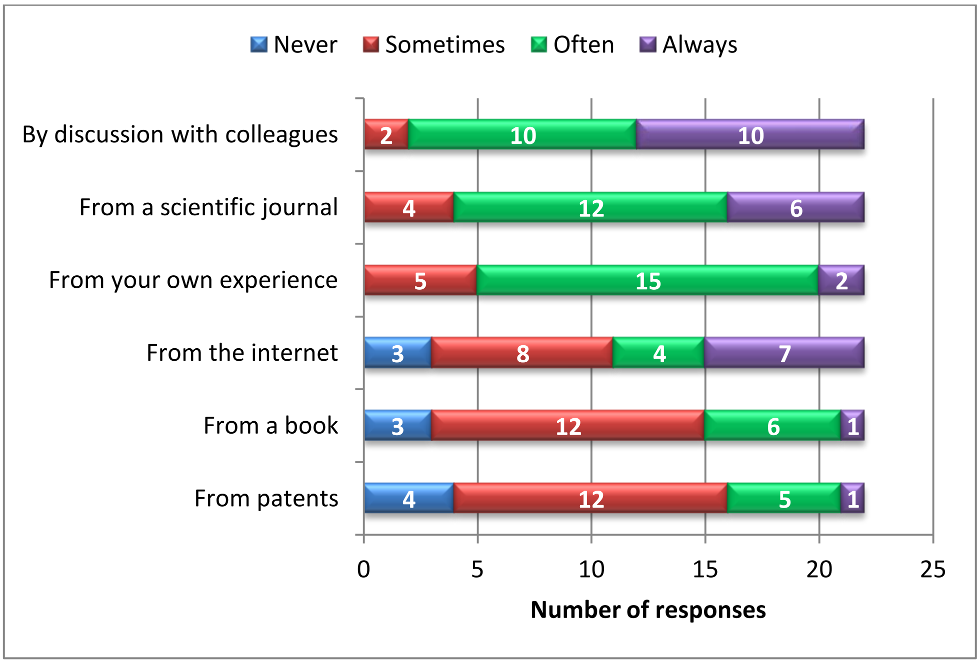


Figure 40: References to physical principles

For the graphical analysis shown above the results were ranked by the frequency of responses in the combined classification “Often + Always”.

- The front-running mechanisms to facilitate the choice of physical principles reported were (1) discussions with colleagues, (2) scientific journals, and (3) personal experience. No respondents declared that they would “never” use these avenues.

- A surprising ~15% of respondents reported that they “never” use the internet in the selection process. The same figure applied for books and patents.

- Nevertheless, in terms of sources “always” used, the internet ranked second only to discussion with colleagues.

- The strong need for discussion with colleagues underlines the importance of the question “How can designers work with objects which are beyond direct human experience, and how can collective discussion take place within teams of designers, and between these teams and other teams responsible for product manufacture?” expressed at the outset of this thesis in 1.1.1 “The problem of unobservable devices”.

Question 2: How does discussion of micro-related design proceed, when the issues lay outside everyday experience at the macro scale? (eg no gravity, high friction, weird fluid behaviour etc...)

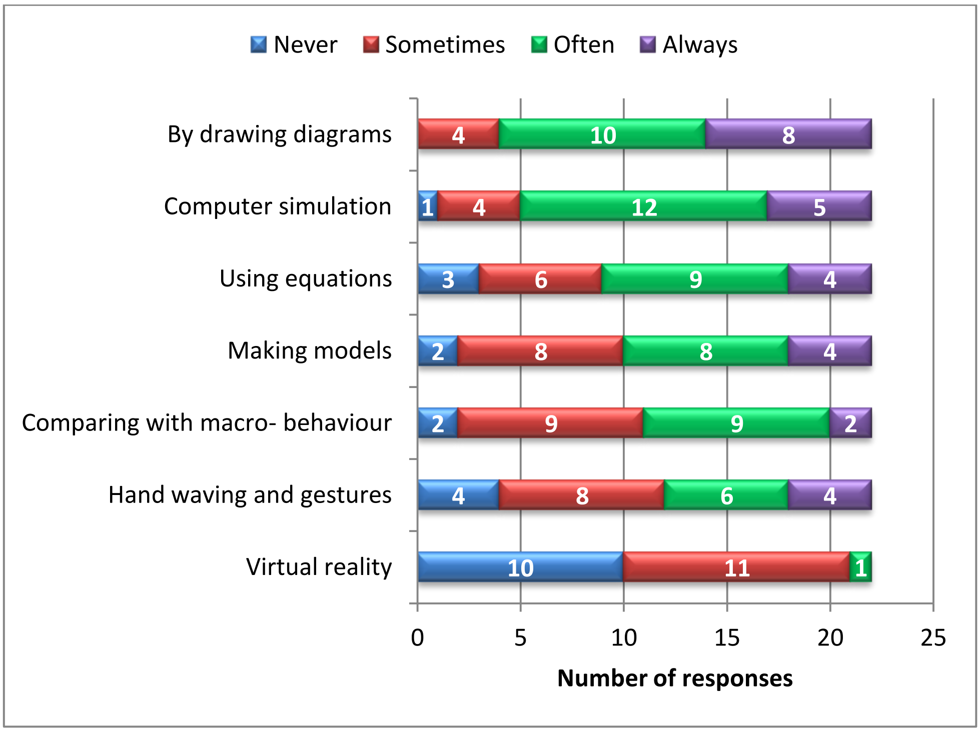


Figure 41: Modes of discussion

For the graphical analysis shown above the results were ranked by the frequency of responses in the combined classification “Often + Always”.

- “Drawing diagrams” was reported as the most prevalent aid to discussion. No respondents declared that they would “never” use this mechanism.

- Computer simulation (which almost inevitably starts with diagrammatic representations) was cited as the second most frequent mechanism used to support discussion, ahead of physical model making, and contrasting surprisingly with virtual reality, shunned by nearly half of the respondents.

- The responses show the use of diagrams as underpinning the progressing of designs where elements lay outside everyday experience at the macro scale. This supports the targeting of the thrust of this thesis – of applying graphical procedures to theoretical diagrams in order to transform them into scalable 3 dimensional devices – as having strong potential to alleviate the difficulties of conceiving of functional structures that, when built, will be too small to experience directly.

Question 3: If, instead of using components, the design approach is to embed microstructures directly into the macro fabric of a 3-dimensional product – how then does discussion of the design proceed?

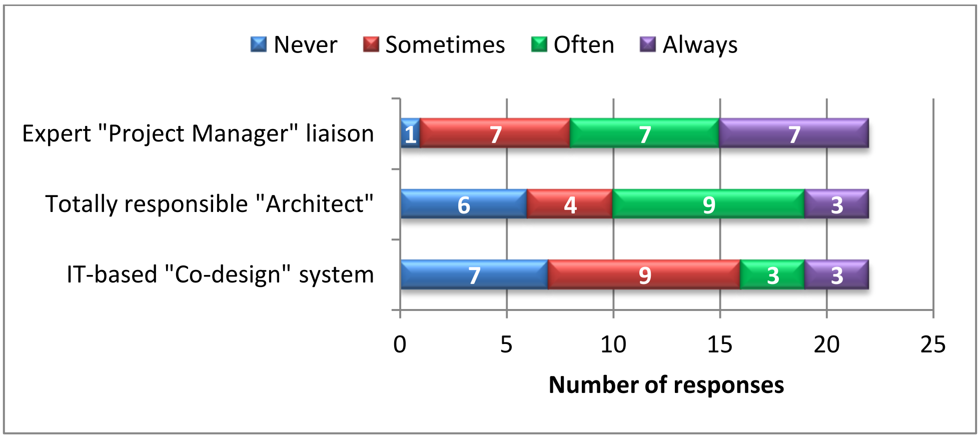


Figure 42: Piecing together the unknown

For the graphical analysis shown above the results were ranked by the frequency of responses in the combined classification “Often + Always”.

- The use of an expert Project Manager to progress designs which embed microstructures directly into the macro fabric of a 3-dimensional product was cited as prevalent, contrasting strongly with the employing of authoritarian architects or IT-based co-design systems, whose use was rejected by over 25% of respondents.

- Some two-thirds of respondents reported that they “often or always” use expert Project Managers, which suggests that inter-personal collaboration and the role of Expert Intermediaries are important and worthy of examination, as embarked upon with the workshop activities of 4.2 below.

4.2 Collaboration and reliance upon expert intermediaries

In the course of the research a hands-on practical workshop was designed and implemented to study the engagement of industry players in the assimilation and application of new design methodologies and unfamiliar manufacturing techniques. All aspects of the workshop were planned, sanctioned and undertaken within the ethical framework adopted by Brunel University London.

4.2.1 Workshop objectives, format and participants

4.2.1.1 Objectives The workshop supported this thesis and also the PhD study of a Brunel co-worker Odette Valentine [14]. The objectives relating solely to this study were to explore:

- The difficulties of conversing about the intangible as increasingly product designers need to use principles which are beyond human experience.
- The degree to which designers and manufacturers depend upon expert intermediaries, and whether there can be realisable benefits associated with design teams being more directly connected to underlying physical principles rather than working through intermediaries.

Further aims were pursued beyond the research study:

- To stimulate partners in the European Technology Platform EPoSS (European Platform on Smart Systems) to consider and adopt a groundbreaking rather than incremental approach to research in Engineering design and Manufacture
- To reinforce the visibility of The Brunel University School of Engineering and Design and the Cambridge University Institute for Manufacturing in the European Framework research collaboration community

4.2.1.2 Venue and format The venue for the workshop, which was held on 6 July 2012, was kindly provided by the Institute for Manufacturing at their premises within the University of Cambridge.

The format comprised:

- An introduction to Open Design, followed by hands-on scenario and product planning in which teams of delegates investigated the application of the design and manufacturing techniques put forward.
- Teams, selected to include diverse abilities, described new products enabled by integrated micro- scale technologies that were impossible to make before. As a relief from the usual post-it note scenario, the ideas were expressed in the form of dressed mannequins, using a diversity of objects and materials provided for the workshop.

- Participants were requested to answer a set of questions related to and focused by the workshop activities. The structure of the questions was devised to facilitate later analysis.

- Experts were made available for teams to interrogate, and observations were made by the workshop researchers Topham and Valentine.

4.2.1.3 Participants were invited from industrial partners within the EU Seventh Framework Programme Coordination Action IRISS "Implementation of Research and Innovation on Smart Systems Technologies". The objective of the IRISS programme was to secure and extend the competitive advantages of European industry Smart Systems research and production.

Smart Systems are technology-based products that combine data processing with sensing, actuating and communication to be able to analyse complex situations, take autonomous decisions, and be predictive. They take advantage of miniaturisation, are highly energy efficient or even energy-autonomous and can communicate with their peers and other systems.

It is in the nature of Smart Systems that their designers encounter:

- unfamiliar technologies and juxtapositions of technologies

- unfamiliar applications environments, including new abilities for personalisation and portability

The 17 IRISS project partners who accepted the workshop invitation were essentially self-selected, but for the hands-on activity they were divided by the researchers into teams of 4 or 5, each team comprising a balance of outlook representing Design, Engineering and Marketing.

4.2.2 Workshop hands-on activity: "Fashioning 2020 Products"

1. Participants were invited to envisage the portable and/or wearable smart products that will enhance the daily life (or special occasions) of the modern lady in the year 2020

2. A briefing session requested participants to consider the following for each product:

- Conception: What is it? What makes it possible? What makes it useful and appealing?

- Technology and manufacturing choices: Can it be made? Where.. ..why there? Is there an inventive leap? Will it work? How?

- Desirability and Acceptance: Are there already expectations, or do they have to be generated? Is there a business innovation? Is it elitist, or is there a "Tipping point" for general use? Standards, regulations and ethical considerations?

3. To generate and depict the new products, mannequins were provided, to be dressed using a diversity of objects and materials provided for the workshop.

4. The participants were then divided into 4 teams of 4, with each team selected to contain a mix of members competent in Design, Engineering and Marketing. The teams were briefed to interact with sources of expertise as follows:

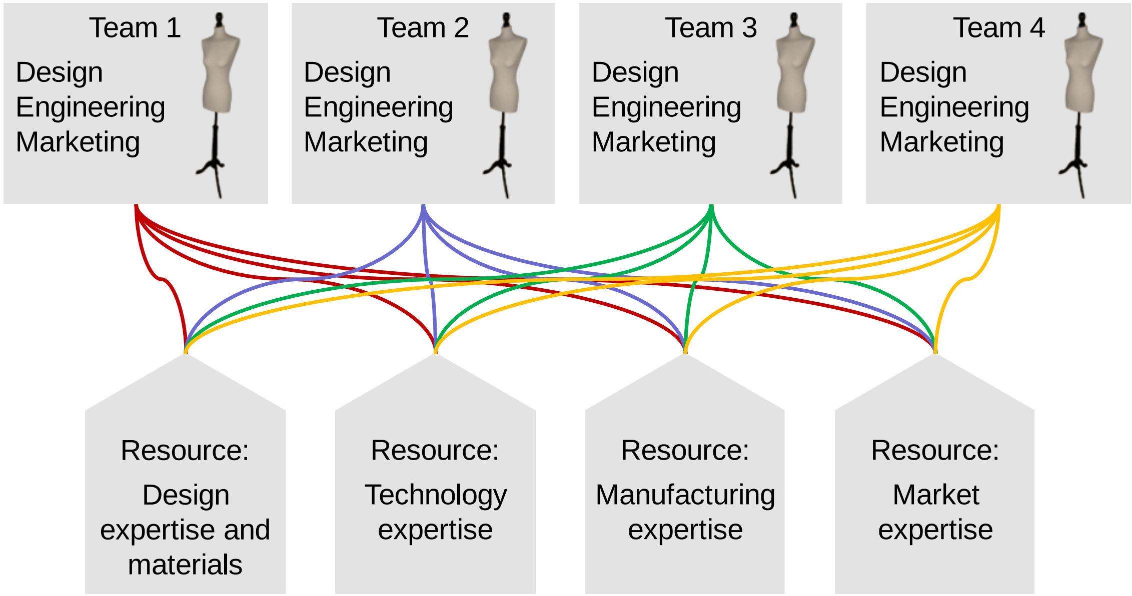


Figure 43: Organisation of workshop teams

5. As a stimulating focus for their discussions, each team was directed to envisage the wearable smart products that will enhance the daily life (or special occasions) of the modern lady in the year 2020, and to dress their mannequin as follows:

   - Team 1: "TravellingGlam", an outfit for travelling and/or mobility
   - Team 2: "SportyLady", for exercise and/or competition
   - Team 3: "YouthOfTomorrow", not what they used to be in 2012
   - Team 4: "MadamMethuselah", to live 1,000 years

6. A common resource was provided for all teams, included tools such as scissors, staplers and pins, and materials as follows:

- Colour printed A3 sheets depicting electronic circuits, solar cells, sensors, indicators, displays and electro-mechanical themes

- Appropriate "party" masks, goggles, hats, cake cases, disposable crockery, toys etc suitable for customised use

- Samples of wires and electronic components

- Equipment to "cannibalise" for parts

- A wide selection of clothing and textile materials

Figure 44: Workshop materials

7. The teams proceeded as follows:

Figure 45: Selecting materials

Figure 46: Teams working in bays

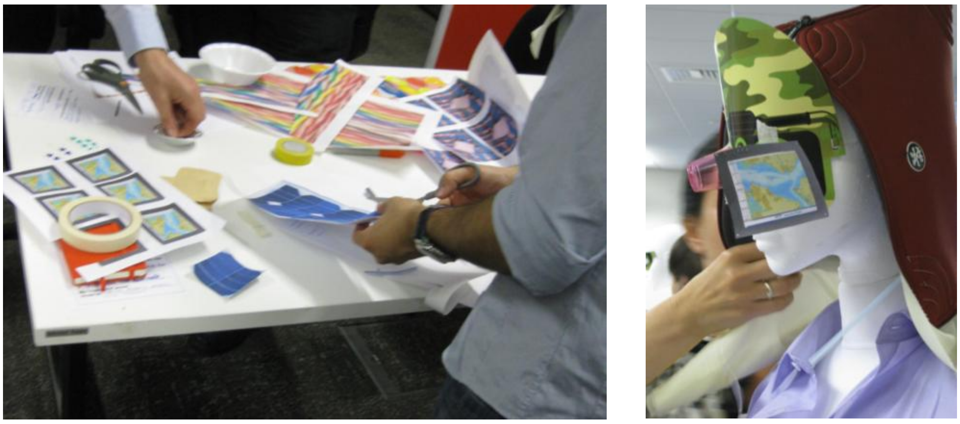


Figure 47: 2D representations conforming to 3D contours

MadamMethuselah	**YouthOfTomorrow**	**SportyLady**	**TravellingGlam**
Spare parts and upgrades for 1,000 years	Wears her emotions on her sleeve	Hot, cold, fast, slow, always compensated	Ready for anything
Always connected – direct to the brain	She will have “reality” wherever she goes	Virtual tracks and virtual competitors	And totally insulated from the experiences and pleasures of travel

Figure 48: The completed mannequins

4.2.3 Workshop questionnaire

At the same time as working on their mannequins, teams were requested to answer a set of questions related to the ideas and thought processes regarding the conception of their ideas, what will make them work, how they can be manufactured, what will makes them useful and appealing, and the team's level of confidence regarding these matters.

		Very confident about this	Not quite sure	Needing expert advice
Idea: What is it? Just a few words about *this* element of the design and why it will be useful				
To make it work, what basic physical principles will need to be understood in the design?		☐	☐	☐
What technology or invention will make it possible?		☐	☐	☐
Can it be made by existing techniques? Anywhere?		☐	☐	☐
Are other products needed before it can be used? (Eg networks, better batteries, etc)		☐	☐	☐
Does it create a new business or service, or expand existing business activities		☐	☐	☐
Will there be an immediate mass market in 2012, or "early adopters", or will it always be specialist – or customised?		☐	☐	☐
Will there need to be new regulations or standards?		☐	☐	☐

Figure 49: Workshop questionnaire

4.2.4 Analysis of completed questionnaires

17 product ideas / capabilities were recorded, along with the principles that would make them work:

“TravellingGlam”	Plane sleeping hood - neck support - light block - sound block
	Data store - booking - directions - ID
	Personal doctor - monitor health - assist in sleeping
	Jet pack - to escape crowded situations
	Adaptive comfort function - temperature - humidity - ventilation
	Cloaking - Invisibility
“SportyLady”	Cloud doctor: Distributed sensors monitor state of body and warn of problems / provide treatment and also advise on training
	Augmented reality and navigation projected directly into the eye. Makes exercise in ugly city surroundings more pleasant
"YouthOfTomorrow"	Electronic pocket money to educate young people regarding use of money
	Flexible display to show colours, pictures or advertising
	Emotion reflecting accessories (necklace). Teenagers use as another medium to express themselves. It works by monitoring functions such as temperature and heart rate and gives a response.
	Smart glasses including loudspeaker, video display and energy scavenging. Tomorrow's smart phone.
	Cooling / heating clothing - keep warm in less clothing - keep cool when the sun is hot
"MadamMethuselah"	Gradual replacement of vital organs by exo-systems. - Brain is sole survivor - organs designed for 1000 year operation
	Brain communication interface - with intelligence amplification - can control a swarm of droids to be physical agents in the world
	Fusion power unit
	Hovercraft propulsion system

Figure 50: Workshop product ideas

The confidence of the respondents regarding the practicality of being able to design and manufacture their ideas in practice is consolidated as follows:

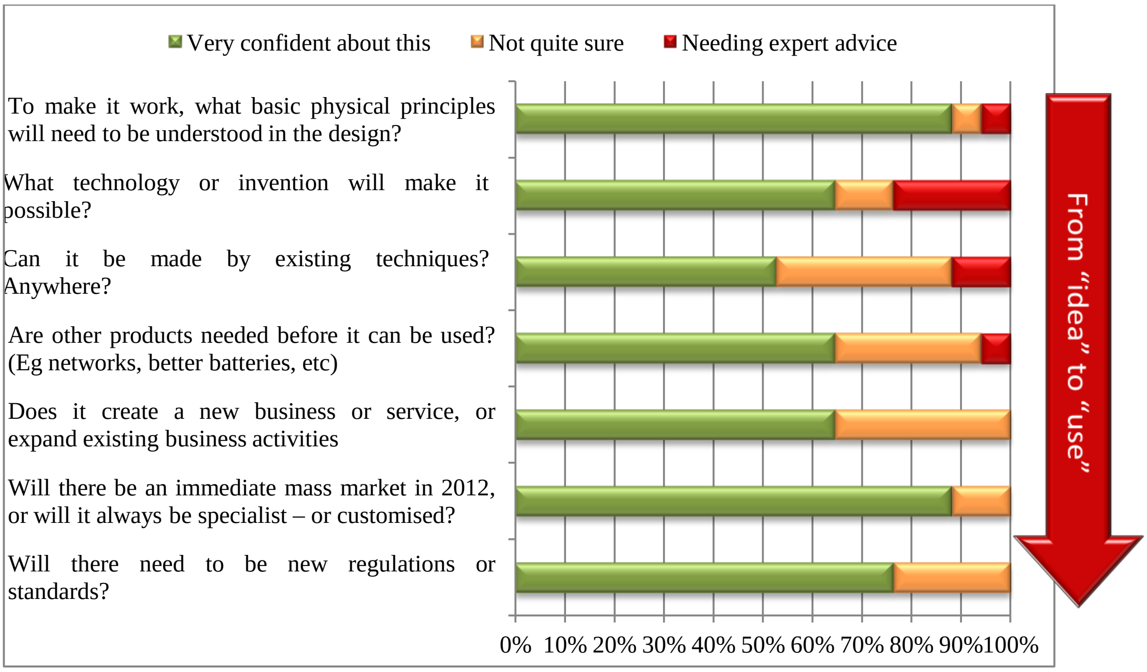


Figure 51: Confidence levels from "idea" to "use"

The graphical analysis shown above follows the sequence of the questionnaire, with its questions being couched in a progression from "idea" to "use". The percentages in the chart relate to the percentage of the 17 product ideas that scored each level of confidence.

- Overall, the need for expert advice was reported as only being required in the earliest stages of the design-manufacture-use progression
- The participants reported the largest need for expert advice in the selection of technology or the identifying of a required invention
- Regarding the availability of suitable manufacturing, the teams were "very confident" for only 50% of the cases of new products
- They did not report a need for expert advice in the close-to-market aspects of product introduction
- The highest overall confidence levels appeared to be that, perhaps optimistically, the great majority of ideas would gain market acceptance

4.2.5 Workshop observations

The following are the primary observations regarding the interaction of the workshop participants during the design activity:

- The unexpected (by the participants) use of human-form mannequins successfully promoted an atmosphere of “working with the unknown”

- The availability of physical resources – even in the form of pieces of paper and novelty toys – strongly encouraged debate and creativity. Teams clustered around the “props” table to form ideas

- Instead of the usual flipchart and “Post-It®” notes-on-a-wall workshop format, the mannequins stimulated the imagining and portrayal of 3D features, starting from only 2D flat printed cut-outs

- The level of engagement and concentration of the teams was quite amazing. Far beyond that expected in normal workshop surroundings

4.2.6 Reaction to workshop

The workshop activity and results were presented at several industry-facing events, inspiring very positive debate, with a number of companies seeing the value of convening a similar activity within their own workforce. The primary presentations were shown at:

- EPoSS Annual Forum, Paris, 26-28 September 2012

- Forum “Be Flexible”, Munich, 21/22 November 2012

- Mecatronic Connection 2012, Turin, 27/28 November 2012

Perhaps the most important reactions to the presentations were:

- A consensus that the work was original and valuable

- As a further step in a series of presentations to the “smart systems” community based on this research, the topic of design was finally adopted as a session topic at the community’s annual international conference Smart Systems Integration, held in Copenhagen 11-12 March 2015. The session, “Design of Smart Systems”, commenced at 13:30 on 11 March and was co-chaired by Dr. Christian Hedayat, Fraunhofer Institute for Electronic Nano Systems ENAS, and Dr. Reinhard Neul, Robert Bosch GmbH. The topic of this research was debated with fervour in the panel discussion.

4.3 Case study: 3D-MINTEGRATION research project

This study examined the discussions and interactions that took place during the course of the EPSRC-funded 3D-MINTEGRATION [1] Grand Challenge project, which was concerned with "The Design and Manufacture of 3D Miniaturised/Integrated Products."

From the outset, even though "Design & Simulation" was the subject of one of the project's five work packages, the aspect of "design" was restricted to focus upon assisting designers to chose and use the project's developing manufacturing processes, and to assess the benefits and risks of using these processes.

A series of loosely-defined demonstrator products was incorporated within the project plan for the purpose of testing the new manufacturing processes being developed but, unexpectedly, the manufacturing process developers found it difficult to conceive of demonstrator products, prompting the realisation that the actual conceiving of design had not been recognised as a necessary component of the Design & Simulation work package.

This situation was rectified by introducing conceptual design as a topic which, in addition to progressing the 3D-MINTEGRATION project, provided an excellent opportunity to study the implementation of conceptual design within an environment of unfamiliar product requirements based upon unfamiliar physical principles and unfamiliar technologies.

4.3.1 Effects of lack of experience

The 3D-MINTEGRATION research team was comprised primarily of relatively inexperienced young researchers, as is typical for such publicly-funded research projects. Accordingly, a criticism might be that basing observations upon this population might not accurately reflect the actualities of the product design community at large.

Liikkanen and Perttula provide a very useful paper [50] concerning problem solving amongst novice designers. The paper describes lack of domain knowledge as a significant barrier, and furthermore shows a reliance upon hierarchy by inexperienced designers, who are shown to be less equipped to tackle "big" (ie whole product or whole system) problems.

However, on p53, the notion emerges that the decomposition of problems into parts that populate an extended domain of experience (as introduced in 2.3.2 Poli, [24]) may have limited applicability in the design of radically new kind of products, because according to Liikkanen and Perttula "designers cannot possess an accurately fitting model for a novel artefact."

Consequently, it may be safe to take the competence of fresh minds to solve fresh problems as indicative of the behaviour of the general designer population when faced by the unfamiliar.

4.3.2 Communal idea generation

The 3D-MINTEGRATION project spanned 8 institutions and 20 companies. It comprised a community of some 70 researchers and industrialists. Moreover, the project was essentially multi-disciplinary, with a structured yet complex matrix of research topics and demonstrator activities.

Accordingly, face-to-face meetings and workshops were a vital element to co-ordinate thought, associate ideas and familiarise the community with the direction of the project, its individual threads, and the capabilities and knowledge of individual people.

Community and networking events involving design matters included the following:

- Cross-institution teams worked together on each of the project's five individual research themes and the three demonstrators
- Seven workshops related specifically to individual demonstrators
- Three annual "community" workshops, enhanced project familiarisation, further refined the demonstrators and generated new product ideas

A workshop challenge for a community event took this form:

- For a given market sector, conceive of a product or subsystem, built at the macro-scale but dependent upon micro-features
- What are the physical effects that it depends upon at the micro-scale?
- How are the micro-structures to be fashioned and integrated into a 3D macro structure?
- What are the challenges? In Design? In manufacture? In test?

Two examples of generated ideas were as follows:

4.3.2.1 Petri Cube

- Petri Cube was conceived as a low-cost robust micro-satellite designed to expose biological material to the space environment, to manipulate it and to analyse it

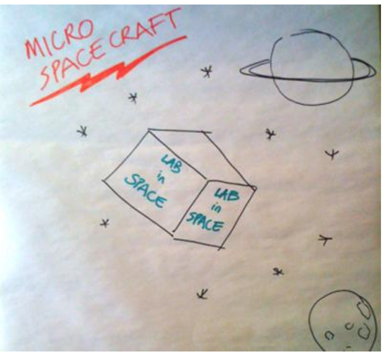


Figure 52: Petri Cube

- Integrated 3D minifluidic channels and reservoirs allow experiments upon very low masses of material

- High capillary forces should protect organisms from the high accelerations of launch, and yet allow manipulation in zero gravity

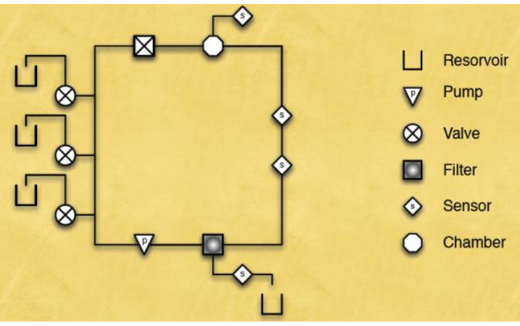


Figure 53: Petri Cube - workings

4.3.2.2 i-ball

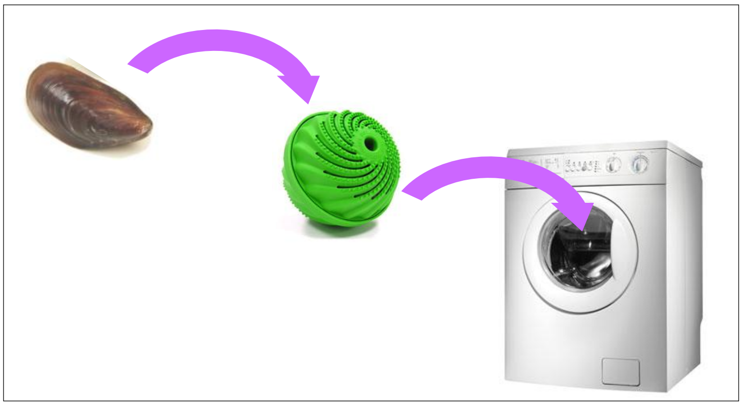
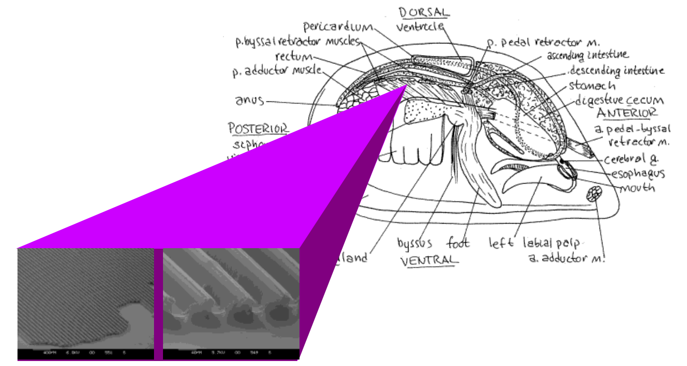


Figure 54: i-ball

- i-ball is a biologically-inspired washball, tossed in with the laundry to sample the wash water. Wireless connectivity will allow it to monitor and adjust detergent levels and wash cycle energy, and to minimize the use of rinse water. It will analyze for health-indicating trace materials from soiled clothing



Sealed microchannels with a width of 50um and a height of about 72um.

Figure 55: i-ball internal workings mimic the organs of a mollusc

Observations during the workshop recorded that in both the above examples:

- Idea generation was driven by diagrammatic representations and highly verbal interaction
- The generation of the product idea preceded the conceiving of how it might work
- The choice of the working principles of microchannel fluidics were strongly influenced by the front-running demonstrator product, which had been discussed beforehand
- The justification for the use of microfluidics (ie capillary and osmotic effects, not just small size) was teased out only through questioning following the presentations made by the design teams

4.3.3 Pitfalls of analogues and assumptions of authority

The discussion recorded in 4.3.1 “Effects of lack of experience” led to an assertion that “it may be safe to take the competence of fresh minds to solve fresh problems as indicative of the behaviour of the general designer population when faced by the unfamiliar.”

However, observations during the 3D-MINTEGRATION project did highlight some pitfalls arising from a lack of accumulated broad experience leading to flaws in the comprehension of effects at the micro-scale, as illustrated by the following four examples:

4.3.3.1 Micro CMM probe

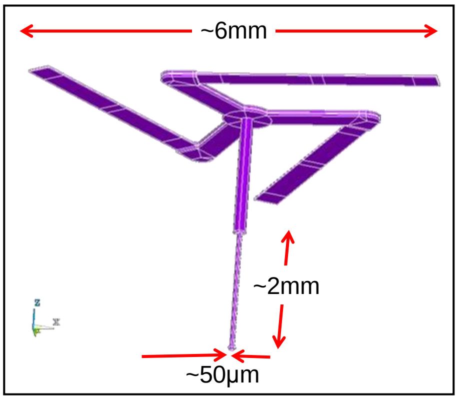


Figure 56: Micro CMM probe

The project designed and produced a small scale Co-ordinate Measuring Machine (CMM) stylus as a demonstrator for Ultra-Fast Laser machining.

In discussing the initial idea, the “fragility” of the assembly, with its flexible 3-legged piezo-electric spider actuator and 50 µm diameter probe, to be fashioned in tungsten, caused concern.

During the period of idea generation, in which many configurations were discussed, there was not sufficient time or resource for computer modelling. One “fixed” idea was that the very thin 2mm long probe would be very “wobbly” in practice, illustrated in the discussion by waving a “limp” arm, and also comparing the tiny probe with the leg of an ant.

Following computer simulation the “limp arm” gesture and “ant leg” analogue proved to be incorrect, but their prevalence and visual impact in the discussions caused delays in finalising the concept. A paper presenting prototyping and simulation of the Micro CMM probe was presented at the 2nd Electronics System-Integration Technology Conference in 2008 [72].

- Mentally scaling up the dimensions of the probe by a factor of 100 would have provided an image of a tungsten rod 5mm in diameter and 20cm long. Such a rod would not be considered “wobbly”.

- Designers unfamiliar with the field, and lacking broad experience face the danger of ingrained fixation of incorrect ideas, especially if they are depicted with strong imagery.

4.3.3.2 Microfluidic channels

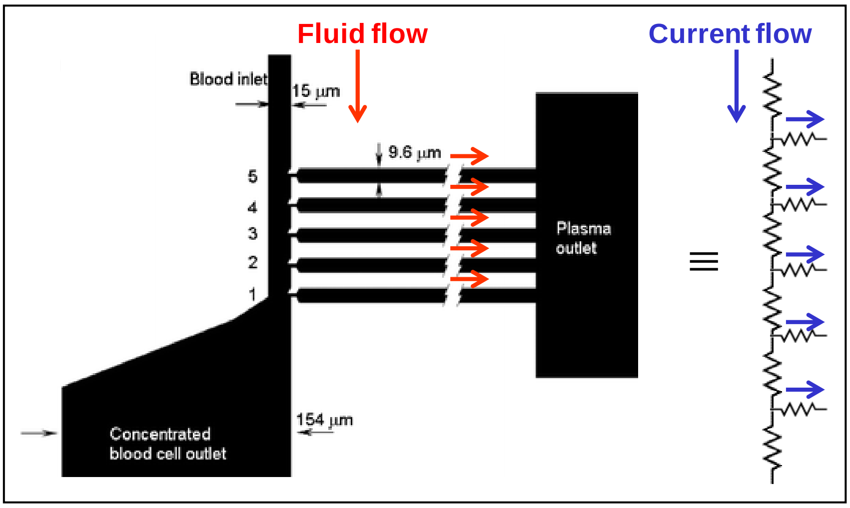


Figure 57: Fluid flow into branched channels

In considering fluid flow in a conceptual blood separation device it was tempting to use an equivalence between the pressure drop in a channel compared with voltage drop in a resistor (Figure 58).

At an overall level this electrical analogue may give insight into optimising the flow rate in the take-off (horizontal) channels as the remaining current diminishes in the vertical channel.

There is a danger in this as that it considers the flow rate of liquids to be uniform across the cross-section of the channel, as is the case for electrical current flow in resistors, at least at DC or low frequencies.

In reality, fluid flow at the boundary with containing walls is essentially zero, with a gradient of increasing flow as distance increases from this boundary layer.

This distinction becomes very important at the micro- scale, as the boundary behaviour can take place at a significant proportion of the channel width if the channel is narrow. This means that the fluid flow at the junctions is determined by behaviour at the boundary rather than that of the bulk flow.

In electrical terms this distinction becomes clear:

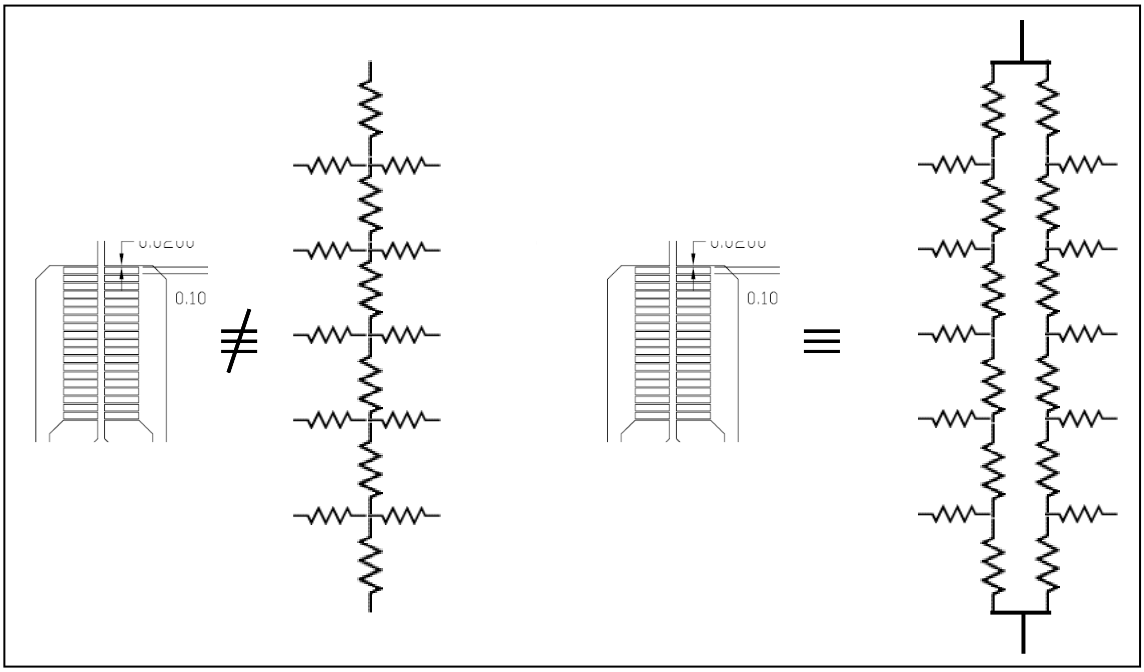


Figure 58: Recognition of boundary behaviour

The importance of this distinction became more significant when the branching concept was extended to “tap” fluid using branches arranged on each side of the main channel: the fluid interactions with the side channels occur independently on the left and right., ie, the leftmost stream in the vertical channel is not strongly influenced by the behaviour of the rightmost stream, because the flow is usually highly laminar in microchannels.

It was instructive in the project to realise that:

- Electrical current does not exhibit turbulence, vortices, etc.
- Circuit diagrams really only relate easily to 2D meshes.
- Designers unfamiliar with the micro- world were led astray by a too-simple analogue that only applies at the macro- scale.
- Electrical analogues failed to explain unexpected behaviour of experimental models. The application of Computational Fluid Dynamics (CFD) analysis resolved the issues.

4.3.3.3 The Fantastic Voyage

In considering the separation of red blood cells from whole blood, as in one of the 3D-MINTEGRATION demonstrators and also the subject of this thesis, visualisation of blood flow containing red blood cells is central. Within the project it became clear that the image of blood flow in the movie “The Fantastic Voyage” had become almost culturally engrained.

The Fantastic Voyage depicts the *purely fictional* insertion of a hugely shrunken submarine into the blood flow of a patient requiring specialist surgery.

Erroneously, the movie depicts a very sparse distribution of red blood cells, allowing the submarine to navigate freely.

It became evident in the 3D-MINTEGRATION project, with ideas such as “skimming” the plasma away from blood flow and similar notions, that the currency of discussion, at least among the majority of researchers, was based upon the idea that blood is typically free-flowing.

The reality of red blood cell distribution in whole blood is that the cells occupy some 45% of the fluid volume. As the cells are in disk form, this allows for the inclusion of just sufficient “lubricating” plasma to allow flow, thus maximising the oxygen-carrying capability of blood.

- Designers unfamiliar with the micro- world were led astray by a false community-wide “experience” stemming from a purely fictional motion picture, perpetuated by a plethora of internet images.

4.3.3.4 Red Blood Cell / Plasma Separation

The separation of red blood cells from whole blood, as in one of the 3D-MINTEGRATION demonstrators and also the subject of this thesis, has already been touched upon in the observations regarding visualisation above.

The requirement for such separation was initially put forward as a constituent part of a more extensive system, a Foetal Cell Monitor, allowing an applications-derived approach to the partitioning of design and manufacture.

It was agreed that across the whole system the number of processes and materials should be optimized as a minimum, and that if a fishbone (Ishikawa) diagram were to be drawn, it should be as simple as possible.

Furthermore, as one step towards clinical acceptance, the behaviour of all processes and materials, and the performance of the product itself, should be predictable from physical principles.

The complete system would analyse the DNA of foetal red blood cells found in maternal blood. The foetal cells would be separated as follows:

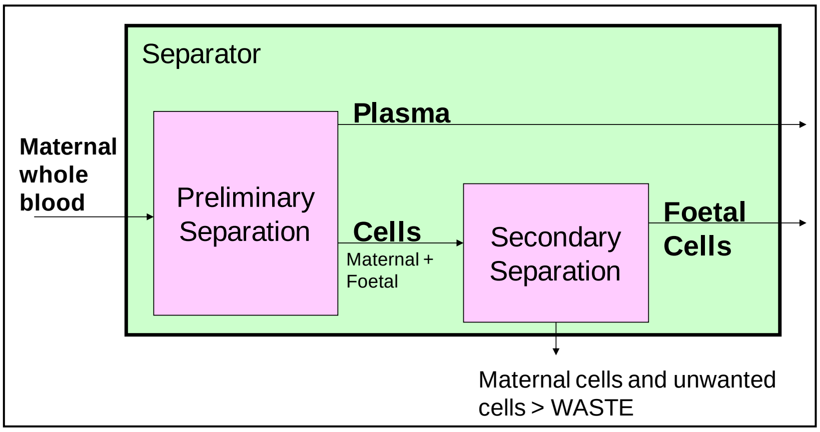


Figure 59: Separation of foetal cells from maternal blood

Practical experience regarding the design and construction of the preliminary separator was identified as being appropriate for considering and demonstrating the benefits of a 3D miniaturised/integrated approach.

The selection of the physical principle to be used in the preliminary separator was arrived at through a literature search, followed by the deriving of a short-list of candidate principles by eliminating those requiring complex geometries, the use of electrodes or the use of moving parts.

A very useful compendium of separation principles was derived from the work supporting the demonstrator and developed further as a Critical Review “Micro-scale blood plasma separation: from acoustophoresis to egg-beaters” [56] .

The purely fluidic principle adopted by the project concerned the behaviour of a particle-bearing fluid at a junction between channels, which has gained currency as the “Zweifach-Fung” effect.

In their publication “Major advances via miniaturisation” Roche (F. Hoffmann-La Roche AG) usefully describe the identification of the effect as stemming from the1968 observation by Svanes and Zweifach [73] that at branching points in very fine blood vessels (capillaries), blood cells tend to flow into the branch with less resistance to flow and a faster flow rate, and that if the flow rate in the two branches differs by a factor of at least 2.5, virtually all the red blood cells enter the vessel with the greater flow rate.

The Roche publication goes on to report that five years later [74] Fung reported that where a blood capillary branches into two smaller vessels of equal diameter and length, virtually all the red blood cells flow initially into only one of the two branches.

Fuelled by the above, the 3D-MINTEGRATION project, in common with Roche and others, engaged in investigating the design and experimental verification of blood separation systems based upon the Zweifach-Fung effect. In particular, a starting point followed the work of Yang, Undar and Zahn [52] from which the following diagrams became a focus of study:

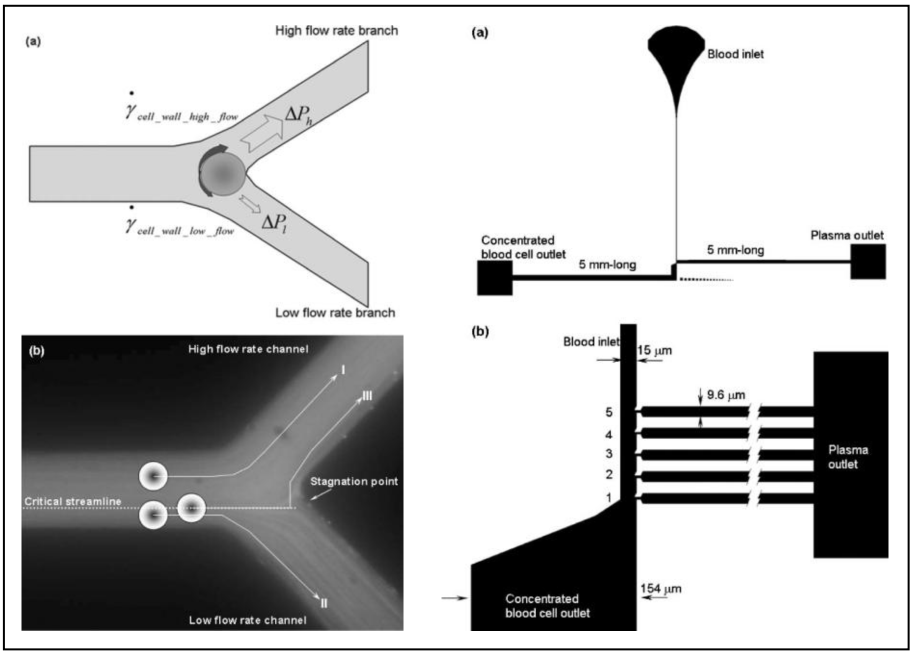


Figure 60: Diagrams from the work of Yang, Undar and Zahn
(Yang et al. [52])

The ubiquity of citations for the Zweifach-Fung effect, plus the endorsement of interest by the major industrialist Roche, conspired to give an authority to the veracity of underlying principles, including furthermore an assumption that a Y-shaped bifurcation could be distorted into T-shaped bifurcations.

In reality, experimental models did not confirm these and other underlying assumptions, the discrepancy being reported variously by the Critical Review [56] already mentioned, which was completed after the 3D-MINTEGRATION experimental trials, and also by an elegant experiment reported by Doyeux et al [75] which casts doubt on the exact nature of the separation process.

As a result of the perceived authority around the original work citing the Zweifach-Fung effect, [73], [74] and [52] a momentum developed in the 3D-MINTEGRATION project to persevere to develop blood cell separation based upon T-junction geometries, despite experimental results failing to produce the separation performance that would have been expected had the underlying physical effects been as assumed.

This matter will be explored further in Chapter 5 “2D to 3D transformation: design study”. However, observations during the 3D-MINTEGRATION project did highlight:

- Designers unfamiliar with the field face the danger of being led astray by newly-developed principles, which, although couched with authority, may require more rigorous proof.

- In developing products to use the results of front-line research, product prototyping may by default become the test bed to refine experimental results.

4.3.4 Formalising a design approach within 3D-MINTEGRATION

The design theme of the 3D-MINTEGRATION project focused upon:

- How can design work better across disciplines including electronics, optics, fluidics and mechanics?

- How can design, modelling and simulation proceed interactively with manufacturing processes that are developing rapidly, or devised solely for the solution of a particular product problem?

- How can these processes assess and mitigate risk, in manufacture and over product life, in this multi-dimensional sea of process and product alternatives?

However, the team assigned to the design work package was heavily canted towards Modelling & Simulation, which was the main intention of the original project proposal.

As the project progressed it became evident that idea generation and the actual conception of products would be of huge relevance if the capabilities of new combined product integration/miniaturisation techniques were to be fully exploited.

Hsu and Liu in their Editorial article for Computer-Aided Design [76] describe how “Decisions made during conceptual design have significant influence on the cost, performance, reliability, safety and environmental impact of a product. It has been estimated that design decisions account for more than 75% of final product costs”. Selecting the most appropriate ideas and approaches is therefore of enormous importance.

As the 3D-MINTEGRATION "workforce" of some 70 researchers was not formally trained in the generation and progression of product design, it was necessary to draw together, develop and channel the talent available within the project.

Accordingly, an activity to focus effort and to provide an instructive depositary for design-to-manufacture knowledge related to the project needs, was commenced in the form of developing a computer-based "Design Assistant" to:

- Collate and build upon methodologies for design stages and associated activities
- Collect the design procedures researched in the project
- Underline the concept of "iterative" design activities and tools
- Integrate third-party software tools for modelling and analysis

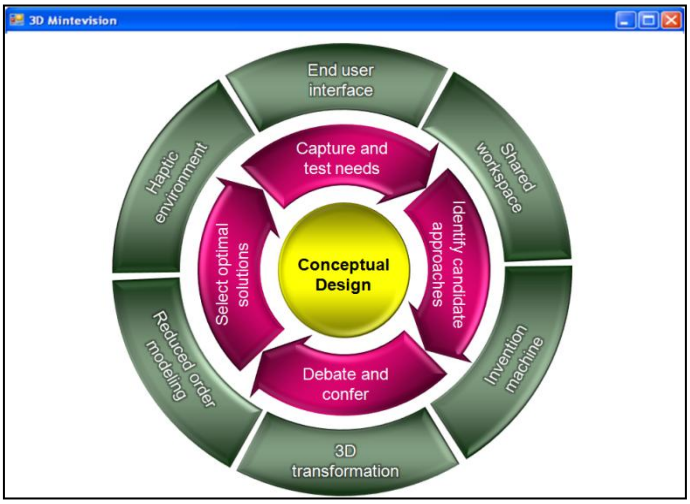


Figure 61: 3D-MINTEVISION, design interface

Conceptual design was presented as an iterative sequence of processes (the inner ring of the screen-shot, left).

The outer ring denoted appropriate activities and resources for progressing conceptual design, each segment being linked to explanatory texts

3D Processing, based upon project developments, was presented as an iterative sequence of requirements (the inner ring of the screen-shot, right).

The outer ring denoted appropriate activities and resources to support manufacturing, each segment being linked to explanatory texts.

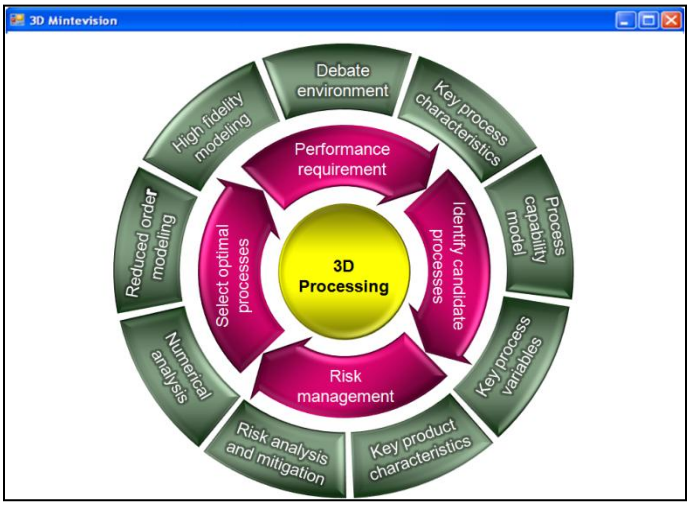


Figure 62: 3D-MINTEVISION, process interface

- Although appearing highly simplified, the system's twin entry points of Conceptual Design and 3D Processing not only provided gateways to a wealth of information, they also provided a degree of instruction to users, and a very effective "filing system" for concepts refined during the project.

A paper describing the simulation of the Micro CMM probe and co-authored by the writer was presented at EuroSimE 2010 [77]. The paper mentions the Design Assistant in context.

4.3.5 The introduction of 2D to 3D transformations

The genesis for the concept that theoretical 2-dimensional diagrams of function may usefully be transformed into 3-dimensional working structures using procedures allied to those used by graphic designers occurred during a 3D-MINTEGRATION project meeting concerned with the preliminary Red Blood Cell / Plasma separator depicted in Figure 59 within 4.3.3 above.

In discussion, the idea of simply creating channels micro-engineered into a flat substrate to replicate the "T-junction" geometries shown in Figure 60 would result in a planar device which, although because of its (shallow) depth might be strictly described as "3-dimensional", would not demonstrate the benefits of a true wholly volumetric construction might deliver.

Debating this point became problematical, words were not properly capable of describing 3D concepts, whilst verbal instructions to draw a diagram on a whiteboard failed. At this moment a pirouette performed by the session chairman Professor W O'Neill, University of Cambridge, interpreted the verbal discussion and marked the starting point for the concept that theoretical 2 dimensional diagrams of function may be transformed into 3 dimensional working structures.

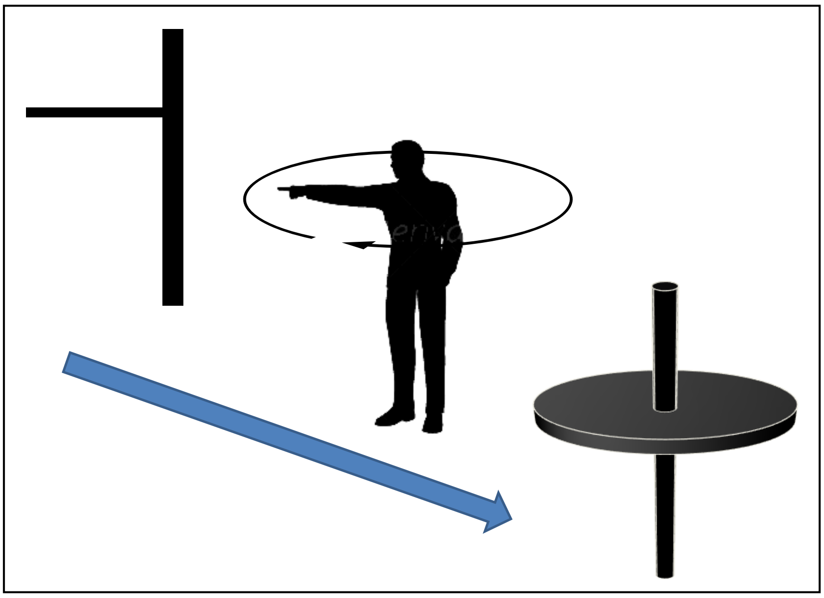


Figure 63: Pirouette demonstrates transform from 2D diagram to 3D object

The above figure records on the left the flat functional diagram of a T-junction between fluid channels being transformed by rotation into a tube intersecting with a hollow disk to create a truly volumetric approach to Red Blood Cell / Plasma separation.

4.4 Collation of Chapter 4 findings

This chapter records the “interpersonal” aspects of idea exchange in the design arena, focusing particularly upon the issues of conversing about the intangible when product designers need to use principles which are beyond their experience.

Through interviews, a survey, a workshop questionnaire, and observations of workshop research project activity, evidence was gathered that supports the following:

4.4.1 Conversing about the intangible

Regarding the issues of conversing about the intangible when product designers need to use physical principles which are beyond everyday human experience:

- The front-running mechanisms to facilitate the choice of physical principles reported were (1) discussions with colleagues, (2) scientific journals, and (3) personal experience. No respondents declared that they would “never” use these avenues.

- A surprising ~15% of respondents reported that they “never” use the internet in the selection process. The same figure applied for books and patents.

- Nevertheless, in terms of sources “always” used, the internet ranked second only to discussion with colleagues.

- The strong need for discussion with colleagues underlines the importance of the question “How can designers work with objects which are beyond direct human experience, and how can collective discussion take place within teams of designers, and between these teams and other teams responsible for product manufacture?” expressed at the outset of this thesis in 1.1.1 “The problem of unobservable devices”.

- In developing products to use the results of front-line research, product prototyping may by default become the test bed to refine experimental results.

4.4.2 The use of diagrams

- Despite perceived progress in co-design and virtual reality, this research upholds the value of building upon the use of diagrams, along with computer simulation.

- "Drawing diagrams" was reported as the most prevalent aid to discussion. No respondents declared that they would "never" use this mechanism.

- Computer simulation (which almost inevitably starts with diagrammatic representations) was cited as the second most frequent mechanism used to support discussion, ahead of physical model making, and contrasting surprisingly with virtual reality, shunned by nearly half of the respondents.

- In the 3D-MINTEGRATION research project, idea generation was driven by diagrammatic representations and highly verbal interaction. The generation of product ideas preceded the conceiving of how they might work.

- The survey showed the use of diagrams as underpinning the progressing of designs where elements lay outside everyday experience at the macro scale. This supports the targeting of the thrust of this thesis – of applying graphical procedures to theoretical diagrams in order to transform them into scalable 3 dimensional devices – as having strong potential to alleviate the difficulties of conceiving of functional structures that, when built, will be too small to experience directly.

4.4.3 Dependence upon expert intermediaries

- Workshop participants reported the greatest need for expert advice in the selection of technology or the identifying of a required invention. Overall, expert advice was reported as only being required in the early stages of the design.

  They did not report a need for expert advice in the close-to-market aspects of product introduction, indeed the highest overall confidence levels appeared to be that, perhaps optimistically, the great majority of ideas would gain market acceptance.

- Designers unfamiliar with the field, and lacking broad experience, are susceptible to become fixated with incorrect ideas, especially if they are depicted with strong imagery. They also risk being led astray by false community-wide "experience" stemming from purely fictional projections of science in the media, and furthermore the reporting of early stage scientific results which may mistakenly be perceived to be authoritative.

  Designers unfamiliar with the micro- world were led astray by a too-simple analogue that only applies at the macro- scale. Electrical analogues failed to explain unexpected behaviour of experimental models. The application of Computational Fluid Dynamics (CFD) analysis resolved the issues.

- A simplified Design Assistant system can not only provided gateways to a wealth of information, but also provide a degree of instruction to users inexperienced in the field.

- Project leadership and "culture" are strong enablers of collaboration, along with a hope for progress in co-design capability.

- The use of an expert Project Manager to progress designs which embed microstructures directly into the macro fabric of a 3-dimensional product was cited as prevalent, contrasting strongly with the employing of authoritarian architects or IT-based co-design systems, whose use was rejected by over 25% of respondents.

- Some two-thirds of survey respondents reported that they "often or always" use expert Project Managers, which suggests that inter-personal collaboration and the role of Expert Intermediaries are important and worthy of examination, as embarked upon within the workshop activities.

4.4.4 Format of design related workshops

- The unexpected use of human-form mannequins successfully promoted an atmosphere of "working with the unknown".

- The availability of physical resources – even in the form of pieces of paper and novelty toys – strongly encouraged debate and creativity.

- Instead of the usual flipchart and "Post-It®" notes-on-a-wall workshop format, the mannequins stimulated the imagining and portrayal of 3D features, transformed from 2D flat printed cut-outs. The level of engagement and concentration of the teams was quite amazing. Far beyond that expected in normal workshop surroundings.

4.4.5 Novelty and acceptance

- Reactions to and participation in the research in terms of the pilot interviews, the survey, the hands-on workshop and the case study showed that the notion of integrating micro-enabled functionality directly into macro products is seen to be novel, yet worthy of development.

- As a result of presentations to the "smart systems" community based on this research, the topic of design was finally adopted as a session topic both at the community's annual international conference, and at the Annual Forum of the EPoSS European Technology Platform on Smart Systems.

Chapter 5 2D to 3D transform: In-practice design study

This chapter records research to investigate the concept that theoretical 2-dimensional diagrams may be transformed into functional 3-dimensional working structures, the study following the outlines put forward in Topic areas 5 and 6:

- Examining, testing and assessing the benefits of the concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures using procedures allied to those used by graphic designers to create solid objects by manipulating 2-dimensional prototypes.

- Through the example of a novel Red Blood Cell / Plasma Separation Device, devising and performing a hands-on simulation and constructional trial to gain insight into the concept-to-embodiment process when including a geometric transformation step.

As reported in this chapter, the above matters were approached through:

- Generating a product concept based upon the needs and traditional approaches researched in sections 2.7.1 and 2.7.2 of the Literature Review.

- Selecting and refining a working principle from those found in section 2.7.3 of the Literature Review.

- Generating and developing a conceptual design based upon a geometric transformation of the working principle.

- Performing computer simulations of aspects of the potential embodiment.

- Performing a practical trial to test the veracity of the concept and to seed a proposal for embodiment.

The above were not performed in isolation, as aspects of the choice of working principle, conceptual design, transformation, simulation and embodiment interacted through iteration.

Addressing the observations summarised in section 2.8.3 of the literature review, the activities of Chapter 5 responded to:

- The need for, and the approaches to, Red Blood Cell / Plasma Separation.

- The caveats around the abstractions of functional diagrams used in both the simulation and construction activities.

In respect of the transformation concept, outlined below, the activities of Chapter 5 addressed:

- How the use of the method, using its currency of functional diagrams, may overcome some of the problems of describing and discussing intangible objects in 3 dimensions.

- How the geometric transformation process can lead to the design of functional structures with improved performance that would not readily be arrived at intuitively.

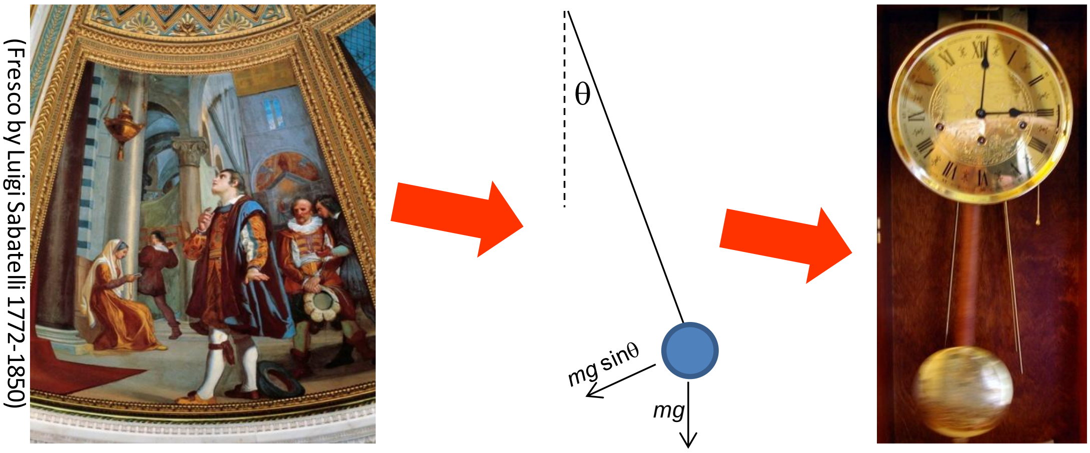

(Fresco by Luigi Sabatelli 1772-1850)

Figure 64: Translation of embodiment via a generalised functional diagram

The stylised *functional diagram* is introduced in section 2.5.2.4 on page 53. Figure 64, above, illustrates the way that a scientific observation, for example Galileo Galilei noticing the behaviour of a swinging lantern in Pisa cathedral, can be condensed to a generalised functional diagram which subsequently may be transformed geometrically to a particular instance of a real product, in this case a clock pendulum.

The geometric transformation used in this example, in addition to scaling, is that of extrusion in a direction normal to the plane of the functional diagram, as illustrated in Figure 65.

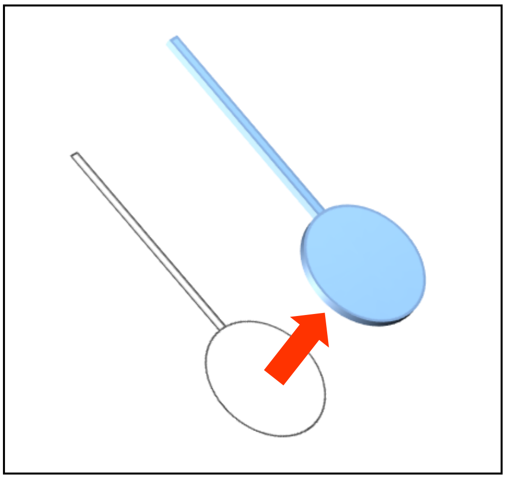


Figure 65: Extrusion normal to the plane of a functional diagram

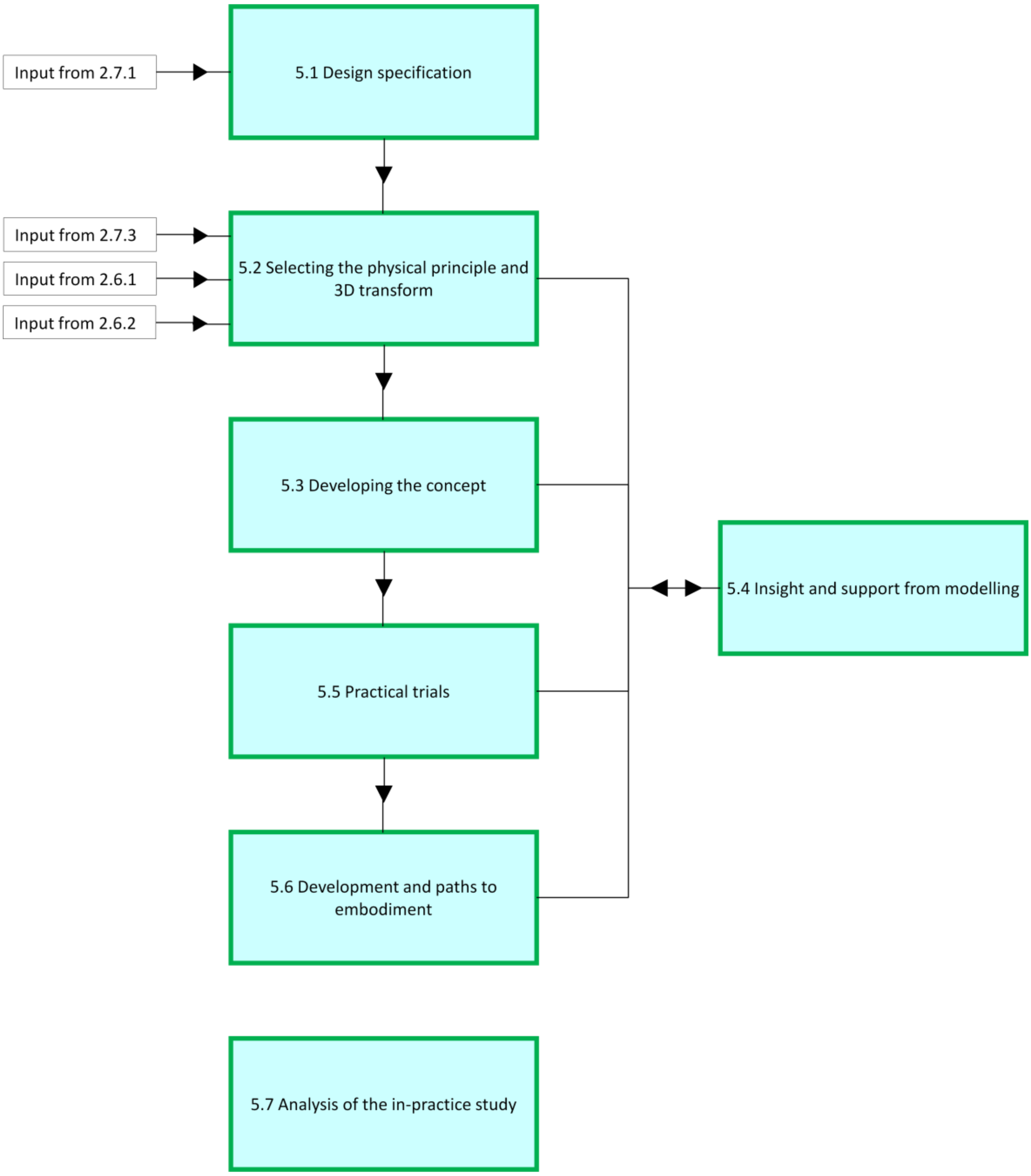


Figure 66: Scope of design study

The design study as depicted above differed from normal product design practice in that:

- Aspects of the design and the design process were developed specifically for research purposes.
- Although product cost and manufacturing ease were taken into account, no specific production plans or investment/amortisation costs were considered.

No study or representation has been made, or implied in any way, as to the safety, standards or legislative matters that might apply to the use of the design or derivative products.

5.1 Design specification

5.1.1 Requirements list

The framework of design put forward by Pahl, Beitz, Feldhusen and Grote, and adopted for this research, introduces on p144 of [8] a process which results in a requirements list. According to the authors this entails answering the questions:

- What are the objectives that the intended solution is expected to satisfy?
- What properties must it have?
- What properties must it not have?

From the options studied in 2.7.1, small volume batch separation was selected for the design study. 2.7.1.1 notes that small volume batch separation is a common clinical procedure, typically following the routine extraction of a blood sample (typically 1 to 5 mL) by syringe for subsequent testing. Whilst some tests can be performed upon whole blood, some sensitive tests... ...would be upset by the presence of red blood cells. Conversely, some tests... ...require the selection of red blood cells alone, free of the blood plasma and other constituents.

2.7.2.2 adds that small volume separation typically commences through the collection of batch samples of the order of 3~10 mL by syringe or a similar device, each sample being obtained in a matter of seconds.

Brunel's Katy Jenkins, a contributor to this research, outlined the needs in her 2008 "Blood Separation Syringe: DM3306 Major Project Report". Categorised extracts are as follows:

5.1.1.1 Objectives

"To design a product that allows blood separation to be undertaken on a sample of blood at the point-of-care. It is to be used to facilitate immediate diagnosis of disease.

This product is aimed primarily at medical professionals such as General Practitioners who take blood from patients. It would also be used in situations where a centrifuge is not necessarily available, such as for self-testing by patients, in a surgery, or in hospital".

5.1.1.2 Required properties

"It has been found that current systems for blood separation are time consuming and costly.

The system should separate blood quickly and continuously."

5.1.1.3 Properties to avoid

"It must not need detailed instructions or be difficult to use

It is to be designed for single use. It must therefore not be expensive to produce."

5.1.2 Essential problems

Page 161 of [8] concerns the identification of those elements from the requirements list which are the crux of the problem to resolve by design. This is achieved by a process of "abstraction", reducing complexity to a generalised abstract level.

At the generalised level, devoid of fixation upon product-specific ideas, it is easier to see alternative parallel approaches, possibly even derived from other products which share the same issues when seen at the most generalised level.

Note that functional diagrams represent abstraction to a fundamental level (as illustrated in Figure 64).

For this design study, the essential problems to overcome were determined as:

- Blood sample collection using a familiar method, sample size and time to collect
- A Red Blood Cell / Plasma Separation as a continuation of the collection method, with a volume and rate compatible with that of the collection method
- A connection between the collection and separation processes
- Sources of energy and the control of parameters

These factors are collated in the block diagram shown in Figure 67.

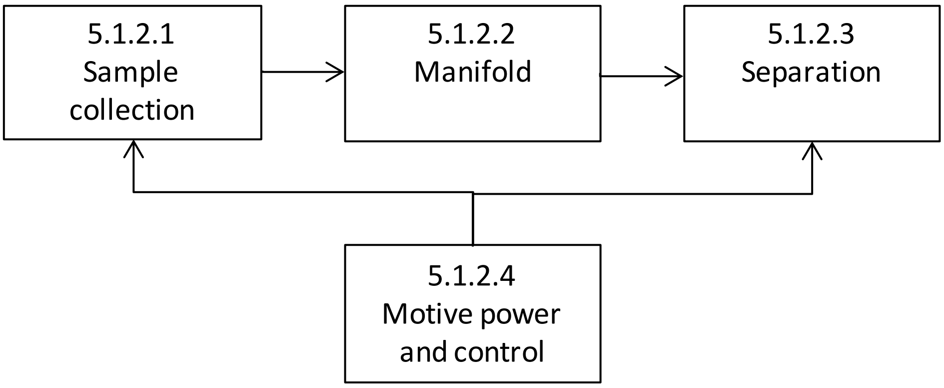


Figure 67: Essential problems

5.2 Selecting the physical principle and 3D transform

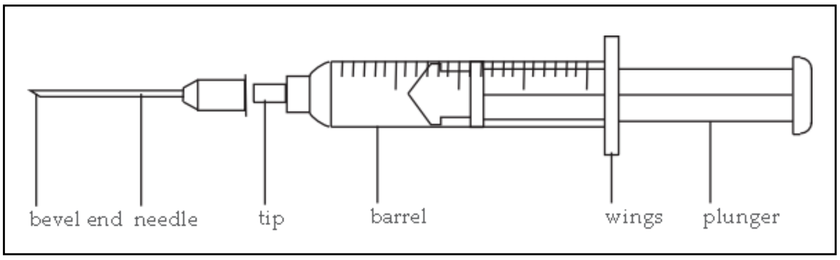


Figure 68: Structure of a syringe

(From Katy Jenkins “Blood Separation Syringe: DM3306 Major Project Report”)

The structure of a standard syringe displays the traditional approach to the four essential problems outlined in the block diagram of Figure 67 as follows:

5.1.2.1 Sample collection:	Needle
5.1.2.2 Manifold:	Tip to barrel expansion
5.1.2.3 Separation:	None
5.1.2.4 Power and control:	Wings and plunger

The above four essential problems, will be consistently referred to during the design study.

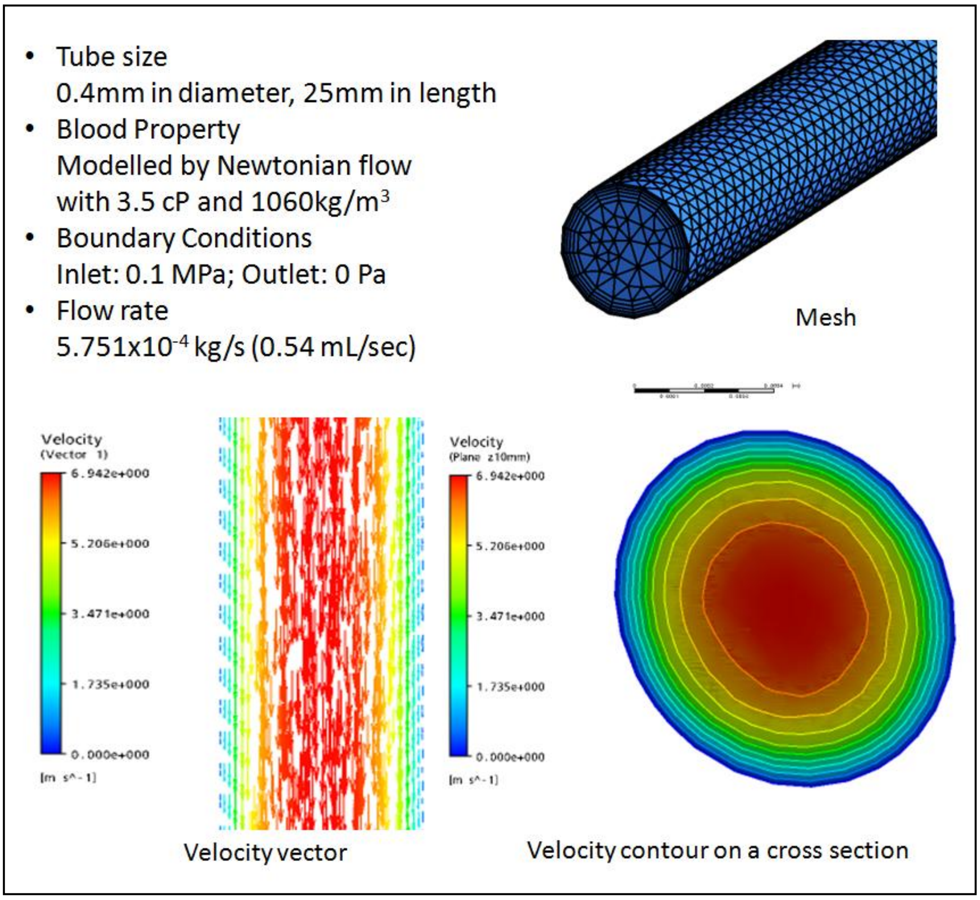
5.2.1 Sample collection

The 5.1.1.1 Objective “To design a product that allows blood separation to be undertaken on a sample of blood at the point-of-care” and the 5.1.1.3 Properties to avoid “It must not need detailed instructions or be difficult to use” led to the idea that sample collection should be through the tried-and-tested and familiar needle.

Computer modelling of a typical syringe needle, as shown in Figure 69, provided useful insight into the parameters of sample collection by this method.

The sampling rate depends upon:

- Geometry: Cylindrical, with internal tube diameter 0.4 mm and effective length 25mm
- Pressure differential: 0.1MPa, ie, atmospheric at the inlet (patient), vacuum at the outlet
- Fluid parameters: Newtonian flow behaviour, viscosity 3.5cP, density 1065 kg/m^3



- Tube size
  0.4mm in diameter, 25mm in length
- Blood Property
  Modelled by Newtonian flow
  with 3.5 cP and 1060kg/m^3
- Boundary Conditions
  Inlet: 0.1 MPa; Outlet: 0 Pa
- Flow rate
  5.751x10^{-4} kg/s (0.54 mL/sec)

Figure 69: Computer modelling of typical syringe needle

The inside diameter of needles used for sampling blood ranges from 0.34 mm to 0.51 mm, suggesting cross section areas between 0.09 and 0.2 mm^2. Choosing the mid point of these areas results in a typical inside diameter of 0.4 mm.

With the parameters as selected, the flow conditions at the outlet derived by the modelling are:

- A flow rate of 0.54 mL/sec (which corresponds well with the practical experience of providing 5 mL samples with extraction times of the order of 10 seconds)

- A maximum linear flow velocity of the order of 7 m/sec, contoured radially across the tube, with, based upon the cross section area and volumetric flow rate, an average linear flow velocity of approximately 4.3 m/sec (about 10 mph, cycling pace)

The above results are fundamental data regarding the fluid flow that the separation process should handle in order to satisfy the essential problem of 5.1.2.3 “Separation as a continuation of the collection method, with a volume and rate equal to that of the collection method”.

It is as well to mention here the caveats and limitations of modelling blood flow, as noted by Xue et al. in [4] *and as discussed in section 5.4.1 of this thesis.*

5.2.2 Power and control

Although the essential problem 5.1.2.4 “Power and control” is listed last under Figure 68, its resolution is required early as it will affect the solution of the remaining problems of the manifold and separator.

In the operation of a manual syringe the motive power is provided by applying tension to the plunger by fingers whilst anchoring the body through grasping the wings. The flow rate of the blood is very largely determined by the “resistance” of the needle, as modelled in Figure 69, unless there is a constriction in the patient’s blood vessel.

Similar conditions apply with the use of an evacuated tube such as a Vacutainer®, with the advantage of avoiding the skill requirement of maintaining a vacuum by pulling a plunger.

Relying upon the application of a vacuum and the resistance of the needle to regulate the flow of sampled blood is a reasonable concept, as long as the flow resistance of the manifold and separator together remain sensibly constant and, if varying, do not represent a significant extra resistance to flow.

Referring to Figure 70, in electrical terms, with a fixed pressure differential the flow rate needs to be dominated by the flow resistance of the needle, ie: $R_{Needle} >> (R_{Manifold} + R_{Separator})$

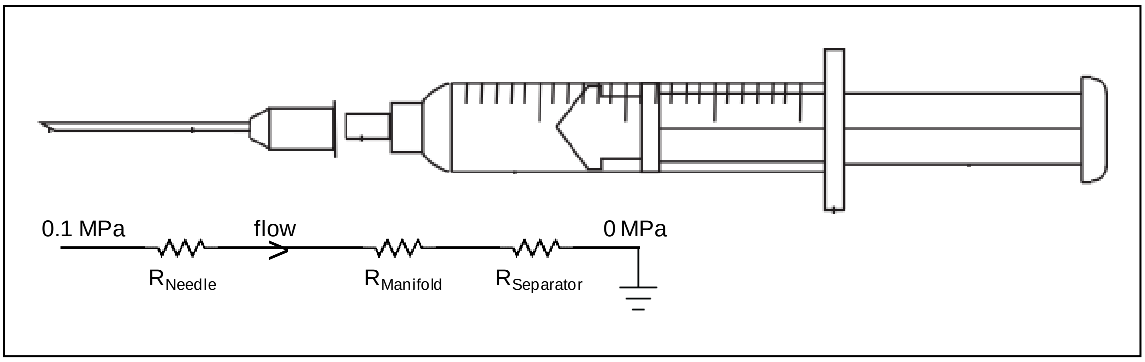


Figure 70: Electrical analogue of Needle→Manifold→Separator

It is important to appreciate that the resistors depicted in this particular electrical analogue represent resistance to total volumetric flow, and have no bearing upon the variation of flow velocity across the cross-sections of the components. A typical velocity contour is shown in Figure 69, and a relevant example of the misunderstanding of an electrical analogue as observed in the section 4.3 Case study is discussed around Figure 58 on page 113.

5.2.3 Manifold and separator

The sample collection method arrived at in 5.2.1 and the power and control solution of 5.2.2 bracket the design choices for both the manifold and the separator.

- A flow rate of 0.54 mL/sec
- The flow arriving from a 0.4 mm diameter tube, with an average linear flow velocity of approximately 4.3 m/sec
- A need to keep the pressure differential across the manifold and separator combination << 0.1 MPa

The manifold and separator need to be discussed together, as their configurations may be inter-dependent. Moreover, they may only work effectively over a relatively narrow range of flow rates, hence the need to ensure that the flow rate is determined primarily by the sample collection needle and the applied vacuum of the control method.

5.2.3.1 Choice of separator principle

Figure 21 on page 63 provides examples of micro- scale cell separation techniques. Satisfying the essential problems

- “Blood sample collection using a familiar method, sample size and time to collect”
- “Plasma Separation as a continuation of the collection method, with a volume and rate equal to that of the collection method”

meant avoiding *filtration* methods due to their rather low flow rate capacity (stated in the figure as 0.02 μL/min to 50 μL/min) and a potential for clogging, and avoiding *active* and *alternative* extraction methods due also to their low - or “no” - flow rate capacity, and their added complexity.

The *cell deviation mechanisms* show promise, as flow rates from 0.16 μL/min to 8 mL/min are cited, still way below the 0.54 mL/sec requirement for the current design, but orders of magnitude higher than the other mechanisms in Figure 21, and so providing a promising starting point.

2.7.3.2 introduces the fundamentals of junction-based *cell deviation* separators using pure viscous forces. These operate using channel dimensions of typically < 50 μm so that the formation of a cell-free layer as observed by Fahraeus [61] is encouraged. A helpful diagram by Tripathi et al. [60] is included in 2.7.3.2 illustrating the extraction of liquid from the cell-free layer through a side channel, reproduced for convenience below:

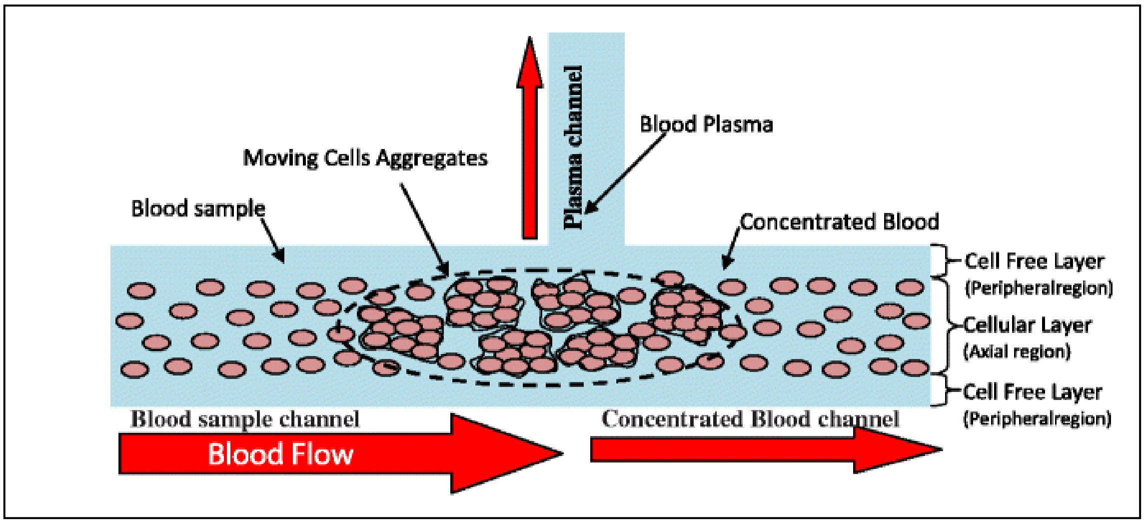


Figure 24: Plasma extraction via a side channel and aggregate formation
(Adapted from Tripathi et al. [60])

Figure 24 shows the cell-free layer occurring at the channel sides, and also an aggregation effect, as also mentioned by Fahraeus in 1929. For completeness, one should also appreciate other mechanisms potentially at play: an element of “transverse filtering” through the narrow side channel impeding the flow of larger particles, and possibly a form of “skimming”, seemingly undefined rigorously but held as a common everyday experience.

Undoubtedly while testing particular theories the experiments of the “microfluidic separator” authors cited variously in this thesis are also perturbed by a matrix of possibly lower order effects. A practical design will take into account the primary effect, but also be cognisant of second order effects that may come into play when realistic operating and manufacturing parameters are applied.

Notwithstanding the above, a rule of thumb for the likely throughput of a side channel separator can be arrived at by noting that in the work of Kersaudy-Kerhoas et al. [63] that “A high flow rate ultimately... ...increases the risk of damaging the cells through greater shear rate forces”. Rupturing the red blood cells could release agents and fragments that are detrimental to sensitive medical tests.

[63] records experiments applying flow rates of 2, 5 and 10 mL/hr through a channel 20 µm deep and with minimum width 40 µm. A flow cytometric study showed no cell damage, although the paper did not record which of the 2, 5 or 10 mL/hr flow rates were used.

Choosing the middle value, 5 mL/hr one can extrapolate that ~1,000 such devices would need to be harnessed in parallel to achieve the 0.54 mL/sec throughput required to match the inflow from the typical syringe needle modelled in Figure 69, as dictated by the essential problem:

"Plasma Separation as a continuation of the collection method, with a volume and rate equal to that of the collection method".

Choosing the lower value, 2 mL/hr, would result in a requirement to parallel ~400 such junctions.

In 2.7.3.3 "Improvements upon junction-based separators" Kersaudy-Kerhoas et al. [63] and Rodriguez-Villarreal et al. [64], [65] both similarly describe the formation of a cell-free zone following a modified geometry. This is further explored in section 5.4 commencing on page 144 below, concerning "Insight and support from modelling".

For the purposes of this section and the following section 5.3, "Developing the concept", the simple side channel geometry will be the chosen separator principle, much as in Figure 60

5.2.3.2 Manifold

Following the choice of separator principle the requirements of the manifold to connect the collection needle to the separator system become clear.

Figure 71 illustrates a collection needle branching to just 10 separator modules, each featuring 5 junctions (which do not materially affect the flow rate but should each extract a further proportion of plasma).

To reach the required total flow rate of 0.54 mL/sec, some 1,000 separators would be needed, requiring a 10x10x10 matrix (Figure 72), along with a complex manifold of tubes to connect them to the needle. This would entail enormous manufacturing costs and undoubtedly display poor reliability due to clogging through flow disruptions at the many junctions.

Evidently a better approach is required.

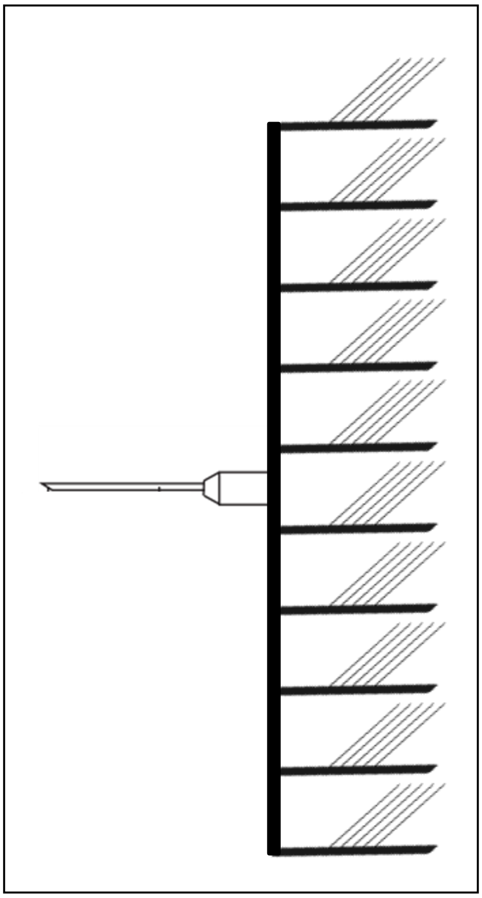


Figure 71: Simple manifold

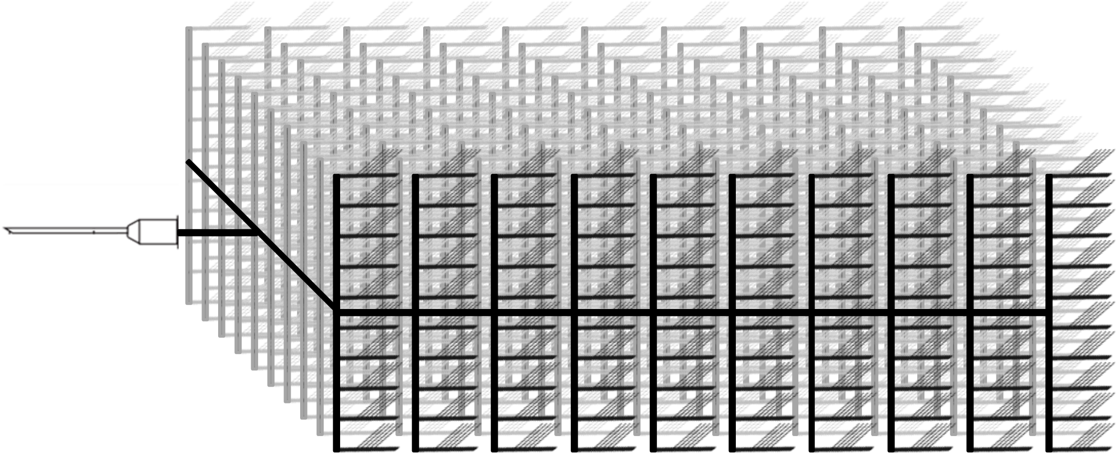


Figure 72: Notional 10x10x10 matrix of planar separators

5.2.3.3 Transformation to 3D

The cuboid arrangement suggested in Figure 72, although filling 3D space, is only a ranked disposition of planar mechanisms. For simplification it also avoids the question of how all the 5,000 plasma side channel outlets and all the 1,000 concentrated blood outlets are gathered together (1) so that the motive vacuum can be applied and (2) so that the separated materials can be collected.

Section 2.6.1 on page 55 describes some of the procedures adopted by graphic designers to create 3-dimensional objects from prototype cross-sections, whilst section 2.6.2, commencing on page 56, introduces the idea of applying those transforms to 2D functional diagrams to become the basis of 3D functional objects.

The current section considers the application of the processes of 2.6.1 and 2.6.2 through three illustrative cases:

Case A: Extrusion

Figure 18 from 2.6.2 and reproduced here for convenience is based upon a configuration by Jaggi et al. [53]. This approach, as illustrated in Figure 18 “B”, extrudes the functional diagram of Figure 18 “A” in the Z direction such that the critical dimensions that maintain laminar flow are retained, but rather between parallel plates rather than channel walls. In this case an implementation to secure a 1,000-fold increase in flow rate would entail a Z dimension of around 5 cm.

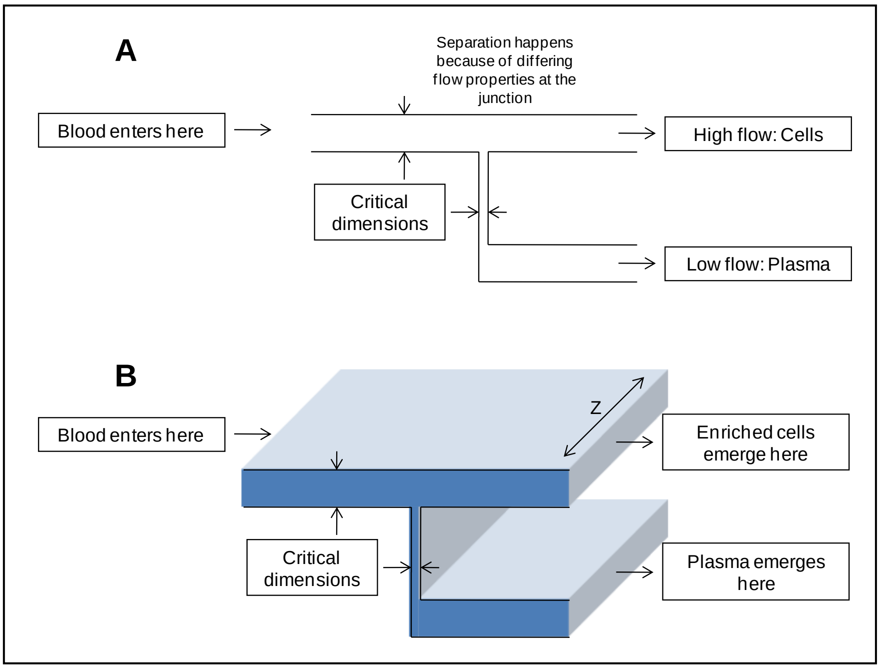


Figure 18: (A) Functional diagram (B) Extruded 3D functional object

Figure 73 sketches in, notionally, the addition of the collection needle and a manifold to spread the incoming flow over the 5cm width of the separator.

Cavities having similar simple geometry could be provided as collection reservoirs at the outputs, including ports for applying the motive vacuum.

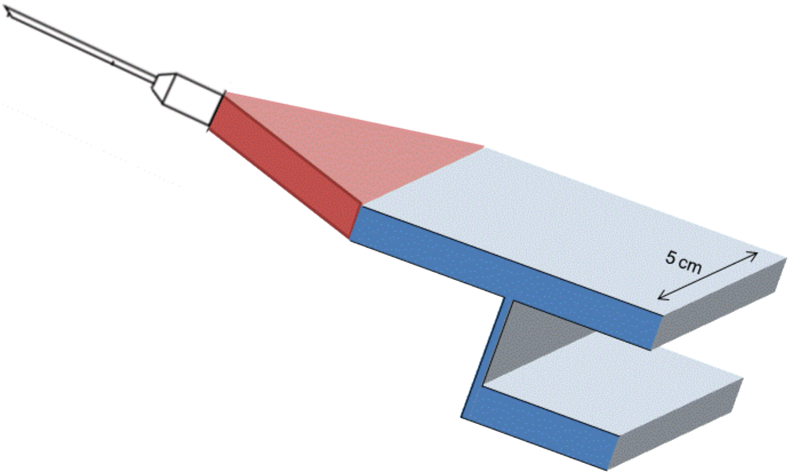


Figure 73: Extruded separator with added needle and inlet manifold

The reduction in complexity depicted in Figure 73 compared with the arrangement shown in Figure 72 is striking. Manufacture could prove relatively simple, and the broad channels for fluid flow should be resistant to clogging.

The arrangement does however appear rather unwieldy, and would struggle to solve one of the essential problems - “Blood sample collection using a familiar method...”

Case B: Rotation (1)

Figure 74 extends the rotation performed bodily by Professor W O'Neill, as described in section 4.3.5, to cover the case of multiple side branches emanating from a single main channel. The branches transform to parallel disks.

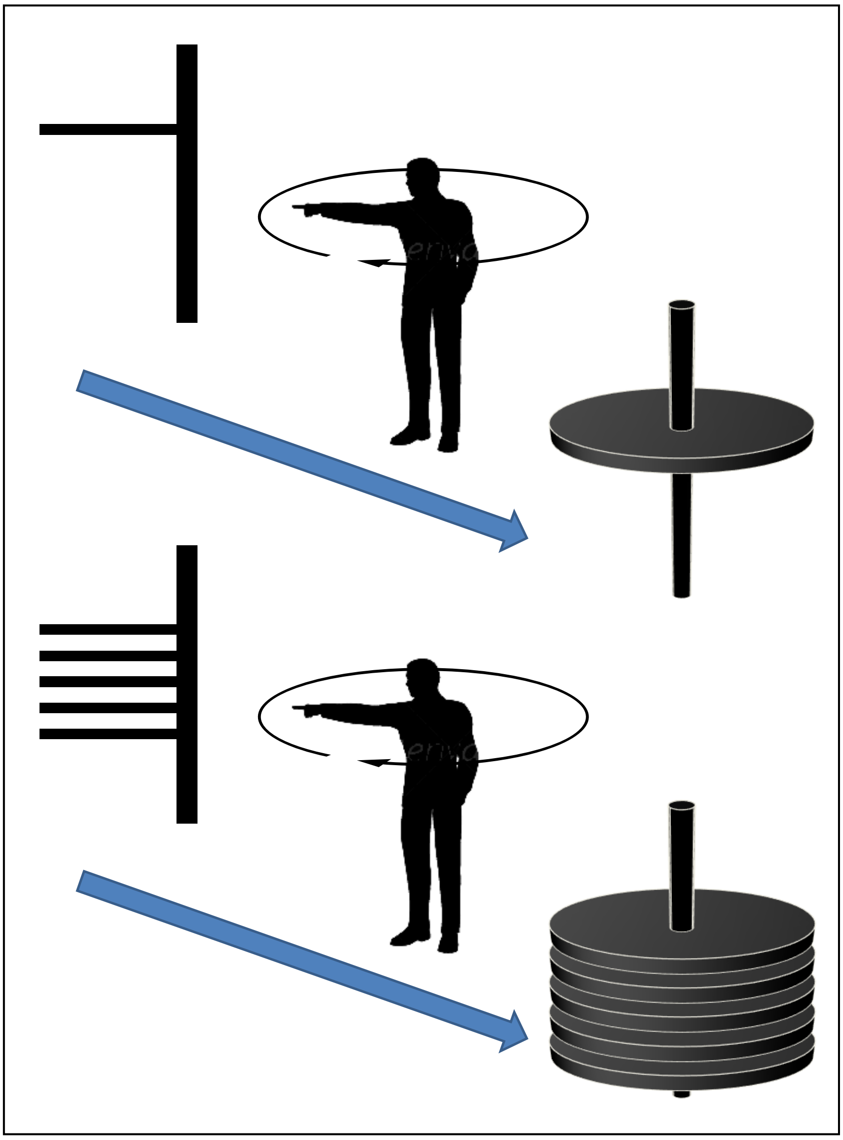


Figure 74: Extension of the rotation introduced in Figure 63

The original reasoning behind this rotational transformation was that previous experiments to achieve plasma separation using micro- scale effects had attempted only to extract from one side of a rectangular channel formed in a planar substrate, as in for example the research apparatus of Yang et al. [52] shown in Figure 26 on page 69 of this thesis.

As shown in Figure 75, the rotational transformation of “A” allows the extraction of plasma radially from the whole circumference of the main channel, which has become tubular in “B”, in which the original side channels have become disk-shaped voids.

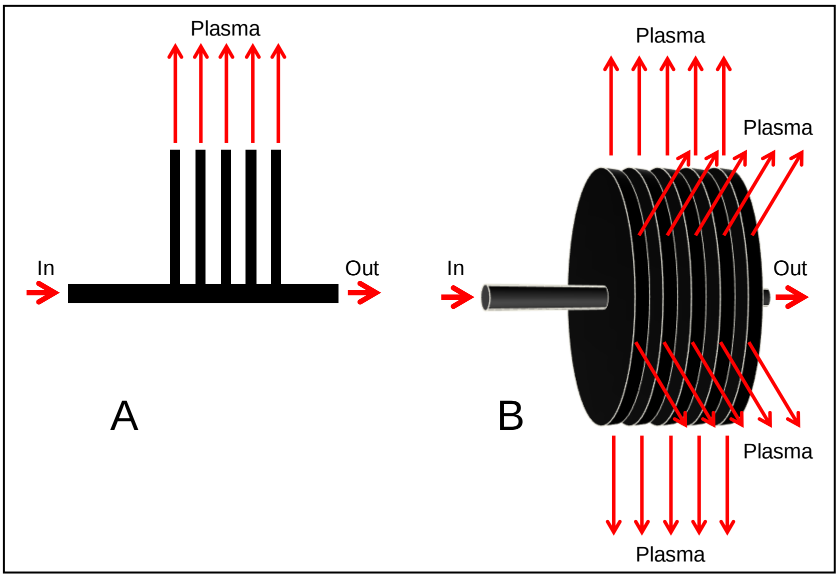


Figure 75: Improved plasma extraction

Although this transform will improve extraction, it does not increase the throughput of the separator by a factor of 1,000. In reality, the side channels of [63] only extract through one 20 µm high side wall. The circumference of the rotated 40 µm wide main channel, all of which is available for plasma extraction, would be π x 40 µm after the transformation, so a gain in throughput of some 40π/20 = 6.3x might be expected, implying that around 160 of such transformed separators would still be required in parallel to meet the essential problem of achieving a collection and processing flow rate of 0.54 mL/sec.

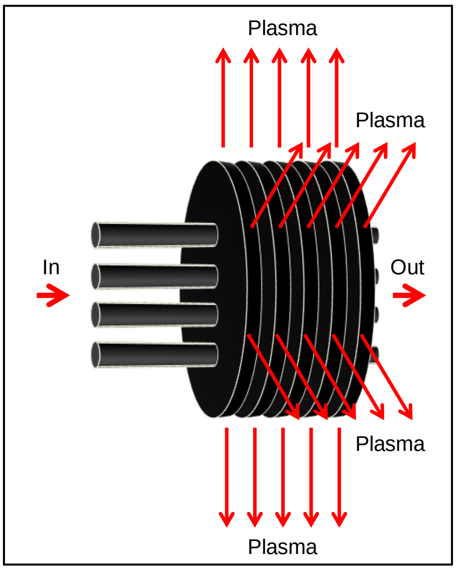


Figure 76: Parallel processing of several "main" channels

The arrangement illustrated in Figure 76 is a potential approach to achieve the needed100-fold parallelism. By extending the disk planes as necessary in principle any number of main channels could pass through and be catered for.

Inlet and outlet manifolds could readily be achieved through conical vessels, and a tubular overall container could collect the extracted plasma. Nevertheless, manufacturing may be complex, with difficult geometries and tight tolerances that are difficult to control.

Case C: Rotation (2)

The third case illustrates how a change in the choice of axis of rotation can have a profound effect upon the format of a 3D functional object transformed from a 2D functional diagram. At the same time, this case, as developed in the following section 5.3, will demonstrate operational and manufacturing advantages over the two previous cases.

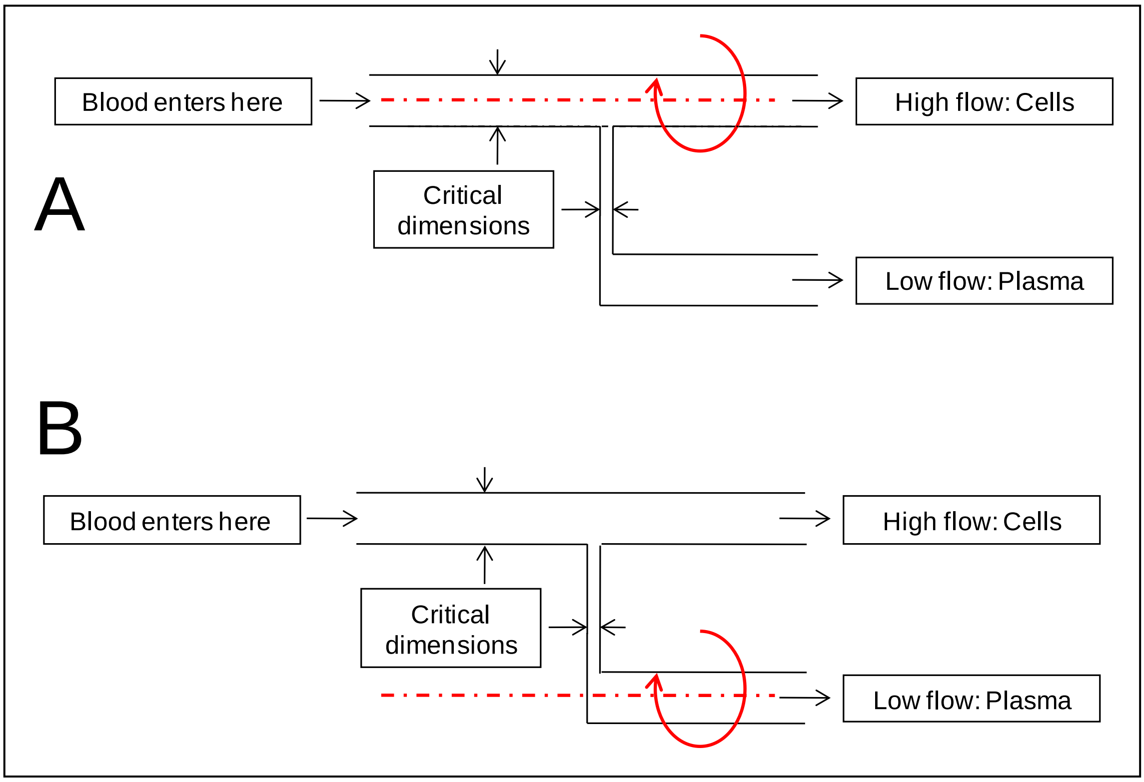


Figure 77: Shifting the axis of rotation

The 2D functional diagram at “A” in Figure 77 will result in a “tube and disk” geometry when rotated along the indicated axis, as per Figure 75, the blood entry channel becoming the tube.

Changing the axis of rotation to that indicated by diagram “B” in Figure 77 results in the inlet channel becoming an annulus around the outside perimeters of the disk, which now discharge the extracted plasma to a central tube in line with the axis of rotation. Figure 78 clarifies.

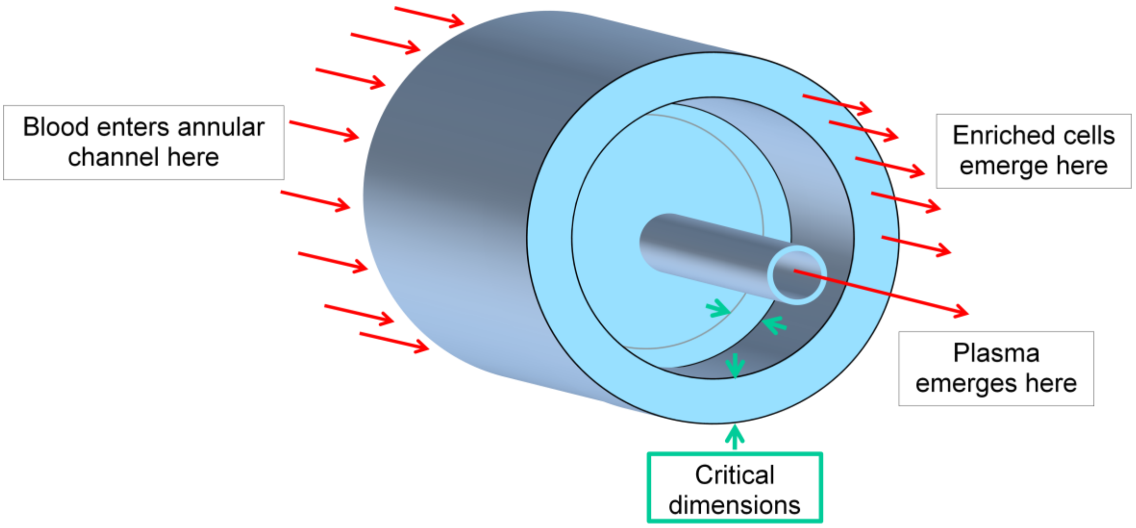


Figure 78: Cylindrical separator, annular main channel, axial plasma channel

To match the performance of the extruded separator of Case A the perimeter of the annular blood channel should be ~ 5 cm (see Figure 73), which corresponds to a diameter of some 1.6 cm, of the order of the barrel diameter of a 10mL syringe.

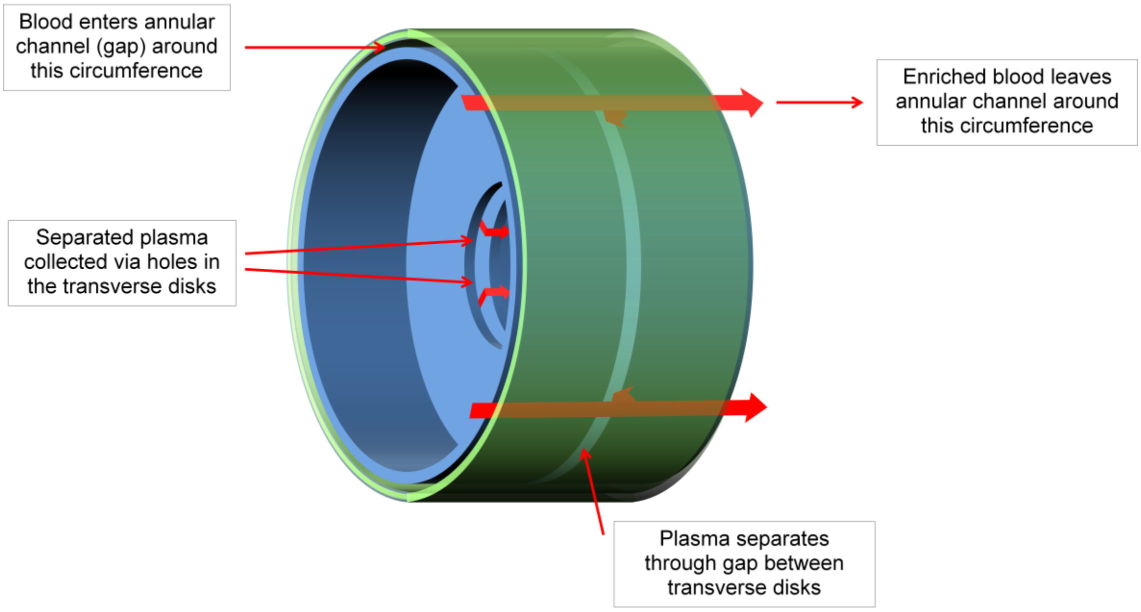


Figure 79: Cylindrical separator, alternative view

Figure 79 provides an alternative view to aid in understanding the structure.

The critical dimensions indicated are in the range 10 µm – 100 µm, depending on detail design. As per the arrangement shown in Figure 75, the cylindrical separator may include a number of separator disks in order to maximise the quantity of recovered plasma.

The arrangement arrived at in Case C could result in a complete separator being included within a standard syringe body, still leaving 5 mL available to receive the separated fluids, as suggested in the conceptual model of Figure 1.

Figure 1: Concept model of Red Blood Cell / Plasma Separation Device

As recorded in the following section 5.3, the Case C concept can be developed, with advantage, in several ways.

5.3 Developing the concept

This section records options considered for the evolution of products based upon the transformations described as Cases A, B and C of section 5.2.3.3

5.3.1 Case A: Extrusion

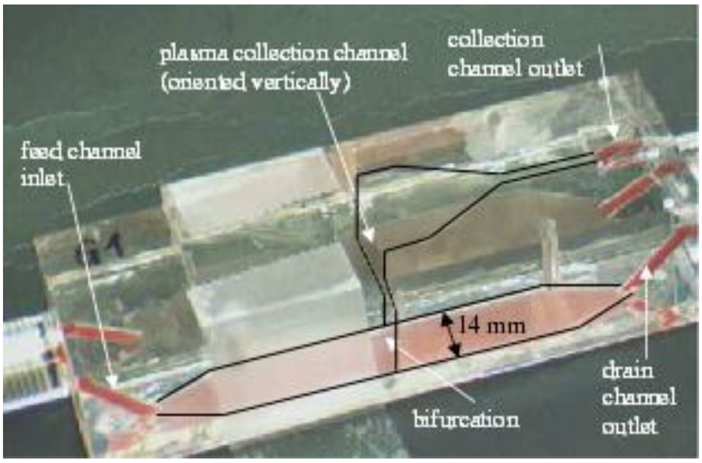


Figure 35: 3D separation device with high-aspect ratio channels

> From Jaggi et al. [53]: *“Channel boundaries are outlined with black lines for clarity (optical refraction gives rise to multiple images of the feed and the drain channel)”*

There is no evidence that this configuration has progressed beyond laboratory trials.

5.3.2 Case B: Rotation (1)

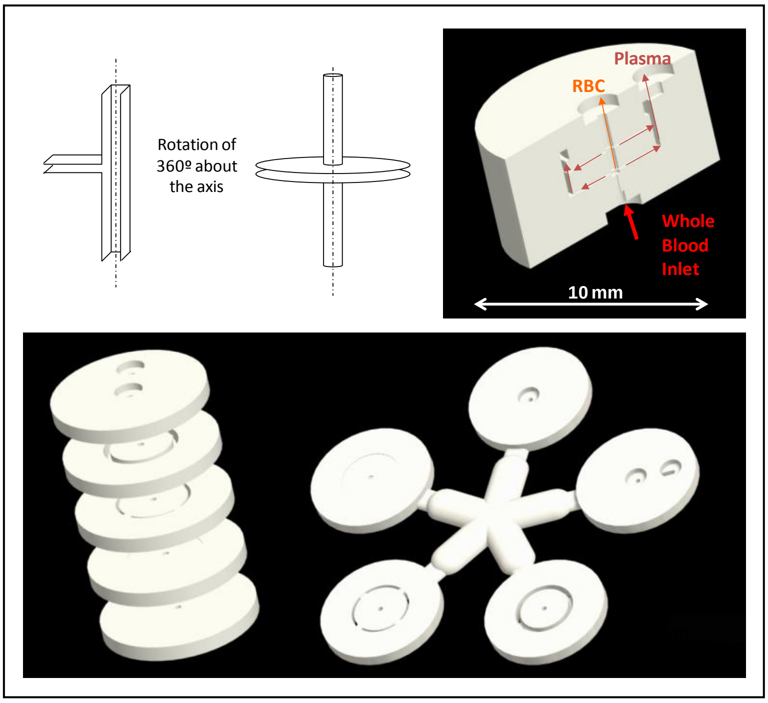


Figure 80: Micro- injection moulded separator test piece
(After Marson et al. 3D-MINTEGRATION)

The device pictured in Figure 80, although suffering from the limitation described on page 137, was constructed by Marson et al [78] to explore precision-milled tooling and moulding tolerance capabilities at the micro- scale.

Figure 81: Mould design and structure
(After Marson et al. 3D-MINTEGRATION)

Apart from valuable insight gained into aspects of micro- mould design, fabrication and operation, the viability of mass manufacture of this design was not proven.

5.3.3 Case C: Rotation (2)

5.3.3.1 Plunger actuated

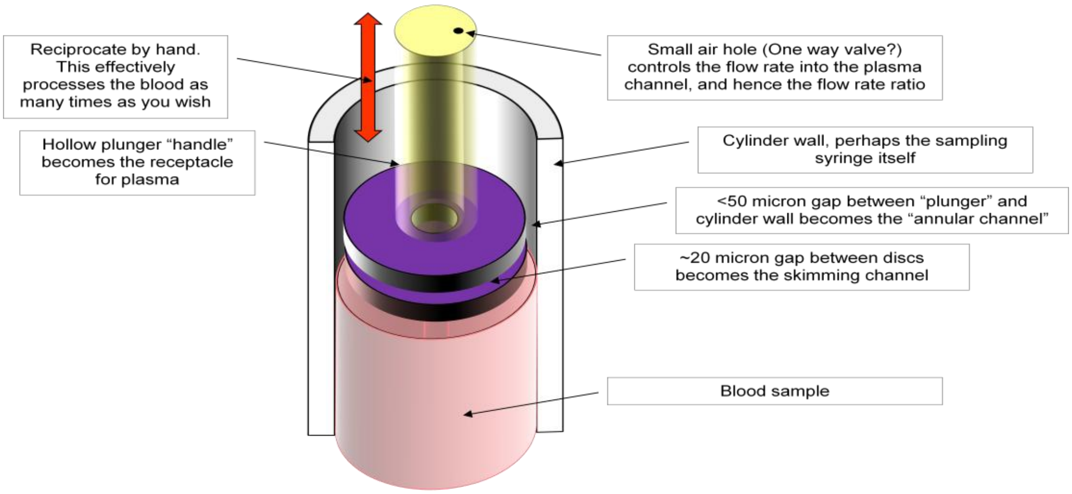


Figure 82: Principle of a plunger actuated device

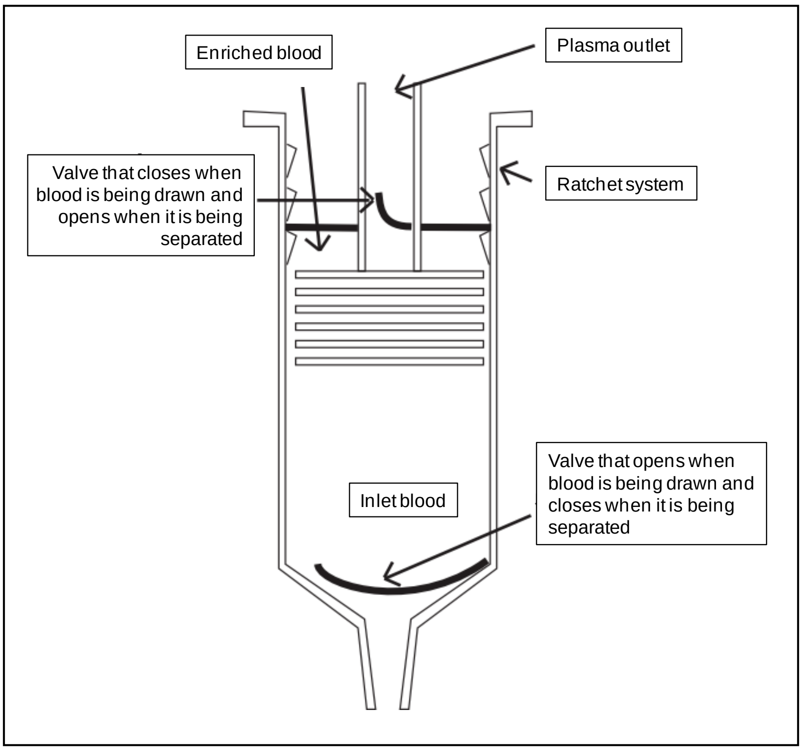


Figure 83: Development of plunger activated device
(Adapted from Katy Jenkins "Blood Separation Syringe: DM3306 Major Project Report")

Here a multiplicity of disks is moved reciprocally through the extracted blood, extracting plasma incrementally during each stroke. The concept of integrating the separator through a specially-valved syringe, seeded by the model shown in Figure 1, is due to Brunel's Katy Jenkins, a part time contributor to this research.

5.3.3.2 Vacuum actuated

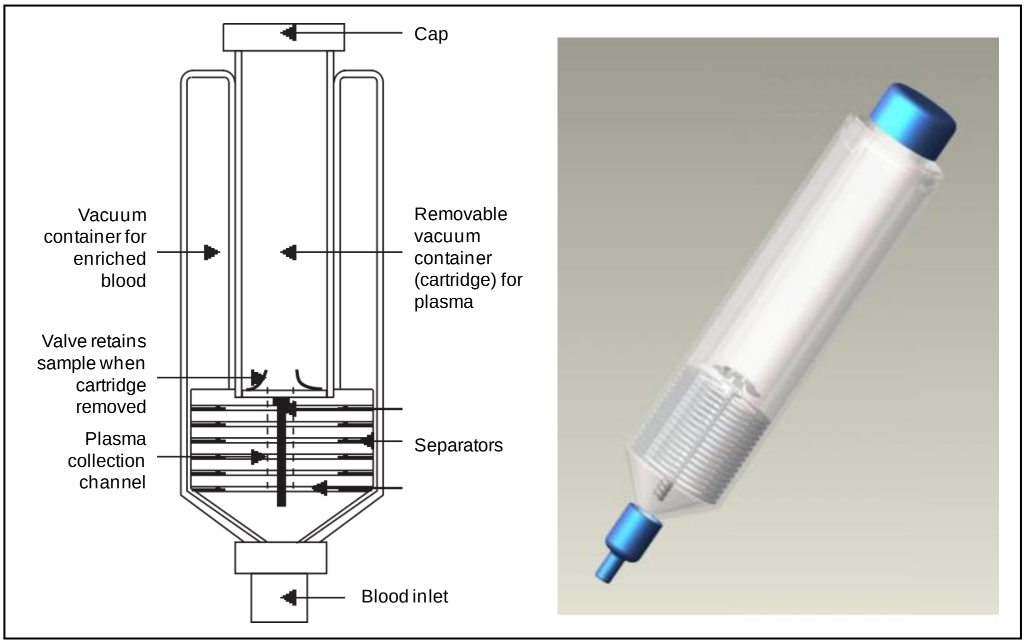


Figure 84: Integration within a Vacutainer®-style device
(Adapted from Katy Jenkins "Blood Separation Syringe: DM3306 Major Project Report")

The second Case C development example, illustrated in Figure 84, has the potential to satisfy all the essential problems of section 5.1.2:

- Blood sample collection using a familiar method, sample size and time to collect
- A Red Blood Cell / Plasma Separation as a continuation of the collection method, with a volume and rate equal to that of the collection method
- A connection between the collection and separation processes
- Sources of energy and the control of parameters

This is a concept which, subject to detailed embodiment design, could become a viable product.

It is very unlikely that the 3D functional mechanism visualised in Figure 78 and Figure 79 would have been arrived at in any other way than the geometric transformation of a 2D functional diagram, with an appropriate choice of rotational axis.

5.4 Insight and support from modelling

Apart from the analogue based upon sheet resistance recorded in section 5.4.6, the modelling described here is computer-aided Computational Fluid Dynamics (CFD). The computer does not do everything. As with all computer aided design the fundamental aspects are "how to put the question and how to evaluate the answers", and this demands knowledge, understanding and experience from the team using the tool, as well as data and information upon which to build the model. The same also applies to the analogue presented in section 5.4.6.

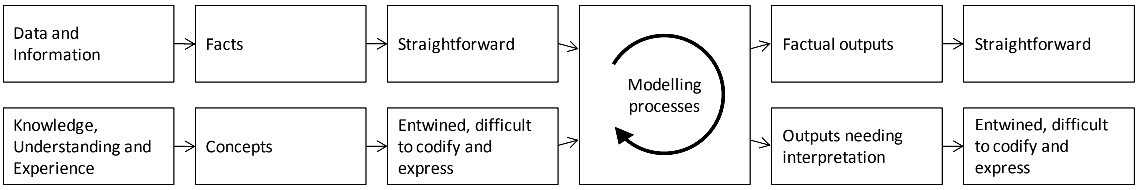


Figure 85: Streams of modelling communication

Figure 85 extends the idea introduced in Figure 7 of 2.4.1.2, "*What is needed to be communicated?"* to illustrate the categories and issues of communications around the modelling process. It is unsurprising that all of the methods discussed in section 2.5: *2D representations used in the design of 3D objects* come into play.

5.4.1 Caveats

Modelling blood flow is not easy, see Xue et al. [4] "Challenges in Modelling Biofluids in Microchannels". Modelling the behaviour of whole blood, which may contain around 50% red blood cells, the plasma behaving almost as a lubricant, is a problem not yet solved in detail, the observations of Fahraeus [61] giving insight into the difficulties including the deformations of cells and their tendency to aggregate in narrow channels.

Xue et al. list the following challenges particular to blood flow in microchannels:

- *Modelling of material properties* that vary substantially with different concentrations of suspensions.

- *Modelling of blood cells,* which not only collide with each other, but also interact with channels.

- *Modelling of the boundary layer.* If the channels have a dimension comparable to the cells the fabrication quality and accurate modelling of wall surfaces are required.

  Modelling of the boundary layer also needs to deal with the high-shear-ratio state. The shear stress in microchannels is so high that sometimes fluids slip on a wall.

- *Modelling of microchannels* which for biofluids have high aspect ratios and large surface to volume ratios. This brings a difficulty for meshing and how to optimise meshing with different types of elements and different densities of meshes.

- *Choice of boundary conditions*. Microfluidic systems generally combine core functionality at the micro- scale, but coupled to the exterior macro- world. Since these very different regions are located within a single system, determining boundary conditions becomes a challenge.

- *Modelling of particle movement*. The viscous and frictional forces are generally governed by equations requiring some parameters and coefficients to be chosen according to the specific situation. Furthermore, with the introduction of particle forces, biofluids are governed with three laws: equations defined by Newton's second law for individual particle movement, viscous forces for interaction between cells and Navier-Stokes equations for fluids. The dominant law or laws will vary according to individual cases of geometry, particle concentration and the nature of the particles.

- *Modelling of particle deformation*. With high viscosities and deformable cells, clogging or congestion becomes a major concern. When a number of red blood cells collide in a flow of a low shear rate, they cluster and aggregate together. The 2007 work of Bagchi [79] makes a start with “plug-flow” effects, but does not properly account for the “stickiness” of aggregation.

5.4.2 Approach to modelling the concept

Precision modelling may be vital for “mission critical” product design, but even with the many imponderables of section 5.4.1, the “in principle” validation of a conceptual design may proceed with a relaxed modelling regime. The strategy adopted for the in-practice design study was:

- Model fluid flow only, or with simple particles, to obtain a sense of the behaviour of blood within the chosen geometries. - *“Factual outputs” according to Figure 85*

- Interpret the potential effects of the indicated behaviour through the knowledge, understanding and experience gained through the study of section 2.7.3: Microscale approaches for red blood cell / plasma separation. - *“Outputs needing interpretation” according to Figure 85*

The CFD was performed by Professor Chris Bailey and his team at the University of Greenwich, who kindly provided resource of appropriate scale to support this thesis.

5.4.3 Communications and debate

Briefing the modelling team required intensive communication and debate based upon diagrams such as those shown in sections 2.7.3 and 5.3 of this thesis.

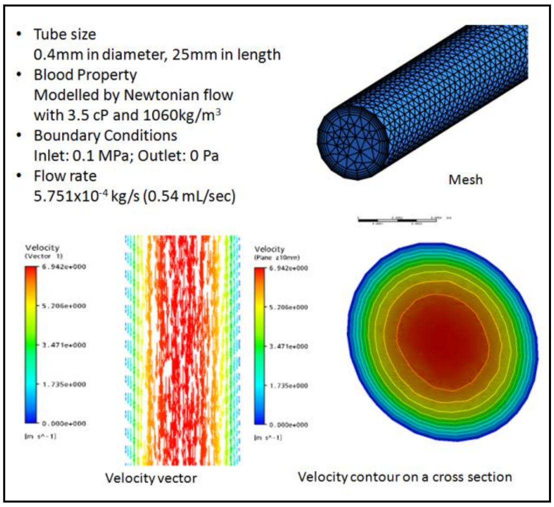
Intensive *factual* and *conceptual* communication (Figure 85) fuelled the discussions concerning both the creation of input models and the interpretation of the outputs, which were typically in the form of on-screen graphic depictions, including animations which are as yet impossible to reproduce in printed form.

The foregoing debate was characterised by a surprising level of inventive conjecture as the team, although deeply experienced in many fields, explored unfamiliar territory in the nature of blood and its flow properties, the behaviour of fluids in micro- scale geometries, and the intricacies of the 3D shapes evolved by geometric transformation from 2D functional diagrams.

Regarding the latter point, it was observed that the 3D shapes could with ease be “flattened” or, where appropriate, “segmented”, where symmetry allowed, to facilitate computationally less-demanding modelling of a sample to reflect the behaviour of the whole. A “duality” of thinking evolved as the operating principle “roots” of the geometry to be modelled were revealed through this deconstruction, followed by the reconstruction of the object - and its internal workings - through the reverse procedure. *In principle, in designs based upon geometric transforms, the basis of this thesis, modelling can start with the 2D functional diagram itself.*

5.4.4 Modelling of fundamentals

The works of Xue et al. [3], [4], [5], [6] and [7] contain much detail regarding the modelling work, its basis, and a large number of examples. Figure 69 and Figure 86 illustrate the two primary results that provided the basics specific for this study.



- Tube size
  0.4mm in diameter, 25mm in length
- Blood Property
  Modelled by Newtonian flow
  with 3.5 cP and 1060kg/m^3
- Boundary Conditions
  Inlet: 0.1 MPa; Outlet: 0 Pa
- Flow rate
  5.751x10^{-4} kg/s (0.54 mL/sec)

Figure 69: Computer modelling of typical syringe needle

The modelling shown in Figure 69 (thumb nail reproduced from page 129) gave insight into the syringe needle collection process described in section 5.2.1. This determined the parameters governing the fluid handling capacity of the subsequent separation process.

The results also revealed the environment imposed upon and survived by red blood cells during normal syringe extraction.

With the fundamental flow parameters determined, attention shifts to the separation process. Figure 86, reproduced from [6], provides a useful visualisation in 2D, but for which the authors assert “Other junctions and other designs show a similar pattern”.

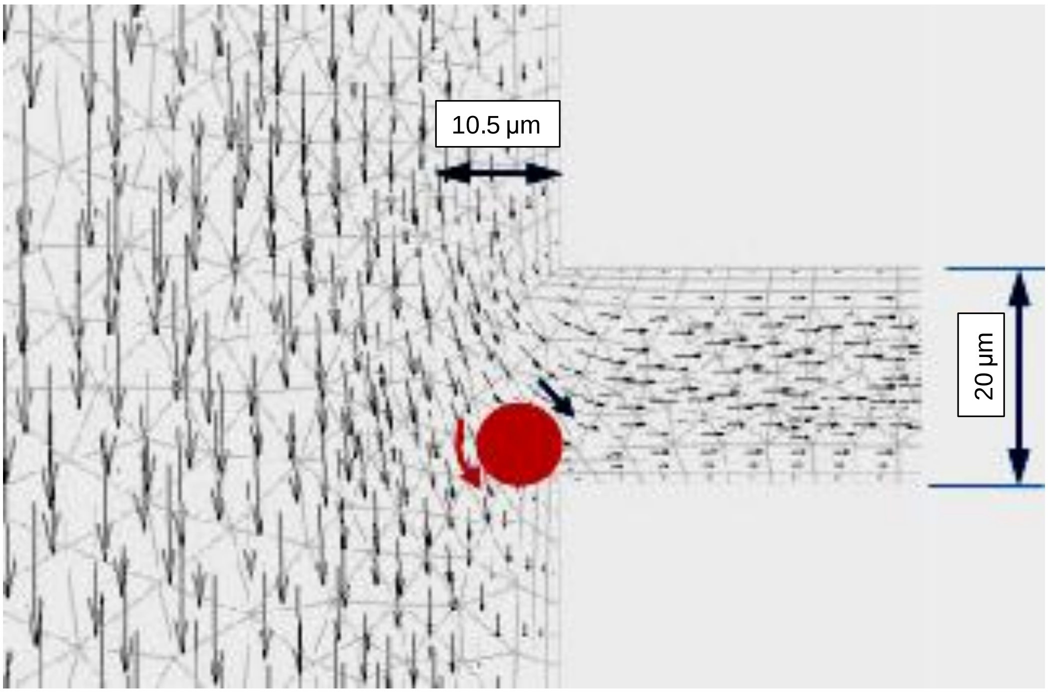


Figure 86: Velocity vectors at a junction
(Adapted from Xiangdong Xue et al. [6])

As shown in Figure 86, [6] explains that for a red blood cell located at the stagnant point, the flow velocity on the main channel side is higher than that on the side nearer the branch channel. Higher frictional force and lower pressure will thus be formed on the main channel side, influencing the movement of the particle towards the main channel.

The paper goes on to suggest also a “Bending channel effect” whereby the blood cell, which has a higher mass density than the surrounding plasma has a kinetic tendency to escape the bending flow and remains in the main channel, and also the Magnus effect and Saffman effect arising through unequal shear stresses across the blood cell due to the parabolic profile of the flow velocities which cause the particle to spin. The whirlfield produced by the spin in turn increases the velocity difference, a pressure gradient is thus formed and a transverse force is induced pointing to the side of higher flow velocity, i.e. the main channel.

Finally, as indicated by Tripathi et al. [60] other matters come into play, such as the aggregation of cells, which may be significant in whole blood separation but less important in the separating of diluted blood. Accordingly, precision modelling can only be applied under precise conditions of use, but discussions around Figure 86 give a helpful general guide to the separation mechanism.

5.4.5 Modelling of rotational transform

Modelling of the Case C separator concept illustrated in Figure 78 and Figure 79 on page 139 was undertaken to check the theory that the geometry would perform as per the 2D prototype from which it was transformed.

The model was confined to a segment of the rotationally-symmetric device to reduce the computational complexity. Even so, it comprised 1,313,010 elements with 969,760 nodes.

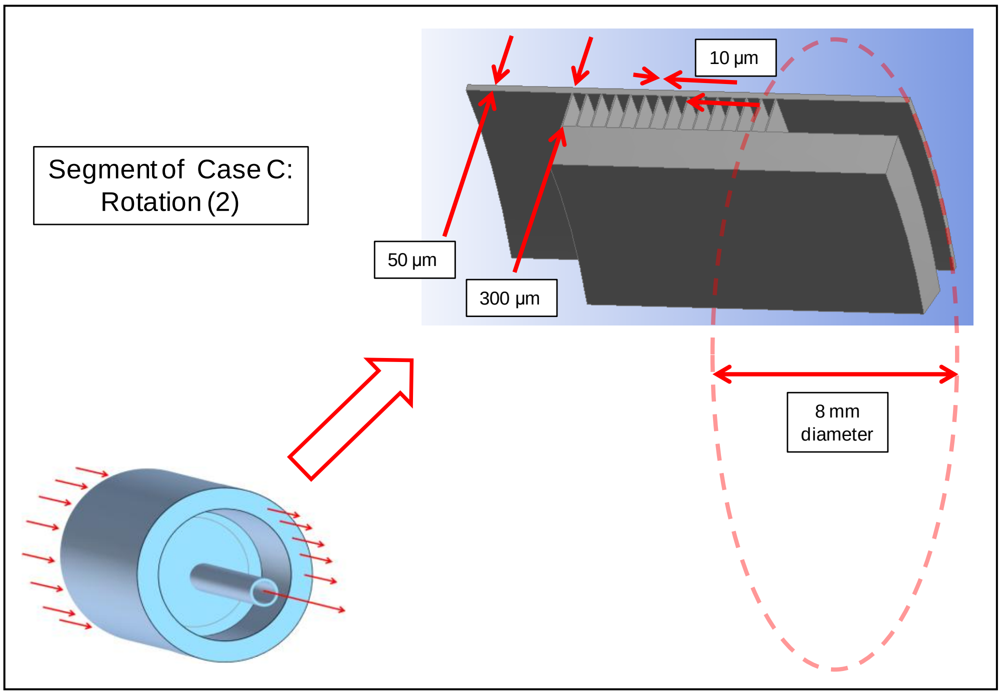


Figure 87: Modelling of segment from cylindrical separator

The velocity vectors at the bifurcations shown below in Figure 88 correlate well with the example shown in Figure 86.

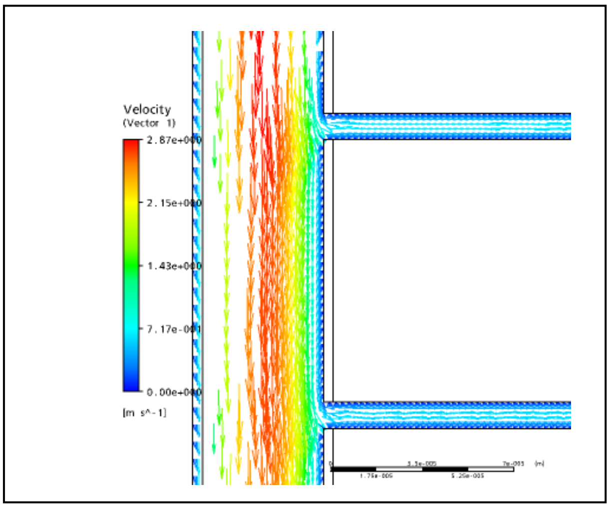


Figure 88: Velocity vectors at junctions

5.4.6 Insight from analogue: sheet resistance

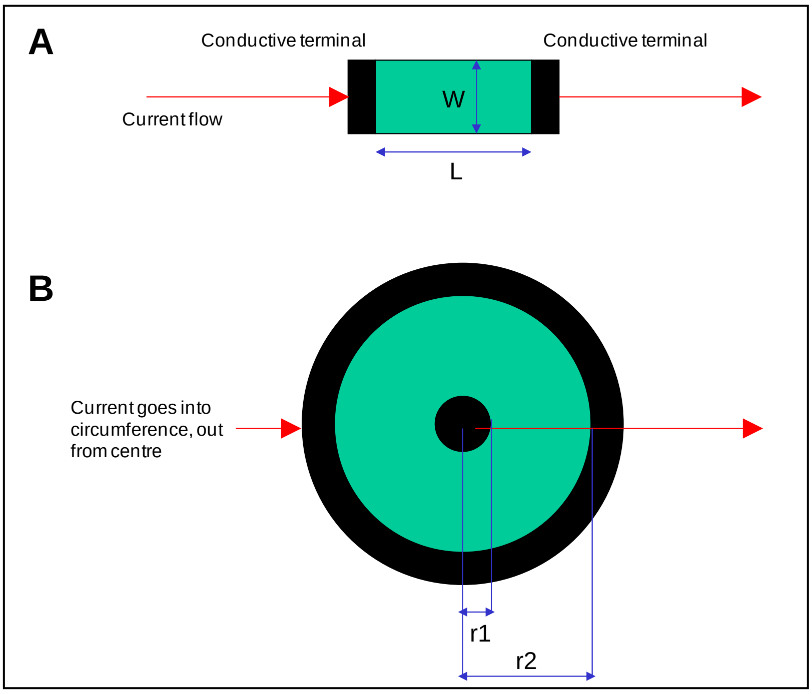


Figure 89: Linear and circular sheet resistors

Resistors made from printed film, such as in thick film microcircuits, are like channels in 2 dimensions. In the following examples the factor "s" is the sheet resistivity.

The resistor depicted in Figure 89 (A) has linear format and resistance proportional to s*L/W, ie a long thin resistor has higher resistance than a short fat one, absolute size being irrelevant.

For the disk geometry of Figure 89 (B) the resistance is proportional to s*ln(r2/r1).

In the simplified example of a disk-shaped separation channel with internal radius 4mm, to accommodate a central plasma collection reservoir, and external radius 8mm, where it would form a junction with the circumferential blood flow channel, the resistance between the inner and outer channels would be s*ln2 = 0.69s.

The "linear" channel case, with width 2*8*π mm (to equal the circumference of the above example), and length 8-4 mm = 4 mm (to equal the span of the disk from the central reservoir to the circumferential junction) the resistance of the channel would be s*4/(2*8*π) = 0.08s.

It can therefore be seen that the disk configuration beneficially "compacts" the collection channels in this case by a factor of 0.69/0.08 = 8.6, shrinking the path because the disk essentially "converges" the streamlines of separated plasma radially towards the central axis, thereby impeding the flow.

5.4.7 Investigation of improved junction geometry

Section 2.7.3.3 “Improvements upon junction-based separators” introduced the observation that the “geometrical focusing of cells” in the 2005 work of Faivre et al. [66], and the T-channel modifications reported by Kersaudy-Kerhoas et al. [63] and similarly by Rodriguez-Villarreal et al. [64], [65], might all be dominated in their effectiveness by the behaviour of the blood flowing past a “step” in the channel wall.

Undoubtedly a preceding constriction might introduce a degree of beneficial cell aggregation as according to Fahraeus [61], but for the sake of examining the development of the conceptual development of the Red Blood Cell / Plasma Separator, the topic of this thesis, the dynamics of flow as perturbed by the step was chosen for modelling.

5.4.7.1 Briefing the modeller, and feedback

The CFD modelling was undertaken at the University of Greenwich by Catherine Tonry, with assistance from Professor Chris Bailey.

The briefing to set up the modelling parameters was by verbal discussion supported by powerpoint slides of pictures and diagrams.

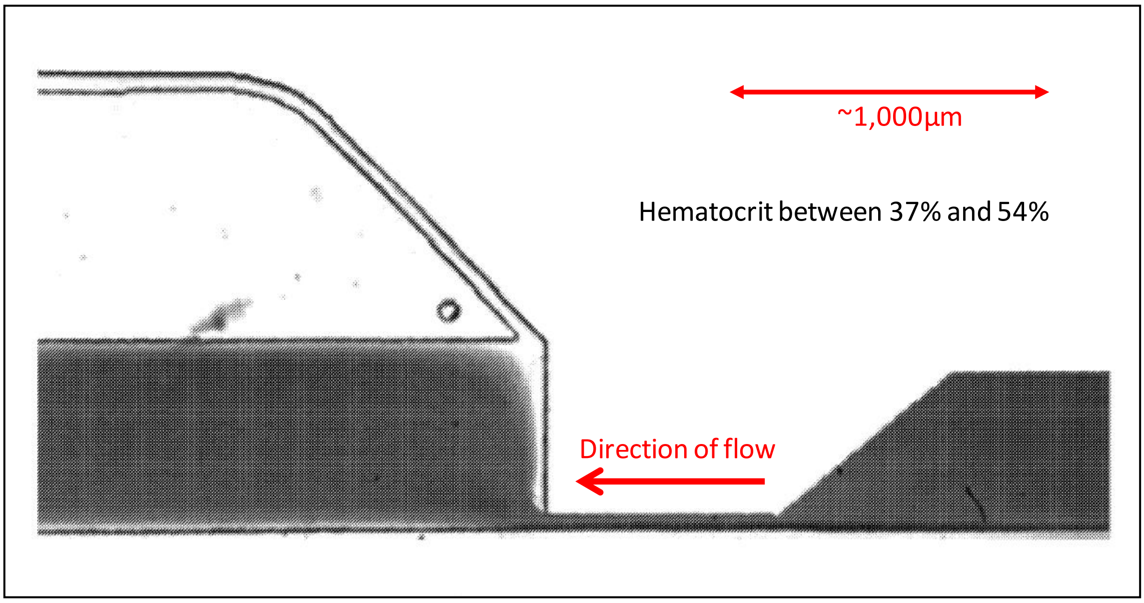
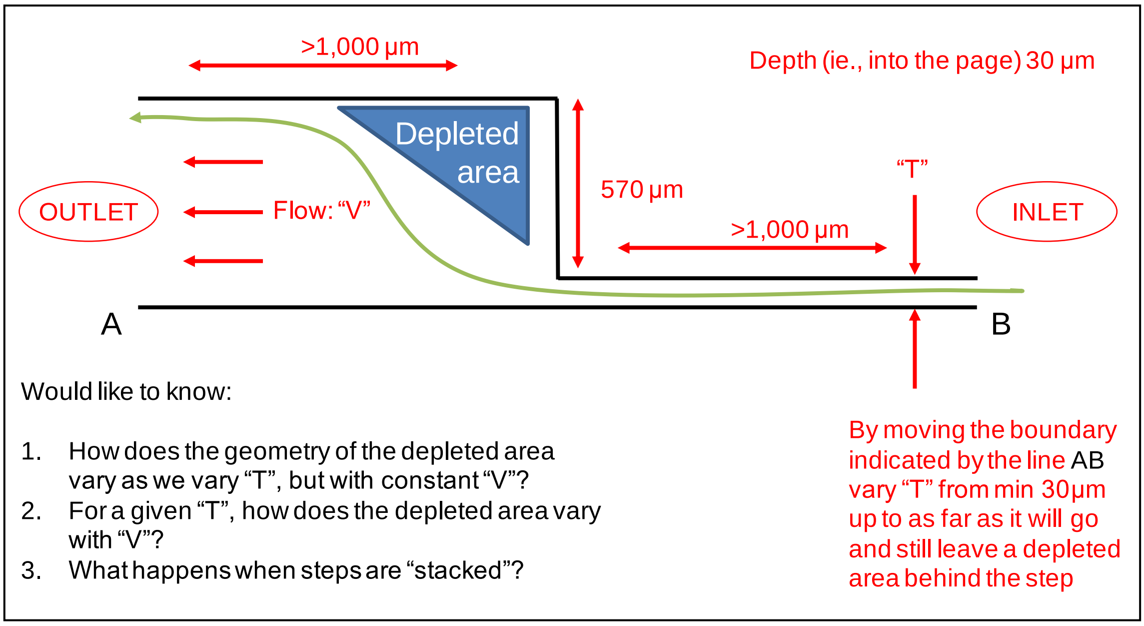


Figure 90: Cell free zone after a step according to Rodriguez-Villarreal et al.
(After US Patent Application 2011/0084033)

The discussions took as a starting point a microphotograph from US Patent Application [65], authored by Rodríguez-Villarreal and Arundell. Dimensions were taken from an associated diagram incorporated in this thesis as Figure 32: Dimensions of junction/ “step” used by Rodriguez-Villarreal et al. on page 72.



Would like to know:

1. How does the geometry of the depleted area vary as we vary "T", but with constant "V"?
2. For a given "T", how does the depleted area vary with "V"?
3. What happens when steps are "stacked"?

By moving the boundary indicated by the line AB vary "T" from min 30µm up to as far as it will go and still leave a depleted area behind the step

Figure 91: Diagram of flow past a step and modelling requests

As a convention, the flow rate "V" was taken, unless expressed otherwise, as the total volumetric flow rate through the system.

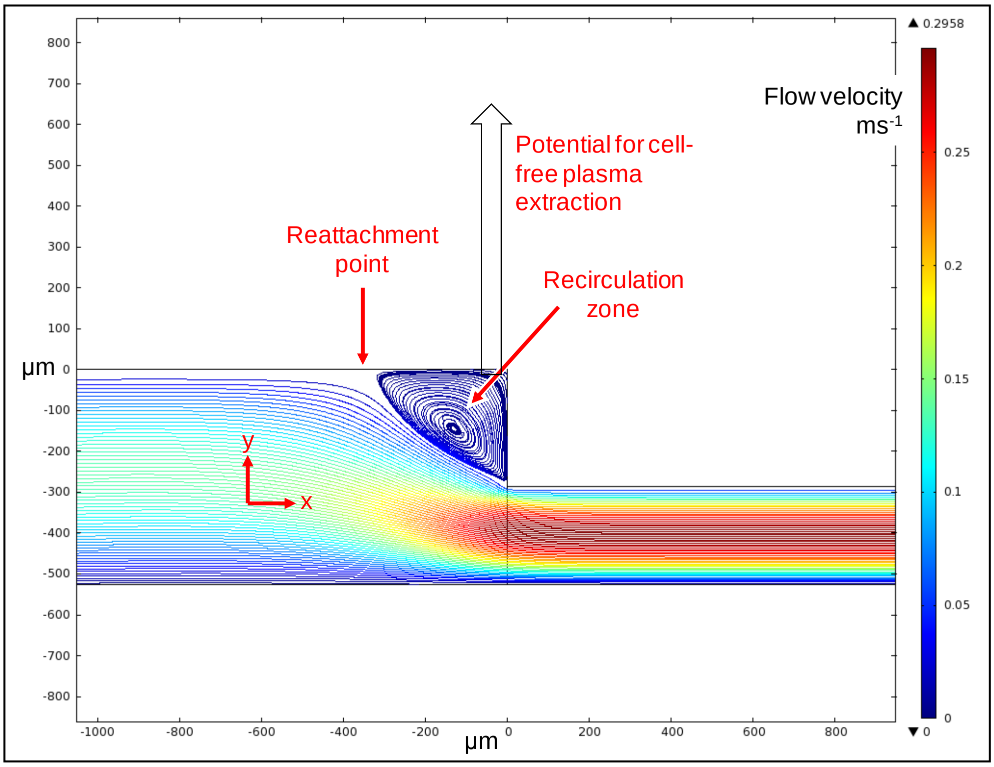


Figure 92: Explanatory diagram of recirculation and reattachment

Initial feedback from Tonri comprised an explanatory diagram of the mechanisms involved, and advice that the reattachment point occurs where the x component of the velocity of flow changes sign along the interface.

5.4.7.2 Response to Figure 91 Request (1)

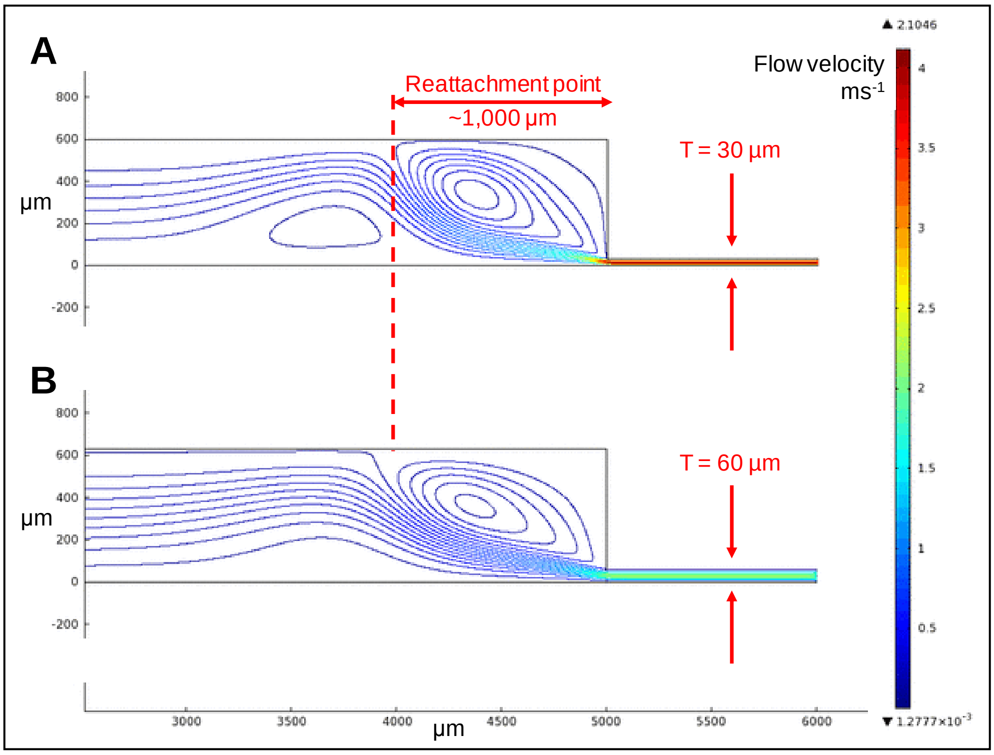


Figure 93: Varying the inlet width at constant volumetric flow

5.4.7.3 Response to Figure 91 Request (2)

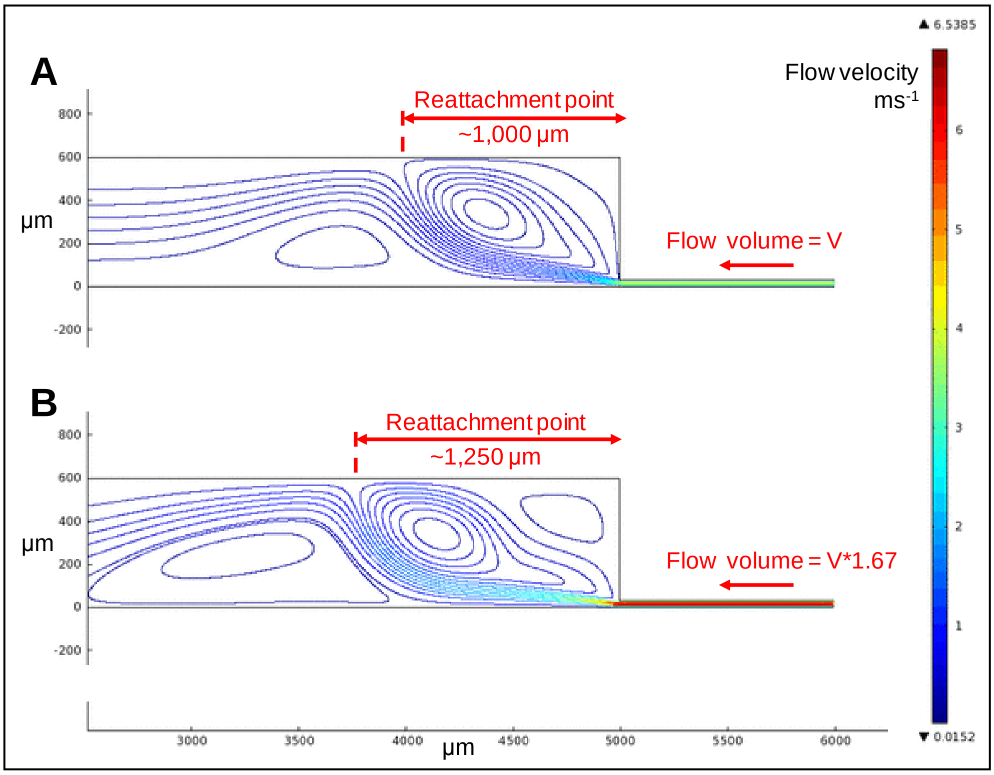


Figure 94: Varying the volumetric flow with constant input width

5.4.7.4 Response to Figure 91 Request (3)

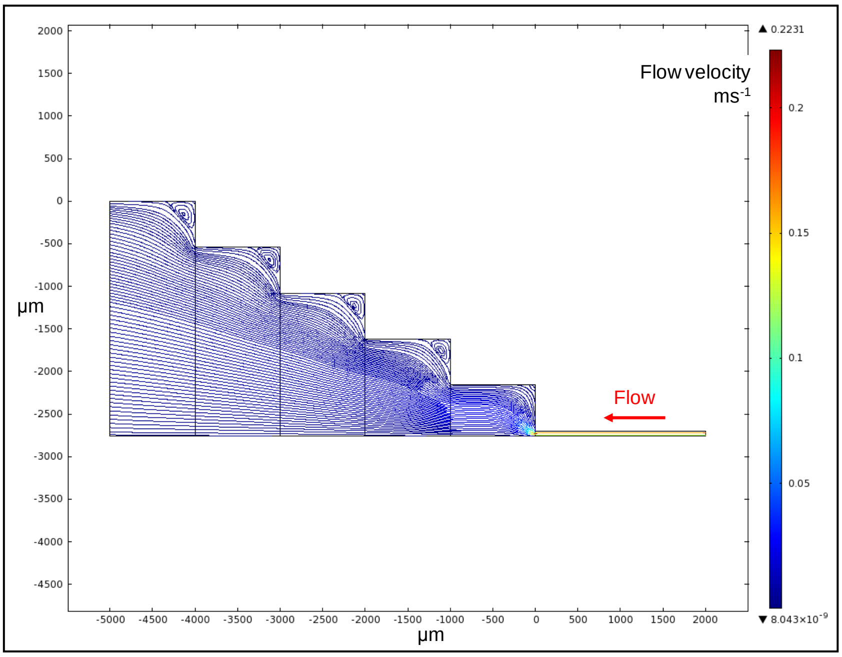


Figure 95: "Staircase" of recirculation zones

5.4.7.5 Evaluating the answers

The following observations arise by inspection of Figure 93, Figure 94 and Figure 95:

- The reattachment point in Figure 93 (A) remains virtually unmoved in Figure 93 (B), even though the inlet width is doubled. This raises the possibility that the reattachment point is determined by the volumetric flow and the step size.

- The reattachment point in Figure 94 (B) moves some 25% compared with the distance seen in Figure 94 (A). This reinforces the possibility that the reattachment point is determined by the volumetric flow and the step size.

- The volumetric flow used in Figure 95 was reduced to 10% of that in Figure 93, hence the length of the recirculation zone being reduced to some 250 μm, providing around 750 μm for straight streamlines to develop again before the next “step”, where the behaviour seems to repeat.

- A further significant observation from Figure 95 is that the “input” to each step, although being of the same volumetric flow rate, is provided from a “channel” of hugely increasing width.

The above observations are explored further in the practical trials of section 5.5 and the development of the concept described in section 5.6.

5.5 Practical trial

A practical experiment was devised to:

- Investigate the concept of the “staircase of recirculation zones” suggested by simulation, as illustrated in Figure 95.
- Judge whether this concept might be incorporated into the embodiment of the product.
- Gain insight into the workings of the designer through recording the flow of communications.

5.5.1 Subject of trial: From staircase to sawtooth

Figure 96 suggests stages of transformation from (A) the “staircase of recirculation zones” of Figure 95 to “D”, a sawtooth pattern retaining the vertical edges of the staircase but eliminating the stepwise widening of the channel at each recirculation zone.

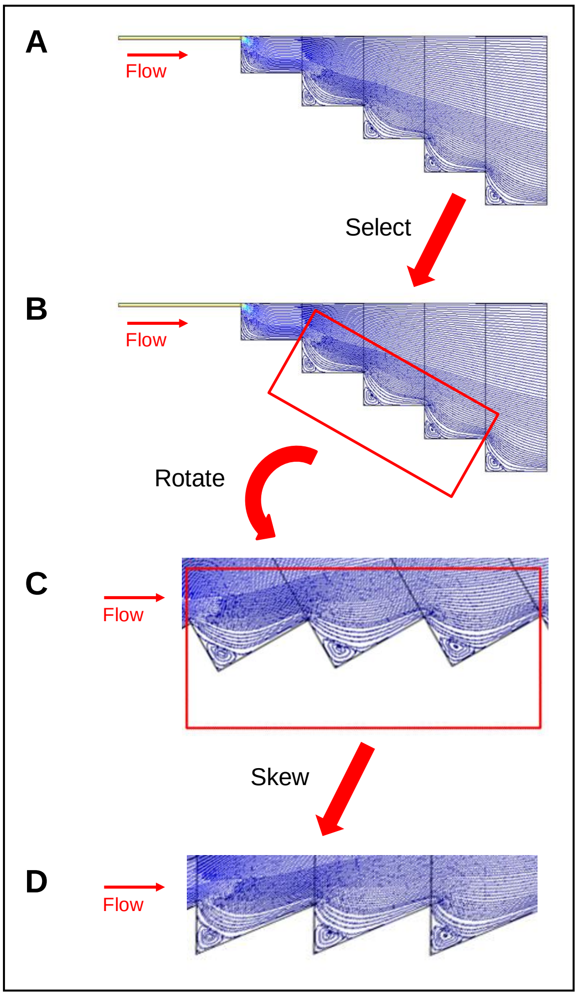


Figure 96: Transformation from "Staircase" to "Sawtooth"

Note that the orientation of this diagram is a rotation of the diagram in Figure 95

The proposal to be tested is that particle-free fractions of a particle-bearing main stream may be drawn from the relatively motion-free recirculation zones formed by the vertical leading edges of the sawtooth geometry, as illustrated in Figure 97.

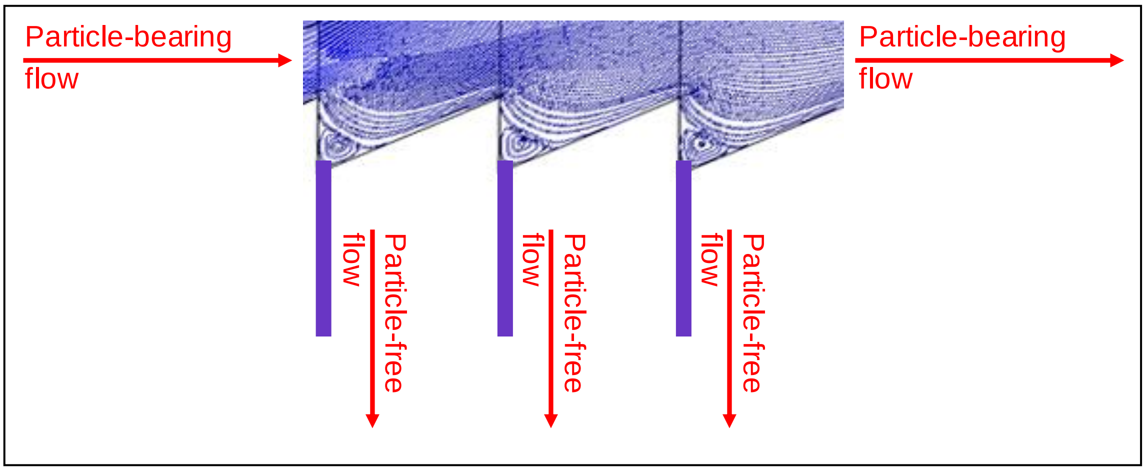


Figure 97: Proposed separation channels

It must be stressed that this is a simple "look see" bench experiment, not a fully comprehensive laboratory research exercise such as those described in section 2.7.3

5.5.2 Experimental approach

A single recirculation zone with extraction channel was fashioned out of three segments of glass cut and ground from a 1 mm thick microscope slide.

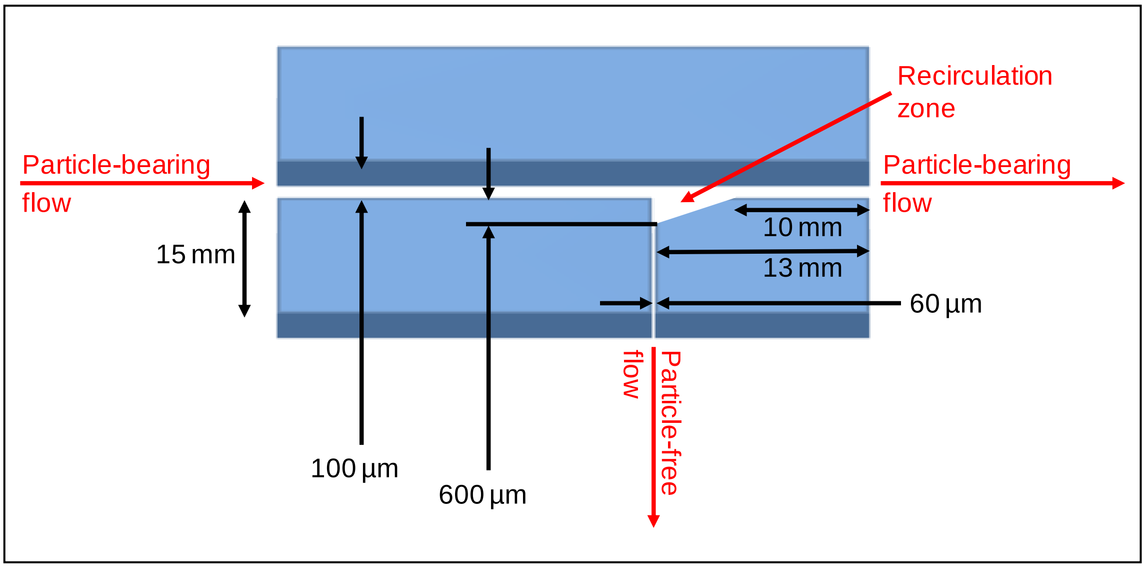


Figure 98: Separation element fashioned from segments of microscope slide

The dimensions of the channels and the length of the recirculation zone were drawn from the simulations in 5.4.7, save that the depth of the channels were increased from the 30 µm of the simulation to 1 mm, to emulate a 1 mm segment of the annular main channel as depicted in Figure 87 on page 148.

The test piece was completed by fixing the three segments of microscope slide to a substrate formed from a second microscope slide, then the channels were “capped” with 2-part epoxy.

The assembly sequence is illustrated below:

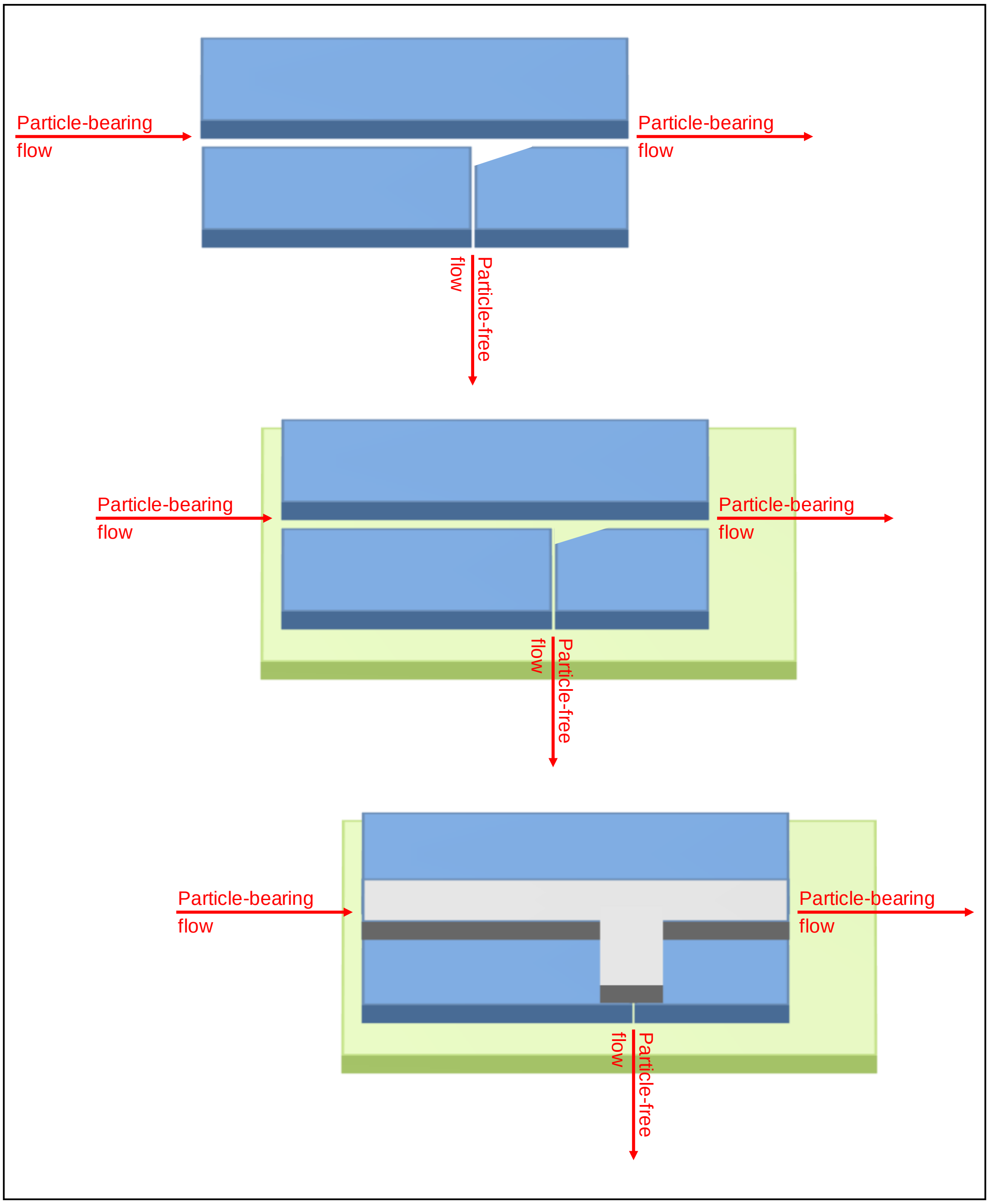


Figure 99: Assembly sequence for test pieces

Figure 100 illustrates the construction of a test piece.

(A) shows the segments of glass slide against 1 mm squared graph paper before alignment. The red mark indicates the position of a carefully ground corner, with radius < 5 µm.

(B) is a microphotograph of the triangular recirculation zone, after alignment, again against a 1 mm grid.

(C) shows a complete test piece including an inlet syringe needle.

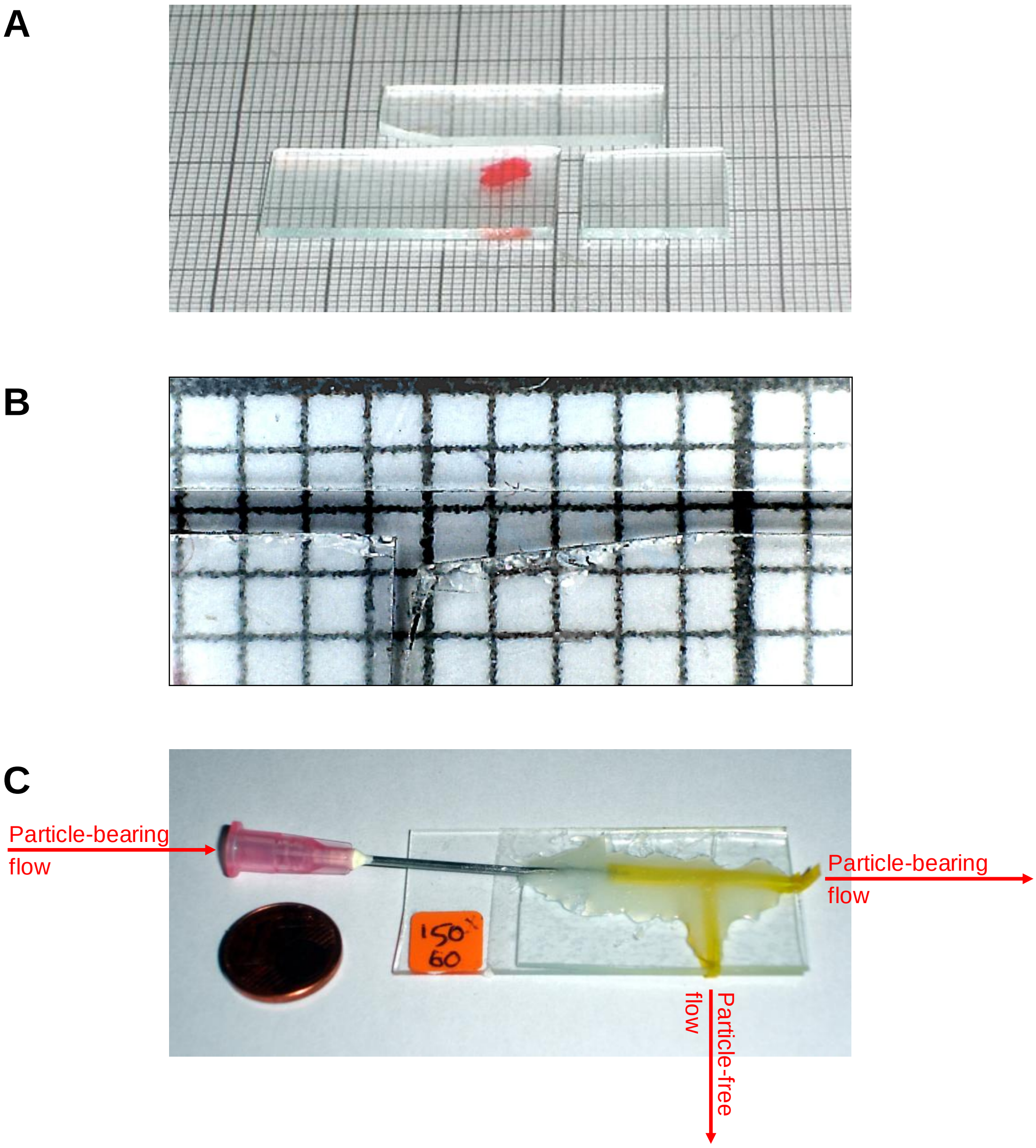


Figure 100: Construction of test piece

5.5.3 Experimental method

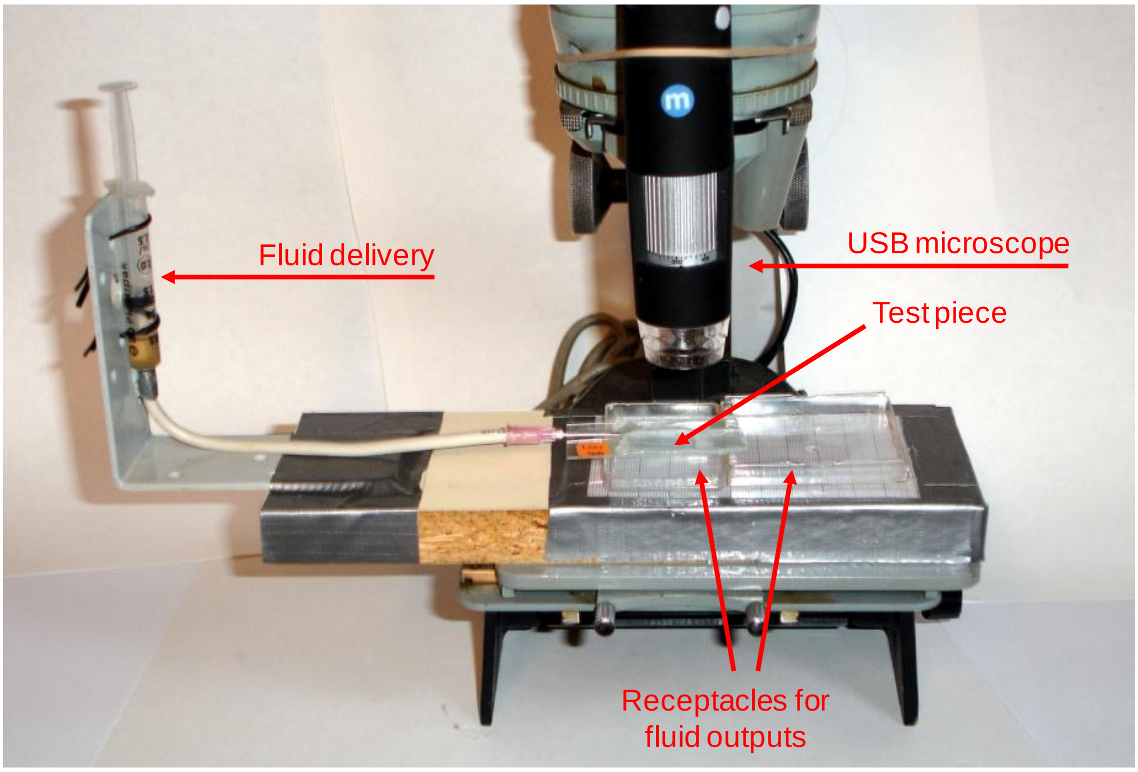


Figure 101: Test jig

The test jig was constructed around a salvaged optical microscope with a serviceable x-y table and smooth rack-and-pinion vertical adjustment. A USB microscope was substituted for the optical system.

The USB device was found to have good calibration at 20x and 400x, a resolution of ~ 1 µm at the 400x setting, and a useful software package with measurement functions.

In operation, the test fluid was loaded into the 2.5 mL syringe to the left of Figure 101, allowing easily-controlled flow of 1 mL of fluid to the test piece over a 10 second period.

The test jig also functioned as an assembly and measurement station during the construction and precision alignment of test pieces.

1 mm squared paper under the fluid output receptacles allowed estimation of the flow rate ratios between the cell and plasma outlets.

Test pieces of varied dimensions were tried, until the dimensions of Figure 98 were arrived at, providing a flow rate ratio of 10:1 between the main channel and the extraction channel. The 10:1 ratio was chosen so as not to unduly disturb the recirculation zone.

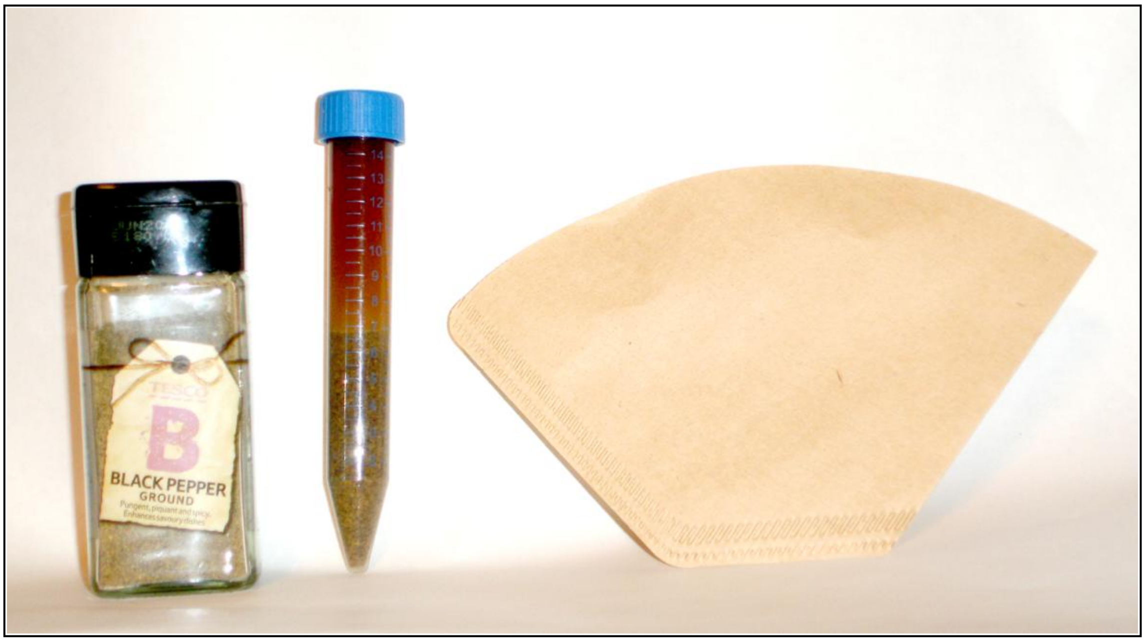


Figure 102: Preparation of test fluid

Ethical, regulatory and handling/storage considerations precluded the use of bio-fluids for this simple trial. Moreover calibrated particles such as latex or polystyrene beads proved prohibitively expensive.

Accordingly, a procedure was developed to generate a low cost fluid containing a suspension of ~ 10 µm particles.

Ground black pepper was selected because it contains finely-milled granules which do not dissolve. It was mixed approximately 50/50 with water and left overnight to settle. The resulting separation caused by the descent of the larger particles can be seen in the Figure 102 test tube.

The top fraction of liquid drawn off was found to contain particles mainly in the range 6 µm to 12 µm across, plus a few larger particles.

The larger particles were easily removed by a filter paper, which had the further advantage that it absorbed some of the liquid thus concentrating the suspension of fine particles. The particle content can be seen on the left-hand panel of Figure 103, which follows.

Note: Some other preparations were tried, as research showed that both toothpaste and hair conditioner also contain fine particles. Unfortunately they also contain surfactants and emulsifiers and so do not exhibit Newtonian flow. This method of particle separation is not suitable for such materials.

5.5.4 Results

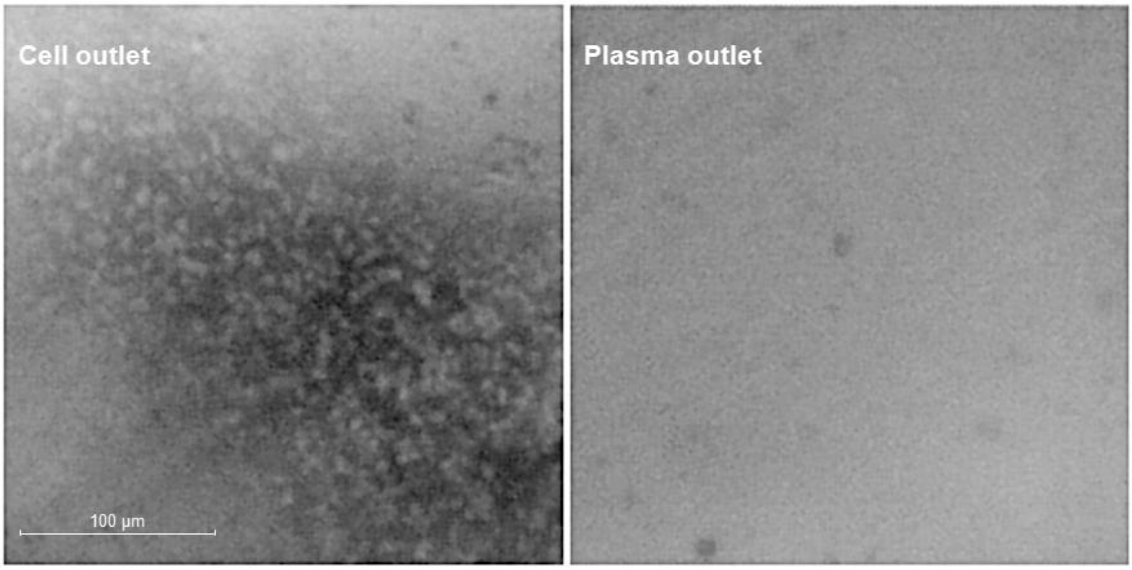


Figure 103: Comparison of outputs from cell and plasma channels

The marked separation shown in Figure 103 is clear evidence that particle-free liquid may be extracted from the recirculation zone formed within the sawtooth geometry.

Moreover:

- The 60 µm width of the extraction channel, along with its 1 mm depth, both exceeding the particle size very significantly, showed conclusively that the separation is due to fluid dynamics rather than simple filtration.
- The 1 mm depth of the channels provided a 30x increase in flow rate compared with the 30 µm depth of the simulated channels, confirming also agreement with the modelling.
- The 1 mm channel depth undoubtedly contributed to the absence of "clogging" that would otherwise result using "odd form" particles - or aggregating bio-fluids.
- The channel dimensions arrived at should not be taxing for common manufacturing processes.

It must be stressed that the experiment depicted is only to explore the concept, not an exhaustive trial which would require a large matrix of tests to thoroughly explore dimensions, flow rates, and pressure drops. Such trials might form a research project of their own, and be based upon bio-fluids under controlled laboratory conditions.

Embodiment and candidate manufacturing processes are progressed in the next section of this thesis.

5.6 Evolution and proposals for embodiment

5.6.1 Basic concept

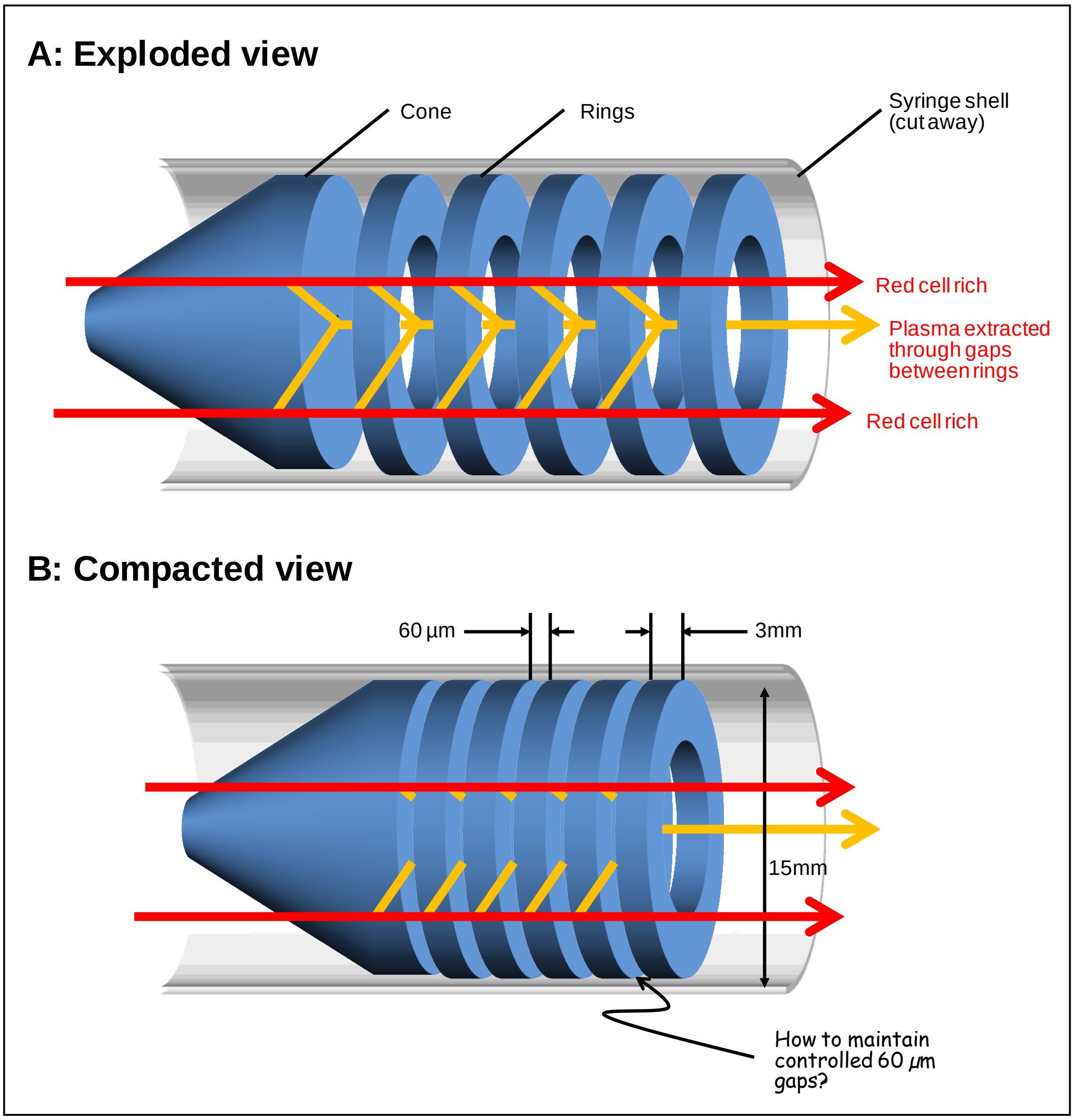


Figure 104: Basic concept of cylindrical separator

The concept illustrated in Figure 104 is an extension of the principle arrived at in Figure 78 and Figure 79 on page 139, adding a conical manifold to spread the incoming fluid around the annular channel formed between the periphery of the rings and the syringe body, and introducing multiple stages of separation.

The compacted view, not to scale, raises the question of how to maintain the 60 µm separation between the rings to emulate the 60 µm width of the extraction channel determined by experiment in section 5.5.3.

5.6.2 Evolving the spacers and flow control

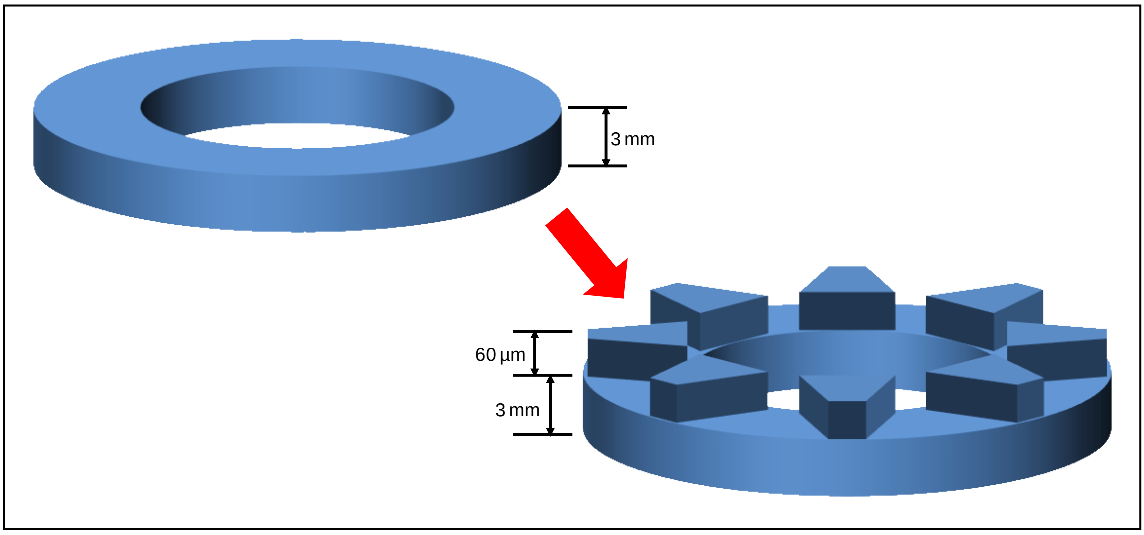


Figure 105: Adding spacers

Adding spacers to define the gaps between separator disks, as shown in Figure 105 (scales exaggerated for clarity), will also impede flow. This may be used to advantage through thoughtful design.

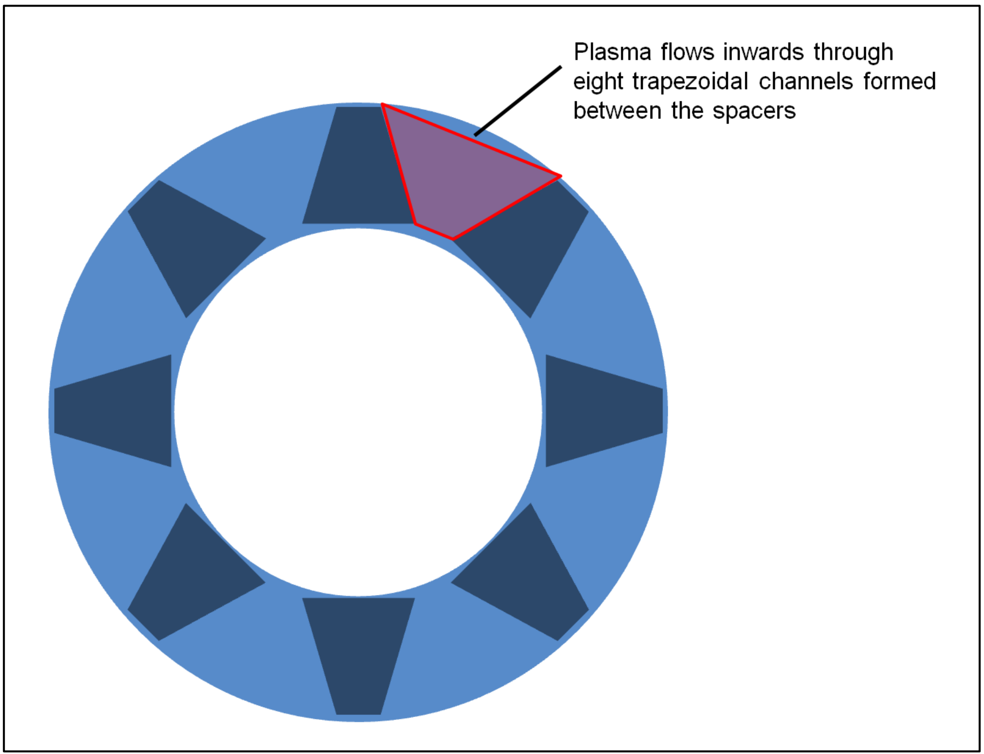


Figure 106: Plan view of spacers and formation of trapezoidal channels

In plan, the spacers form trapezoidal channels whose geometry can be adjusted to increase the flow resistance without increasing the length of the channel. The procedure is similar to that described in section 5.4.6 “Insight from analogue: sheet resistance” on page 149.

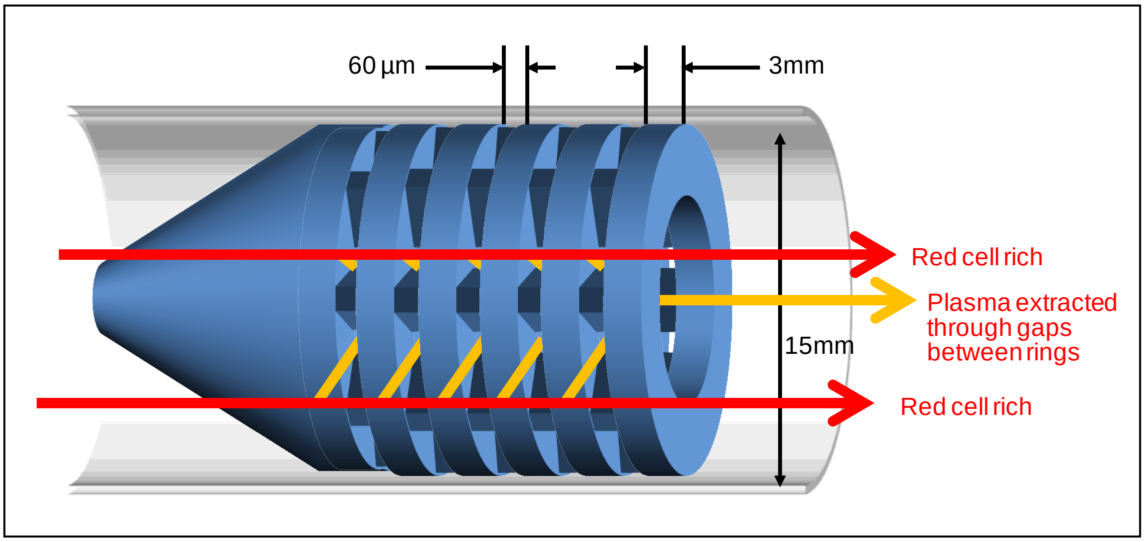


Figure 107: Cylindrical separator with trapezoid spacers

5.6.3 Incorporating the sawtooth improvement

The final evolution of the separator considered here concerns exploiting the sawtooth recirculation zone geometry introduced in section 5.5.1.

Particle-free fractions of a particle-bearing main stream may be drawn from the relatively motion-free recirculation zones formed by the vertical leading edges of the sawtooth geometry, as illustrated in Figure 97, this time the sawtooth being defined by bevelling of the separator rings (bevel exaggerated in Figure 108):

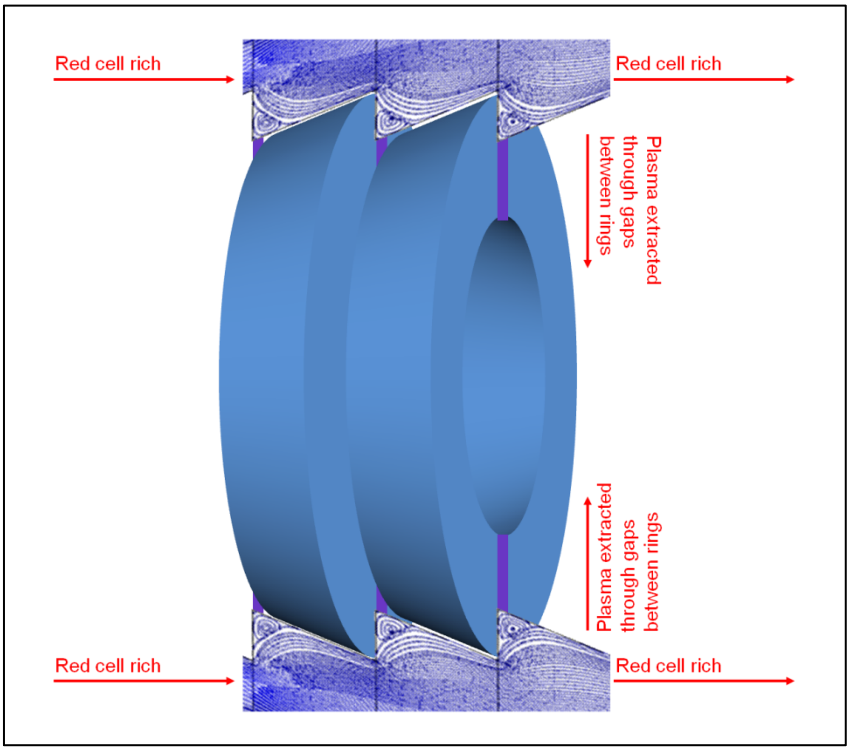


Figure 108: Sawtooth recirculation zones formed by bevelled separator rings

Adding trapezoid spacers forms the finalised stackable component illustrated in Figure 109.

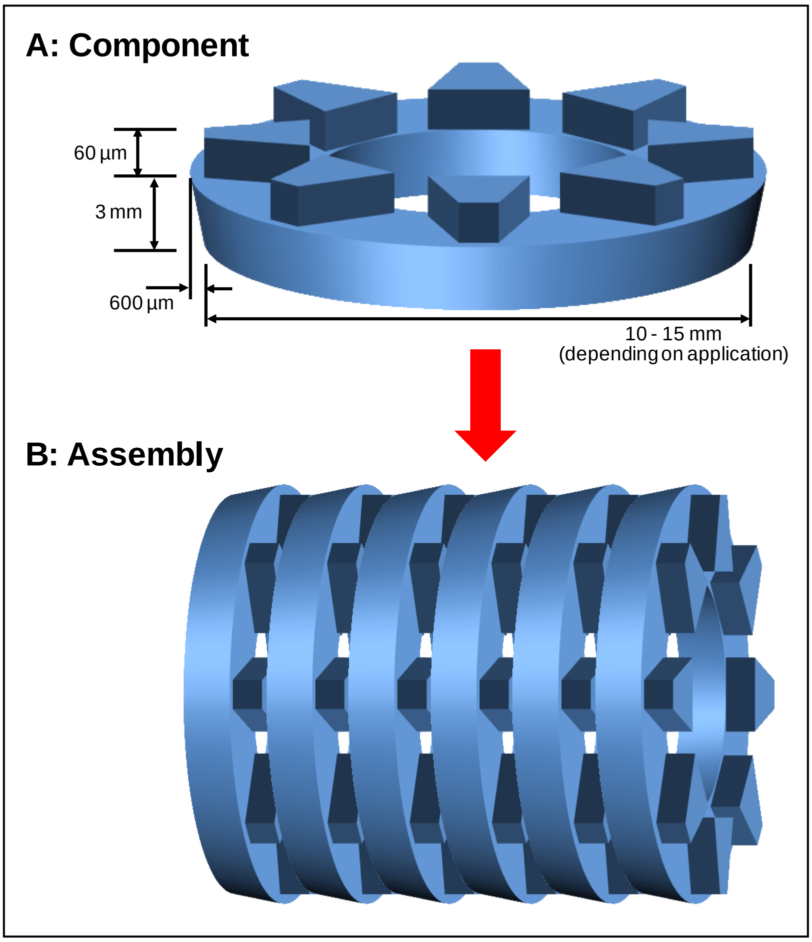


Figure 109: Bevelled separator component and assembly

5.6.4 Proposals for embodiment

The component of Figure 109 is a simple shape that would lend itself to fabrication in many materials, including thermoplastics and thermo-sets, glasses, ceramics, and metals. The choice would depend on use (typically disposable), cost, bio-compatibility, environmental and disposal/re-use considerations.

Whichever, fabrication of the disks could be achieved easily through:

- Injection moulding
- Transfer moulding
- Casting
- Stamping/embossing/coining
- Micro machining

The stackable nature of the components allows for easy assembly into a cylindrical body without adhesives or other joining materials, thus avoiding extra costs and potential bio-compatibility problems, whilst maintaining the ~100 µm critical dimensions:

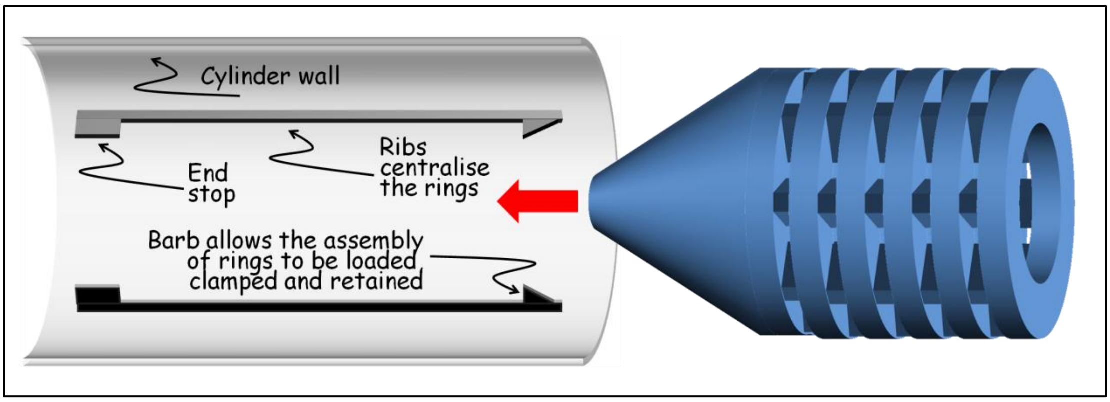


Figure 110: Proposed assembly method

5.7 Analysis of the in-practice design study

5.7.1 Practical involvement

Although the in-practice design exercise was primarily desk-based and cerebral, the need to commission and interpret computer modelling and the challenge of devising and conducting physical testing compelled a level of involvement that to a degree reproduced the drives of a real-life design and prototyping activity.

Following the discipline of generating a requirements list, crystallising the essential problems and selecting an appropriate physical principle to solve the essential problems worked efficiently in practice.

Alternative geometric transformations from the physical principle to create candidate product configurations was revealing, including an observation that an adroit choice of the axis of rotation could radically affect the outcome of the transformation.

A simplified modelling regime restricted the intensity of this activity to a level commensurate with the “look see” nature of the in-practice study, but nevertheless provided indications for geometry improvements that proved viable by physically testing prototype components.

Diagrams featured strongly during all phases of the study. Their evolution contributed strongly to the proposed embodiment that was one outcome of the exercise, the other being the confirmation that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures that would not readily be arrived at intuitively.

5.7.2 Word frequency

The frequency of individual words used to record the in-practice design study in Chapter 5 (excluding this analysis section, 5.7) was employed to provide a dispassionate measure of activity. Figure 111 lists the frequency of word use after omitting the definite and indefinite articles and other common words:

Figure 111: Words used to record the in-practice design study

First 25 words by frequency			**Second 25 words by frequency**	
Frequency	**Word**		**Frequency**	**Word**
71	flow		13	transformation
51	blood		13	principle
46	channel		13	illustrated
37	separation		13	fluid
37	modelling		13	extraction
36	cell		13	dimensions
35	separator		12	velocity
31	design		12	study
31	collection		12	point
27	rate		12	particles
27	plasma		11	problems
22	functional		11	rotation
22	concept		11	product
21	method		10	zone
21	diagram		10	sawtooth
20	channels		10	process
18	syringe		10	parameters
18	sample		10	insight
17	needle		10	embodiment
16	test		10	device
15	resistance		9	width
15	recirculation		9	volumetric
15	particle		9	volume
15	geometry		9	disk
14	manifold		9	step

Some observations from the lists of Figure 111 are as follows:

- The first 25 words, ranked from highest frequency of use to lowest, are predominantly product based in line with the subject of this thesis
- The second set of 25 words is in the main associated with actions and parameters used to resolve the design issues around the product.
- “Diagram” features relatively high on the list, reflecting its central position in the formation, communication and evolution of ideas.

- “Transformation” heads the second set of 25 words, which tend to relate to design activities.

- The most frequently used word, “flow”, suggests that this (invisible) phenomenon attracted the greatest attention

The above can only constitute a crude examination. The following section 5.7.3 provides a finer analysis of the interchange of facts and ideas.

5.7.3 Analysis of design communications

Figure 112 tabulates an analysis of the communication of intelligence noted during the in-practice design process, according to the categories arrived at in section 2.4.1.2 of this thesis, and as illustrated in Figure 7, seen in context on page 38 but reproduced here for convenience:

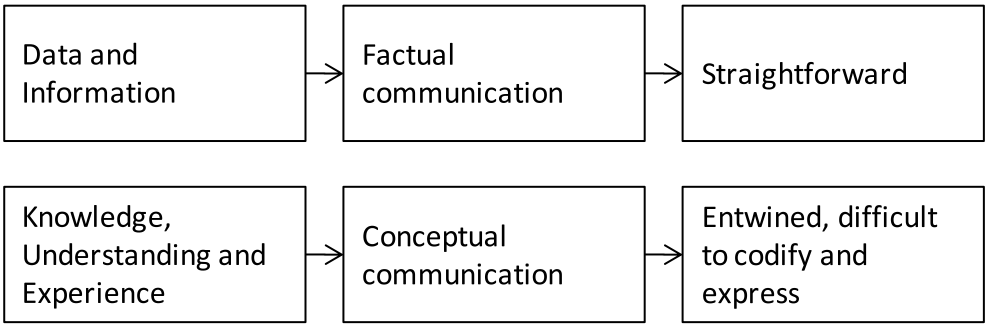


Figure 7: Parallel streams of design communication

As an overview, the frequency of the noted exchanges as listed in Figure 112 is as follows:

Section 5.1, Design specification: 8 exchanges

Section 5.2, Selecting the physical principle and 3D transform: 30 exchanges

Section 5.3, Developing the concept: 8 exchanges

Section 5.4, Insight and support from modelling: 14 exchanges

Section 5.5, Practical trial: 12 exchanges

Section 5.6, Evolution and proposals for embodiment 10 exchanges

Evidently the selection of the physical principle and the 3D transformation concept, both foci of this thesis, were the centre of gravity for the communication of intelligence.

Figure 112: Analysis of design communications		**Factual communication**		**Conceptual communication**		
Reference	**Description**	**↓Data**	**↓Information**	**↓Knowledge**	**↓Understanding**	**↓Experience**
5.1.1.1	Narrative of design objectives			X	X	
5.1.1.2	Narrative of required properties			X	X	X
5.1.1.3	Narrative of properties to avoid			X	X	X
Figure 68	Diagram: Structure of a syringe	X	X			
5.1.2.1	Narrative of essential problem: sample collection			X		
5.1.2.2	Narrative of essential problem: manifold			X		
5.1.2.3	Narrative of essential problem: separation			X		
5.1.2.4	Narrative of essential problem: power and control			X		
5.2.1	Data input for computer modelling	X				
5.2.1	Data output from computer modelling	X				
5.2.1	Narrative of blood sampling experience					X
5.2.2	Narrative of syringe plunger and evacuated tube operation			X	X	
Figure 70	Introduction of electrical analogue: R_{Needle} >> ($R_{Manifold}$ + $R_{Separator}$)			X	X	X
5.2.3	Data input from 5.2.1 and 5.2.2, collection and control decisions	X				
5.2.3.1	Narrative choices of functional principles from Figure 21				X	
5.2.3.1	Flow rata data from Figure 21	X				
5.2.3.1	Flow rate maxima from cytometric study recounted in [63]	X	X			
5.2.3.1	Calculation of number of separators needed for designed flow	X	X			
5.2.3.2	Narrative regarding matrix of separators	X	X			
Figure 72	Conceptual depiction of separator matrix			X	X	
5.2.3.2	Declaration regarding cost, complexity and reliability					X
5.2.3.3	Critique of the arrangement shown in Figure 72					X
5.2.3.3	Case (A) estimate of required width	X	X			
Figure 18	Conceptual depiction of extruded separator			X	X	
Figure 73	Conceptual depiction of manifold					X
5.2.3.3	Case (A) comments regarding the arrangement shown in Figure 73					X
5.2.3.3	Case (B) reasoning behind extraction surrounding the main channel			X	X	
Figure 74	Conceptual extension of rotation concept			X	X	
Figure 75	Conceptual extension of rotation concept			X	X	
5.2.3.3	Case (B) calculation of number of separators to meet designed flow	X	X			
Figure 76	Further extension of rotation concept			X	X	
5.2.3.3	Case (B) comments regarding the arrangement shown in Figure 76					X
Figure 77	Change of rotational axis			X	X	
Figure 78	Conceptual depiction of rotated(2) separator, paired with Figure 79			X	X	
5.2.3.3	Case (C) dimensions to match the performance of Case (A)	X	X			
5.2.3.3	Case (C) declaration regarding manufacturability					X
5.2.3.3	Case (C) suggestion for integration into standard syringe format			X	X	X
Figure 1	Conceptual model syringe			X	X	
Figure 35	Embodiment of Case A transformation			X	X	
Figure 80	Embodiment of Case B transformation, paired with Figure 81			X	X	
Figure 82	Conceptual depiction of plunger actuated separator			X	X	
Figure 83	Development of plunger actuated separator			X	X	
5.3.2	Case (B) geometry and dimensions supplied to researchers	X	X			

Figure 112 Continued		**Factual communication**		**Conceptual communication**		
Reference	**Description**	**↓Data**	**↓Information**	**↓Knowledge**	**↓Understanding**	**↓Experience**
Figure 84	Development of vacuum actuated separator			X	X	
5.3.3	Case (C) geometry and dimensions supplied to researcher	X	X			
5.3.3.2	Case (C) declaration regarding prospect for successful exploitation					X
5.4	Declaration regarding computer aided design					X
5.4.1	Declaration regarding modelling the behaviour of whole blood			X	X	
5.4.2	Defining the approach to modelling			X	X	
5.4.3	Briefing the modelling team	X	X	X	X	X
5.4.4	Determining the parameters governing the fluid handling	X	X			
5.4.4	Determining the environment survived by red blood cells	X	X			
5.4.4	Determining the separation process	X	X	X	X	
5.4.5	Correlation between Figure 88 and Figure 86	X	X			
5.4.6	Identify analogue based upon sheet resistance			X	X	X
5.4.6	Calculate example based upon sheet resistance	X	X			
5.4.7	Consideration of “step” versus “constriction”			X	X	
5.4.7.1	Briefing the modeller	X	X	X	X	X
5.4.7.2 - 4	Feedback from the modeller	X	X			
5.4.7.5	Evaluation of feedback	X	X			
5.5	Selection of objectives for experiment				X	
5.5.1	Staircase to sawtooth transformation				X	X
5.5.2	Devise experimental approach				X	X
Figure 98	Dimensioned test piece	X	X			
Figure 99	Assembly sequence			X		
Figure 100	Construction of test piece			X		
5.5.3	Experimental parameters	X				
Figure 101	Construction of test jig			X		
Figure 102	Preparation of test fluid			X		
5.5.3	Parameters of test fluid	X				
Figure 103	Comparison of outputs from cell and plasma channels	X	X			
5.5.3	Statements regarding experimental results	X			X	
5.6.1	Basic concept of cylindrical separator	X	X			
Figure 104	Basic concept of cylindrical separator				X	
5.6.2	Insight into flow control				X	X
Figure 105	Configuration of spacers	X	X			
5.6.2	Insight into trapezoidal channels				X	X
Figure 106	Depiction of trapezoidal channel	X	X			
Figure 107	Depiction of cylindrical separator with trapezoid spacers	X	X			
5.6.3	Evolution of sawtooth geometry into 3D				X	
5.6.4	Statements regarding simplicity and manufacturability				X	X
Figure 110	Explanation of assembly method				X	

5.7.3.1 Intensity of exchanges regarding modelling

Only two rows in Figure 112 record communication embracing all of the 5 categories Data, Information, Knowledge, Understanding and Experience:

- 5.4.3 Briefing the modelling team
- 5.4.7.1 Briefing the modeller

This probably reflects the breadth of communication demanded to initiate and discuss the modelling process, which involved parameters, physical principles, case histories and observations and examples from other fields.

5.7.3.2 Factual communication: Data and Information

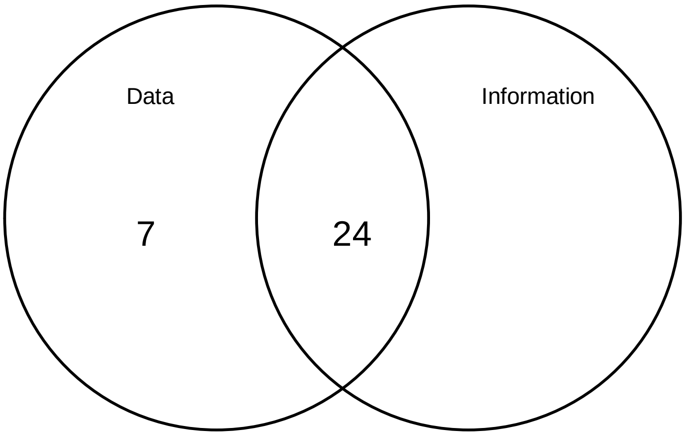


Figure 113: Exchanges regarding Data and Information

- As *information* is described in [27] as "structured data [including] what is said or recorded", it should be no surprise that in the Venn diagram of Figure 113 all the information communications included data.

- Conversely *data* communications relate to facts and quantities, and may on their own contain no additional structure. Referring to Figure 112, solely data communications were typified by parameters provided for modelling and the construction of test pieces.

- During the in-practice design exercise raw data communications represented just less than one quarter of all factual communication, put another way, some 75% of factual communications incorporated structured data in some supporting context.

- Factual communications amounted to some 38% of all communications.

5.7.3.3 Conceptual communication: Knowledge, Understanding and Experience

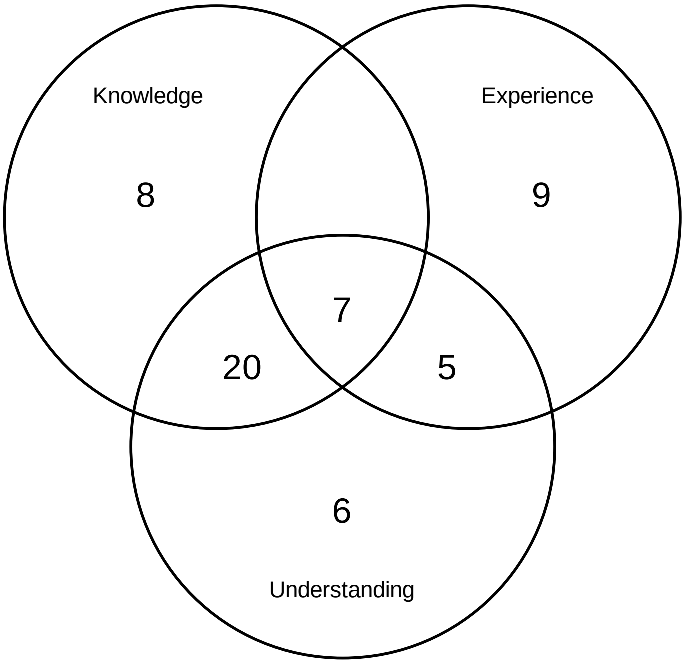


Figure 114: Exchanges regarding Knowledge, Understanding and Experience

- As *understanding* is delineated in [27] as “...human cognitive processes through which associations and inferences can be used to apply knowledge appropriately”, there is no surprise that over one third of the 55 conceptual communications combined knowledge and understanding.

- Pure experience counted almost equally with purely knowledge-based communications, but combinations of the two only occurred together with understanding.

- Conceptual communications accounted for some 62% of all communications, which appears in keeping with the conceptual nature of the in-practice study.

5.7.4 Product outcomes

The in-practice design study resulted in a product proposal for a Novel Red Blood Cell / Plasma Separation Device with the advantages of:

- Simple, familiar, operation at the point of care.

- Sample collection at a comfortable rate, with little chance of disruption by clogging.

- Preservation of body temperature to avoid clotting of the sample, and obviating the need for stabilizing additives.

- Elimination of delays and contamination that could be caused by laboratory transfers.
- Simplicity of parts, with dimensions and tolerances to allow easy, low cost, manufacture.

At October 2015 the product concept appears to be unique, confirming that the geometric transformation process can lead to the design of functional structures which would not readily be arrived at intuitively.

Figure 115 provides a comparison between planar approaches to the product and the 3D transformed approach, the concept to be tested and examined by this thesis.

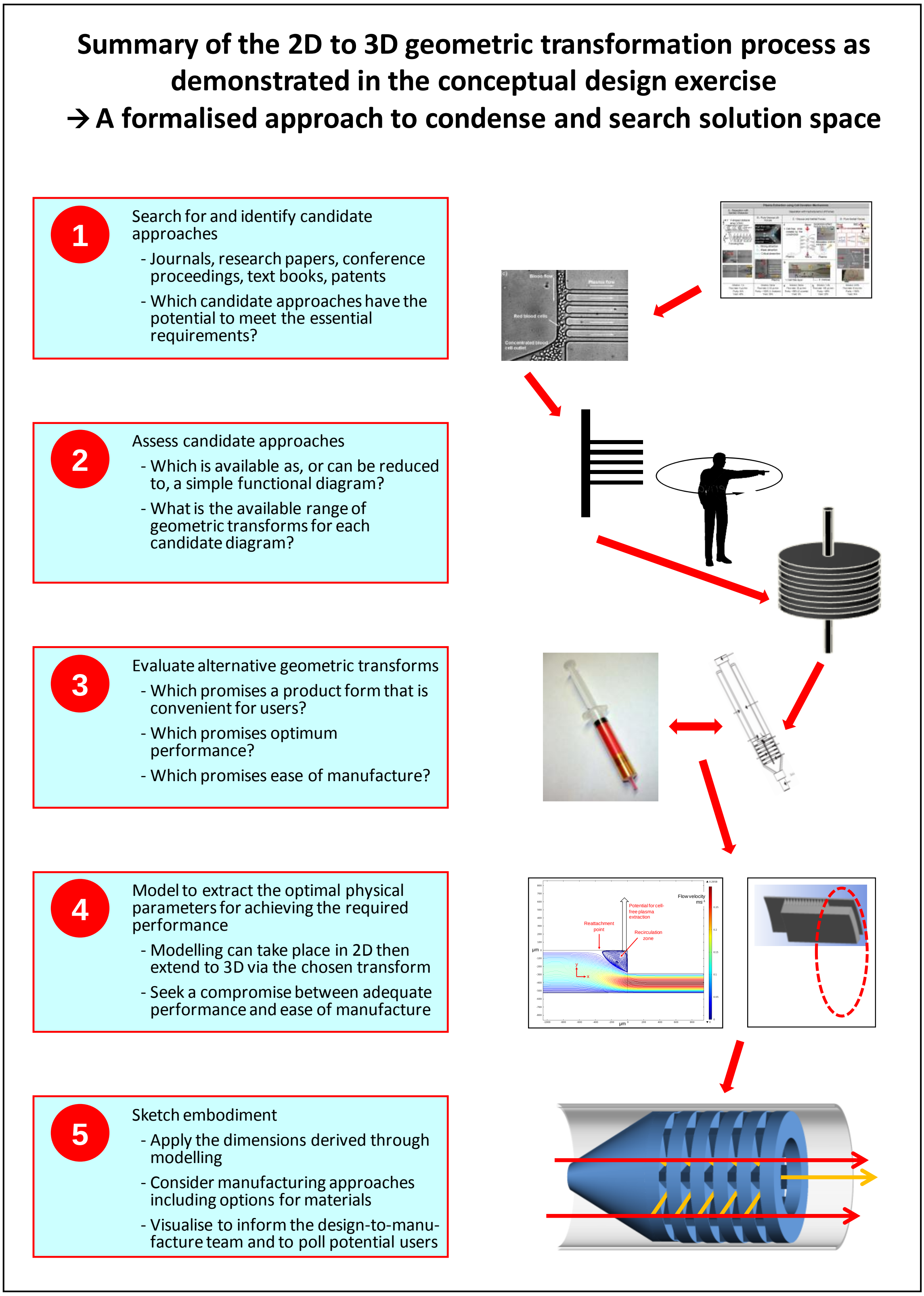
Figure 115: Comparison between planar and 3D transformed approaches

Planar approach	3D transformed approach
The limited throughput of planar devices requires many devices in parallel	One simple device can be scaled to provide almost any required throughput
Complex manifolds are required to connect many devices in parallel	A simple cone-shaped component serves as a manifold to disperse the fluid
Long fine channels are required to limit the flow of extracted plasma	3D construction provides an extra degree of design freedom to control fluid flow
Channels are both narrow and shallow, and therefore prone to clogging	Only one narrow channel dimension, which allows particles to bypass obstructions
Difficult to integrate complex networks of devices into products	Integrated by designing in tandem with the final product
Limited to mimicking a 2D functional diagram	Geometric transforms can result in beneficial non-intuitive creations

The relevance of the product is underlined by its addressing a prime challenge identified by Kersaudy-Kerhoas and Sollier [56], who observe that the “lab-on-a-chip” research community has concentrated upon the analysis of sample volumes in the microlitre range, relevant when the target is highly concentrated, whereas in the case of many applications, such as the amplification of rare circulating DNA from plasma, a blood drop does not contain a meaningful quantity of analyte. They state that *“In these cases, volumes in the range of millilitres are more relevant, and are collected by venous puncture (1–50 mL), but few commercially viable solutions have been proposed for these samples.”*

5.8 Collation of Chapter 5 findings

This chapter records practice-based research to investigate the concept, one of the twin foci of this thesis, that theoretical 2-dimensional diagrams may be converted into functional 3-dimensional working structures through the type of geometric transforms used by graphic designers to generate solid objects from 2-dimensional prototypes.



Summary of the 2D to 3D geometric transformation process as demonstrated in the conceptual design exercise
→ A formalised approach to condense and search solution space

1 Search for and identify candidate approaches
- Journals, research papers, conference proceedings, text books, patents
- Which candidate approaches have the potential to meet the essential requirements?

2 Assess candidate approaches
- Which is available as, or can be reduced to, a simple functional diagram?
- What is the available range of geometric transforms for each candidate diagram?

3 Evaluate alternative geometric transforms
- Which promises a product form that is convenient for users?
- Which promises optimum performance?
- Which promises ease of manufacture?

4 Model to extract the optimal physical parameters for achieving the required performance
- Modelling can take place in 2D then extend to 3D via the chosen transform
- Seek a compromise between adequate performance and ease of manufacture

5 Sketch embodiment
- Apply the dimensions derived through modelling
- Consider manufacturing approaches including options for materials
- Visualise to inform the design-to-manufacture team and to poll potential users

Figure 116: Design steps based upon transforming a 2D functional diagram
(Illustrations adapted from Figures 1, 21, 26, 74, 84, 87, 92 and 104)

The summary set out in Figure 116 of necessity omits some of the detail of design – the inevitable iterations, the sparks of inspiration triggered by the unexpected geometries generated by various transforms (for example, 5.4.6 leading to 5.6.2) and revelations from modelling providing avenues for performance enhancements and efficiencies in manufacture (as reported in 5.4.7.4, 5.5.1 and 5.6.3).

Background from literature regarding the process as a whole is recorded in section 2.6, commencing on page 55. The work recorded in Chapter 5 examined the concept and its benefits by following and recording a worked design example: the Development of a Novel Red Blood Cell / Plasma Separation Device.

The worked design example also provided insight into the second focus of this thesis: the interpersonal difficulties arising in the concept-to-embodiment process when concerned with principles, objects and effects in 3 dimensions which are beyond everyday human experience.

This practice-based research pursued a disciplined sequence of generating a requirements list, crystallising the essential problems, selecting in diagrammatic form an appropriate physical principle to solve them, then applying, as conceived, a geometric transformation to the diagram to create a functional product configuration for modelling, physically testing and evolving for embodiment. The activity provided evidence that supports the following:

5.8.1 Geometric transformation

Regarding the concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures using procedures allied to those used by graphic designers to create solid objects:

- Once the requirements list of 5.1.1 and identification of essential problems of 5.1.2 had been completed, the selection of the geometric transform was found to be a powerful tool to marry the theoretical physical principle of operation into the practical requirements of the solutions to the essential problems.

  Normally a design team would need to search either previous cases or to embark upon a new stage of development to achieve this integration. The geometric transform technique provided a formalised approach in this respect, reducing the search to the trial and selection of a form-fitting transform from a relatively small set of rules.

Regarding the notion that the geometric transformation process can lead to the design of functional structures which would not readily be arrived at intuitively, and that may be effectively and efficiently integrated into host products:

- The rotational transform selected provided two alternate solutions as described in 5.3.2

and 5.3.3 respectively. A further degree of design freedom, the ability to choose the axis of rotation, produced a structure which promised much higher separation throughput, through a geometry that would be difficult to conceive of in any other way.

A further benefit of the 3D transform came to light during the evolution of the design towards embodiment, allowing the use of a further degree of design freedom to control fluid flow by means of the trapezoidal spacers described in 5.6.2

- The chosen transformation married the cylindrical form of the generated separator to match and integrate into the cylindrical form of typical blood sample collection devices - marrying function to form, rather than form to function.
- Product related benefits of the transformation technique are tabulated in Figure 115.

5.8.2 Communicating the intangible

Regarding the issues of conversing physical principles which are beyond everyday experience:

- According to the word frequency list, Figure 111, the most frequently used word, “flow”, suggests that this (invisible) phenomenon attracted the greatest attention during the design process.
- The design method, through its basis upon a common currency of functional diagrams and an easy-to-describe geometric transformations, proved easy to discuss with colleagues rather than the alternative of describing the workings of constructions devised from a hierarchy of building blocks which in turn would require explanation.
- Working from a fundamental diagram of function facilitated debate through reducing the need for shared practical experience.

5.8.3 Experiences from modelling

Regarding further issues of conveying the intangible:

- As described in 5.4.3, a “duality” of thinking evolved as the operating principle “roots” of the geometry to be modelled were revealed when 3D examples were “flattened” to reduce computational complexity, followed by the reconstruction of the object - and its internal workings - through the reverse procedure.
- *In principle, in designs based upon geometric transforms, the basis of this thesis, modelling can start with the underlying 2D functional diagram itself.*

- Very simplified models proved eminently sufficient for establishing the basic parameters for the product concept and moreover provided insight and a stimulus for further evolution of the product.

Regarding the intensity of communication:

- All of the methods of expression discussed in section *2.5: 2D representations used in the design of 3D objects* came into play.

- As analysed in Figure 112, to brief the modelling team, and also to evaluate the outcomes, all the streams of communication foreseen in Figure 85 were used.

Regarding improvements to the design:

- The answer to question 3 of 5.4.7.1 “What happens when steps are stacked?” was both revealing and surprising. Following evaluation of the geometry by the experiment of 5.5, the development was introduced into the design evolution in 5.6.3.

5.8.4 Testing and product evolution

Regarding the practical test:

- The test piece geometry was generated from the functional diagram by extrusion vertically. Accordingly the tests not only confirmed the behaviour predicted by modelling, they also confirmed that the throughput could be extended through a geometric transform whilst preserving the separation capability.

Regarding product evolution:

- Commencing from the rotational transform of a functional diagram facilitated the generation of illustrations which stimulated thought and could with ease become working designs for prototype production.

5.8.5 Modes of expression

- Over 40 function/product diagrams were used in the recording of the undertakings of Chapter 5, underlining the fundamental power of diagrams and geometry to convey product conception and evolution.

- “Diagram” and “transformation” feature relatively high on the word frequency lists, Figure 111, reflecting their central position in the formation, communication and evolution of ideas.

- The careful definition of Data, Information, Knowledge, Understanding and Experience into two streams, “Factual” and “Conceptual”, derived in 2.4.1.7 proved valuable in the cataloguing and analysis of intelligence exchanges undertaken in 5.7.3.

- From Figure 113, factual communications amounted to some 38% of all communications, with most of them incorporating structured data - ie “information” - in some supporting context. As seen in Figure 112, data communications devoid of structure were typically those providing parameters for modelling and the test pieces.

- A further analysis of Figure 114 shows that exchanges containing “Understanding” rank highest, with 38 exchanges, almost matched by the 35 exchanges containing “Knowledge”. The number of exchanges containing “Experience” was significantly lower, at 21, possibly reflecting the lower applicability of experience in a nascent field.

- Again from Figure 114, conceptual communications accounted for some 62% of all communications, which corresponds to the conceptual nature of the in-practice study.

- The analysis by topic revealed, with 30 exchanges, the central importance of *Selecting the physical principle and 3D transformation concept*, both foci of this thesis.

5.8.6 Achievements and limitations of the product development

Regarding the product concept and its evolution:

- Although the work resulted in a feasible product concept capable of meeting the requirements stated in 5.1.1.1, 5.1.1.2 and 5.1.1.3 no study or representation has been made, or implied in any way, as to the safety, standards or legislative matters that might apply to the use of the design or derivative products.

- Exploring and testing the concept was not exhaustive. A large matrix of more precise modelling and tests would be required to thoroughly explore dimensions, flow rates, and pressure drops. This might form a dedicated research and development project, based upon bio-fluids under controlled laboratory conditions, followed by the production of prototypes for clinical trials.

Regarding the geometric transformation concept:

- As reflected in the title of the thesis, the work explored the application of the transformation concept to just one product, utilising just one physical principle. Although three distinct transformations were considered, more do exist, such as coiled tube helices, which are beyond the scope of this thesis.

Chapter 6 Discussion and conclusions

This research has delivered two significant contributions, *Outcome 1* being “Improvements to the concept-to-embodiment process” (Figure 117 “B”), *Outcome 2* being “The evolution of a Red Blood Cell / Plasma Separation Device” (Figure 118 “B”). These primary contributions are accompanied by some useful *additional* research outcomes.

In the course of generating the outcomes the work has identified and tackled many of the obstacles that impede the conceptual design process when it is tasked with integrating micro-enabled functionality directly into 3-dimensional products.

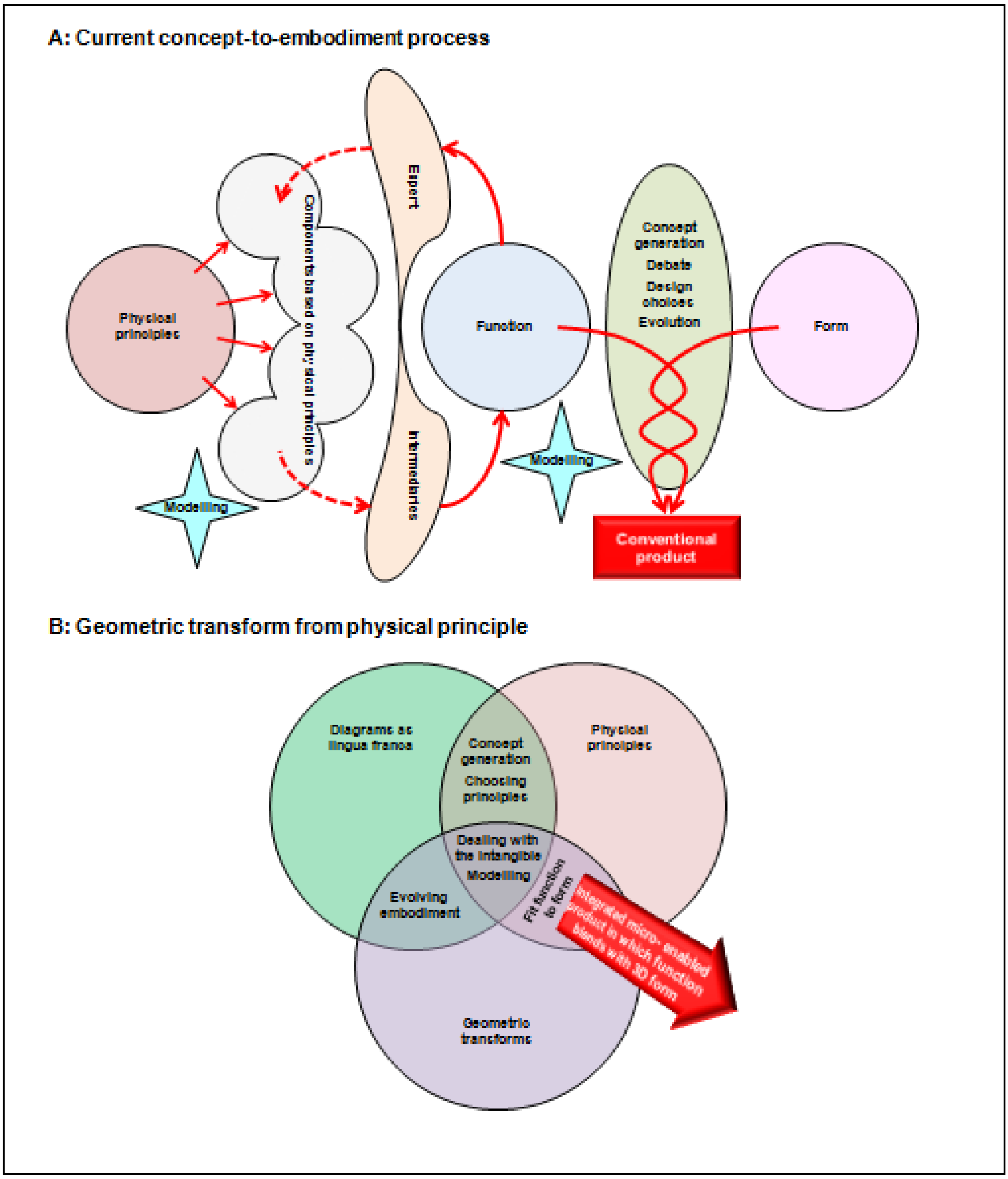
The twin foci of the research were:

- Studying the interpersonal difficulties of conversing about the intangible when product designers need to choose and use principles which are beyond everyday human experience, and the degree to which designers depend upon expert intermediaries.
- Examining, testing and assessing the interpersonal and engineering benefits that could arise from using the concept that theoretical 2-dimensional diagrams of function may be transformed into 3-dimensional working structures, investigated through the practical evolution of a novel Red Blood Cell / Plasma Separation Device.

Improving the capability of designers to integrate micro- enabled functionality into 3D products has become important in order to link and exploit recent progress in the understanding of functionality at the micro- scale with advances in manufacturing, which is finally breaking away from its entrenched capital-intensive planar approach.

The remaining sections of the current chapter comprise:

- Discussion regarding the primary elements that can improve the concept-to-embodiment process, as illustrated in Figure 117 “B” overleaf with an appended short description.
- Discussion regarding the evolved Red Blood Cell / Plasma Separation Device, as illustrated in Figure 118 “B” on page 180, again with an appended short description.
- Additional research outcomes.
- For each of the research outcomes an assessment is provided concerning their application, limitations, and prospects for further development.


A: Current concept-to-embodiment process

B: Geometric transform from physical principle

Figure 117: Improving the current concept-to-embodiment process

The current concept-to-embodiment design process, as shown in “A” above, can be somewhat fragmented, with the design team squeezed between the demands of form and function, and insulated from the underlying physical principles by the lens of expert intermediaries and component devices that shroud their inner workings.

“B” illustrates the seamless design process integration that can result from the diagram-based direct transformation of physical principles to the desired 3D form of the product, together with discussion and modelling, all linked by the lingua franca of diagrams.

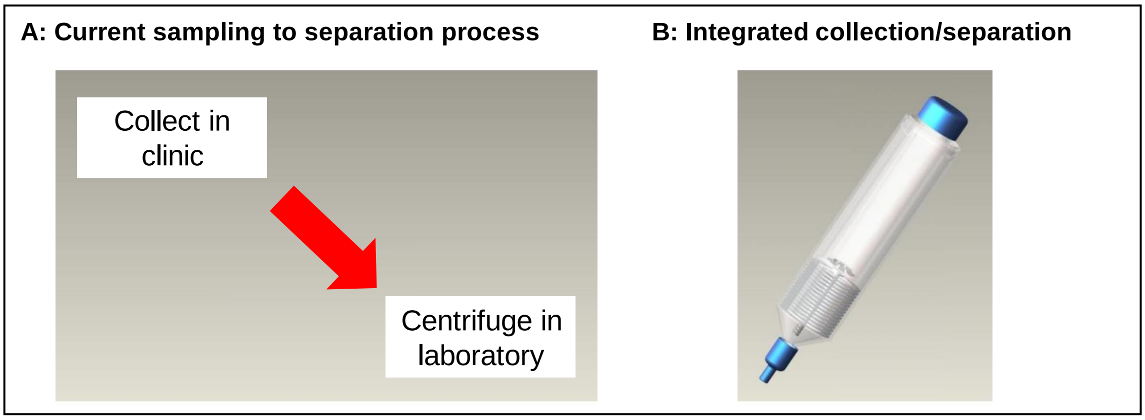


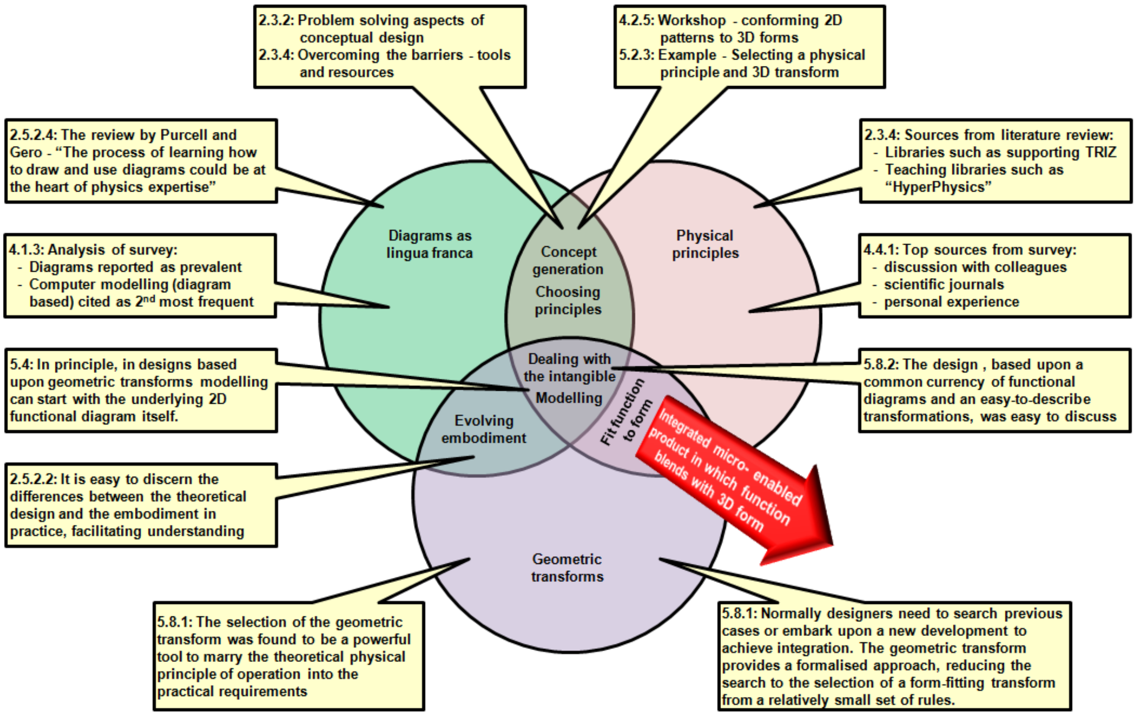
Figure 118: Improving the blood sampling and plasma separation process
(Right hand visualisation adapted from Katy Jenkins "Blood Separation Syringe: DM3306 Major Project Report")

The depiction of the current process in Figure 118 "A" omits important detail in that (1) the laboratory is typically remote from the point of care, and that (2) as a consequence the blood has to be treated so that it does not deteriorate on the journey, and (3) there are opportunities for contamination, delays and mistakes.

The device portrayed in Figure 118 "B", conceived from the 3D transformation of a 2D diagram of physical principle, integrates the sample collection and plasma separation at the point of care, allowing the blood to remain stable at body heat, and avoiding contamination, delay and error.

6.1 Outcome 1: Improvements to the concept-to-embodiment process

It is necessary to appreciate that the set of improvements depicted in the Venn diagram of Figure 117 "B" on page 179, and also below, do not constitute a "tool box" as such, or a fixed procedure. The diagram is intended to illustrate how the duo of physical principles and geometric transforms share a common basis of diagrammatic expression, and that this common "lingua franca" can further facilitate the communications aspects of debate, modelling and evolution to embodiment, especially when the product is enabled by mechanisms normally intangible and therefore outside the shared human experiences that usually form a basis for understanding.



2.3.2: Problem solving aspects of conceptual design
2.3.4: Overcoming the barriers - tools and resources

4.2.5: Workshop - conforming 2D patterns to 3D forms
5.2.3: Example - Selecting a physical principle and 3D transform

2.5.2.4: The review by Purcell and Gero - "The process of learning how to draw and use diagrams could be at the heart of physics expertise"

2.3.4: Sources from literature review:
- Libraries such as supporting TRIZ
- Teaching libraries such as "HyperPhysics"

4.1.3: Analysis of survey:
- Diagrams reported as prevalent
- Computer modelling (diagram based) cited as 2nd most frequent

4.4.1: Top sources from survey:
- discussion with colleagues
- scientific journals
- personal experience

5.4: In principle, in designs based upon geometric transforms modelling can start with the underlying 2D functional diagram itself.

5.8.2: The design, based upon a common currency of functional diagrams and an easy-to-describe transformations, was easy to discuss

2.5.2.2: It is easy to discern the differences between the theoretical design and the embodiment in practice, facilitating understanding

5.8.1: The selection of the geometric transform was found to be a powerful tool to marry the theoretical physical principle of operation into the practical requirements

5.8.1: Normally designers need to search previous cases or embark upon a new development to achieve integration. The geometric transform provides a formalised approach, reducing the search to the selection of a form-fitting transform from a relatively small set of rules.

Figure 119: Selected contributions to improvements in the design process

Figure 119 shows how selected background and findings from the literature review and the interpersonal and practical research streams support each element of the improvements that may be brought about by the duo of physical principles and geometric transforms. These selections are only a small representative sample of the greater body of work recorded in this thesis, notably in the collations of findings in sections 2.8, 4.4 and 5.8.

Application and limitations The application of the elements comprising *Outcome 1* may prove to be of use beyond the original target of the integration of micro- enabled functionality. It is however likely to be most effective in the technology/product maturity space just beyond "blue sky" but not yet pilot-scale manufacture. This is the niche where revolutionary products can evolve, but with necessarily inexperienced design-to-manufacture teams.

The duo of physical principles and geometric transforms is not however put forward as a general panacea for the difficulties of creating highly integrated technology products, but, where geometry and function allow, the procedure should provide a starting point to build upon and apply across a broad family of products, notably in "Smart" products that incorporate sensors, actuators and local data processing into items that retain or mimic their previous, and possibly familiar, "traditional" form.

I discuss the limitations of my research in section 3.2, commencing on page 85.

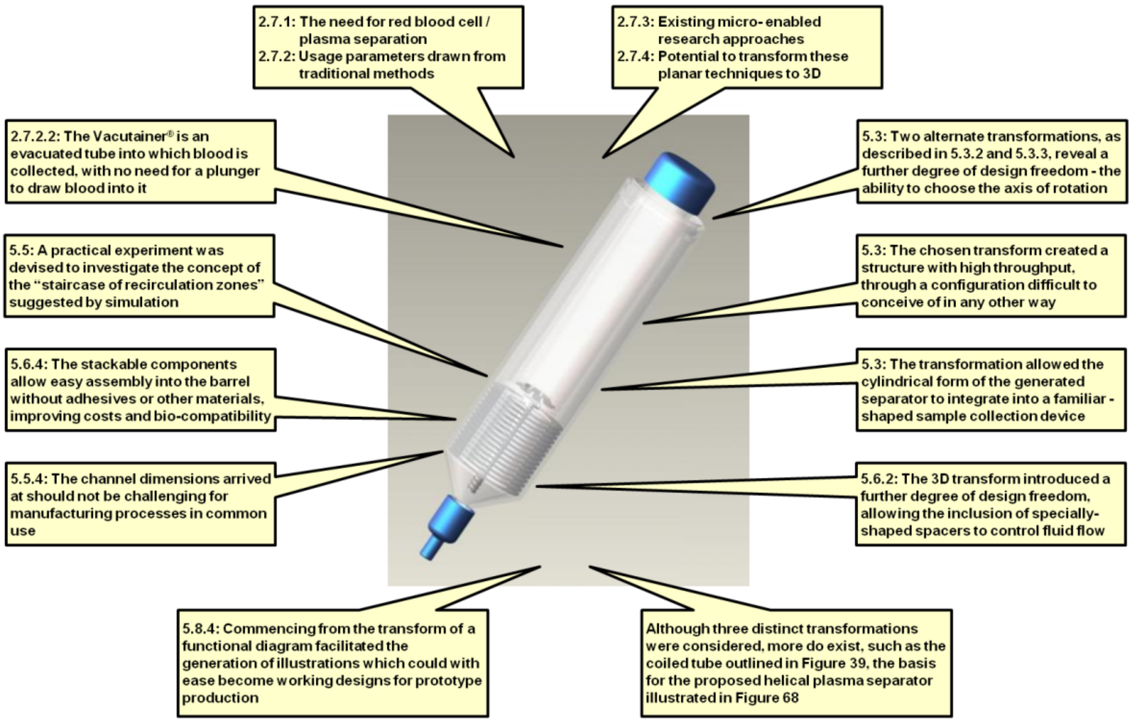
Prospects for further development

- There is as yet no general access to catalogued and classified diagrams of physical principles, save through commercial concerns. It may be possible, for example, to generate a specialised Google® search in this respect. Akin to this, COMSOL features a searchable gallery of 90 case histories.
- There is the potential for research to investigate a wider matrix of physical principles and geometric transforms, developing a taxonomy of combinations, and perhaps multiple combinations of principles and transforms.
- The observed relationship between diagrams of physical principles, computer modelling, geometric transforms and embodiment is worthy of further investigation.
- Although a "tool box" or formalised design procedure is not the current focus of *Outcome 1*, the possibility remains to generate guidelines for its application.
- The advent of "additive" technologies such as 3D printing open up the prospect to *manufacture* products based directly upon diagrams of appropriate physical principles, with geometric transforms from function to form and further transforms from form to embodiment.
- A fusion with biology, one aspect of naturally-inspired manufacturing, might see the deconstruction of micro- biological forms and function to diagrammatic form, then their reconstruction to inorganic artefacts.

The above prospects are listed very much in an order ranging from immediate practicality to longer-term visions.

6.2 Outcome 2: Red Blood Cell / Plasma Separation Device

The concept portrayed in Figure 118 “B”, and below, is a visualisation provided by part-time co-worker Katy Jenkins, based loosely upon the BD Vacutainer®, but fitted at its collection end with the separator assembly shown in Figure 110 on page 165.



2.7.1: The need for red blood cell / plasma separation
2.7.2: Usage parameters drawn from traditional methods

2.7.3: Existing micro-enabled research approaches
2.7.4: Potential to transform these planar techniques to 3D

2.7.2.2: The Vacutainer® is an evacuated tube into which blood is collected, with no need for a plunger to draw blood into it

5.3: Two alternate transformations, as described in 5.3.2 and 5.3.3, reveal a further degree of design freedom - the ability to choose the axis of rotation

5.5: A practical experiment was devised to investigate the concept of the “staircase of recirculation zones” suggested by simulation

5.3: The chosen transform created a structure with high throughput, through a configuration difficult to conceive of in any other way

5.6.4: The stackable components allow easy assembly into the barrel without adhesives or other materials, improving costs and bio-compatibility

5.3: The transformation allowed the cylindrical form of the generated separator to integrate into a familiar - shaped sample collection device

5.5.4: The channel dimensions arrived at should not be challenging for manufacturing processes in common use

5.6.2: The 3D transform introduced a further degree of design freedom, allowing the inclusion of specially-shaped spacers to control fluid flow

5.8.4: Commencing from the transform of a functional diagram facilitated the generation of illustrations which could with ease become working designs for prototype production

Although three distinct transformations were considered, more do exist, such as the coiled tube outlined in Figure 39, the basis for the proposed helical plasma separator illustrated in Figure 68

Figure 120: Selected contributions to the separator device
(Visualisation adapted from Katy Jenkins “Blood Separation Syringe: DM3306 Major Project Report”)

Figure 120 shows how selected background from the literature review and the practical research stream contributed to the conceiving and evolution of a novel Red Blood Cell / Plasma Separation Device. The device itself was not a primary objective of the research, or a deliverable item, it was rather a vehicle upon which to examine the issues concerning the conceptual design of 3D miniaturised / integrated products and to demonstrate the improvements to be brought about the notion of integrating function into form through the application of geometric transforms upon diagrams of physical principles.

Although a finished device was not intended as a physical deliverable, a sample element was constructed, and, as reported in section 5.5, tested.

As a result of the research closely associated with this demonstrator, as opposed to the wider observations which contributed to *Outcome 1*, the following new results were obtained through the testing:

- Validation of the computer modelling performed to explore design parameters
- Real-life demonstration of a new separation geometry suggested by the modelling
- Confirmation that the transformation of a diagram of physical principle into a 3D component would deliver the expected benefits in terms of throughput and elimination of clogging without compromising separation efficiency.

Section 5.7.4 lists, commencing on page 171, the advantages of the envisioned device, whilst Figure 115 records the benefits of the 3D transformed approach.

At October 2015 the device appeared to be unique. This view was confirmed by the signing of a non-disclosure agreement with The Medical Device Company, an organisation that assists companies to protect their ideas, develop their products and take them to market.

Application and limitations The application of the *Outcome 2* device, when fully developed, is detailed in 2.7.2.2 “Small volume separation”, in that the device should perform exactly as a regular sampling device, as it has the same form. The significant difference is that reagents may be introduced or pre-loaded into the plasma receptacle to provide point-of-care diagnosis, or the device may be loaded directly into a diagnostic instrument to perform more searching analysis.

The research has only taken the idea as far as proof of concept and a vision of how the finished product might be. A proper matrix of more detailed computer modelling and full-product prototypes tested with appropriate bio-fluids is needed. Following that, a major limitation of the work to date is that it is a very long journey from concept to use in the medical world, through safety, user and clinical trials, requiring significant investment and the will of a potential manufacturer to disrupt a well-established market that uses legacy technology.

Prospects for further development

- The need for a matrix of more detailed computer modelling and full-product prototype testing with appropriate bio-fluids is mentioned above.
- There is a research opportunity to investigate the effect of different surface finishes upon the separator elements, whether they should wet well or not, and whether in some locations an intentional texturing may be advantageous. These matters are made more relevant due to the larger surface areas presented by the transformed geometry.

- Practical comparisons of the manufacturing options tabled in section 5.6.4 on page 164 could be rewarding, as would be the consideration of 3D-printing a complete device comprising barrel and separator combined.

6.3 Additional research outcomes

Here I provide brief notes regarding some additional outcomes that should prove of further use:

Classifying design communications A scheme identifying parallel streams of design communication is illustrated in Figure 7 on page 38 and was used effectively in the analysis of communication in Chapter 5. Section 2.4.1.2 refers to the differing viewpoints of other researchers, which were resolved in a non-contradictory way for this thesis.

Diagrams in microbiology A parallel was recognised between needs for explanatory diagrams in cellular biology and similar needs in the discussing, understanding and communication of micro- scale technologies (see Figure 89: i-ball internal workings mimic the organs of a mollusc on page 125). Diagrams are therefore also a lingua franca from biology to engineering.

3D-transformed workshop The workshop activity reported in section 4.2 piloted a novel format in which, rather than the usual fixing of “Post-It®” ideas on flip charts or walls, 3D mannequins were provided, along with 2D-printed artefacts that could conform to or “dress” the mannequins. The activity was successful in that it:

- Took the participants into, for them, an unexpected zone
- Related directly to the application topic of wearable technology
- Emphasised the desirability and benefits of conforming the technology to the product

I can recommend extending this idea to other sectors, such as automotive, furniture and agriculture, and wherever technology is becoming embedded into everyday life.

6.4 Coda

The Novel Red Blood Cell / Plasma Separation Device evolved during this research demonstrates one instance of how to bring hidden, almost invisible, extra functionality to an otherwise mundane clinical device.

But the incorporation of extra functionality into familiar objects is not the end of it: On-body wearable systems and in-body smart prosthetics extend the need for technology to adapt to humans rather than the other way round.

Kelley and Littman describe in “The Art of Innovation” [80] how the IDEO design offices each curate a “Tech Box”, a series of drawers containing hundreds of tagged parts, materials, mechanisms and toys, which, along with internet and database resources, inspire designers and engineers to adopt new viewpoints and innovative associations to progress their design concepts and solutions.

In the same book Kelley and Littman cite “Inspiration from adversity” as an idea generator. The challenge of a frustrating silicon-blinkered viewpoint in industry drove this researcher to innovate: the result being the geometric transform from planar diagrams of physical principles to 3-dimensional articles examined and justified in this thesis.

The notion was originally conceived to allow products to be enhanced through the integration of micro- technologies, but the new concept can now be seen, through this thesis and the cadre of researchers and industrialists who have been touched by the research, to offer wider improvements to the design-to-manufacture process, whether venturing into the micro- world or exploring other frontiers where experience has yet to be accrued.

In the vein of IDEO’s “Tech Box” and similar “untidy drawer” assets, surely recognised by all innovators, I have a fervent hope that a well-stirred assortment of physical principles and geometric transformations will find a valued place in the armoury of conceptual design.

I have a similar wish that the thinking behind the Red Blood Cell / Plasma Separator will find beneficial application in healthcare, both in diagnosis and in treatment, and that the ideas generated in this thesis and taken on board by a community of researchers and industrialists will result in the generation of worthwhile new products in many sectors.

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