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Modeling and Imaging the Cardiovascular System

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Abstract. The cardiovascular system is concealed, complex and in a continual state of movement and change. Medical images and physical or computational models give limited representations of the living system which are far from complete, and never entirely accurate. This paper outlines some techniques of cardiovascular imaging and modeling, and considers their limitations relative to the living system. An inclusive, imaginative approach to cardiovascular study is proposed, guided by observations and information from a variety of sources, including direct study of vascular tissues and casts, imaging, critical use of published information, and interactive experimentation in the limited but adaptable context of physical and computational models. Models enhance understanding of principles relevant to cardiovascular dynamics and allow exploration of interactions among selected parameters, but limitations should be recognized. The living cardiovascular system is extremely complex, with flexible, continually changing inter-dependency of parts. It maintains unity in complexity, and continuity through continual change.

Keywords: Circulation; Heart; Flow; Haemodynamics; Mode

1. Introduction

The aims of cardiovascular imaging and modeling include diagnosis and comprehension of patho-physiology, and progress towards improved interventions for cardiovascular disease.

But the human cardiovascular system is well hidden, extremely complex and in a continual state of movement and change. To what extent are we able to image, understand and simulate the reality of our cardiovascular system? Medical images and physical or computational models, however sophisticated, are always far from complete. They represent only limited aspects of the living system, never with complete accuracy, and always leaving unseen or un-modeled far more than they represent. Images and models are inevitably selective. If blood flow of a single organ or limb, let alone the whole body, were depicted fully, there would be so much detail of branched, superimposed streams, micro-streams and counter-streams that the whole would be incomprehensible in a single image. Anatomical images are always selective, usually in favor of larger-scale structures, perhaps depicting one slice only, or, as in angiography, projecting to a plane the 3-dimensional distribution of contrast that has arrived in certain vascular branches. Living tissues are permeated through-and-through with movement and change, across all scales from the whole organism down to the inconceivably small scales of molecular and atomic components.

The limitations of particular imaging or modeling approaches may not be obvious, especially to those who work with the most sophisticated equipment and software. The aim of this paper is to recognize limitations of imaging and modeling relative to the complexity of the living cardiovascular system, and to consider how living reality may be questioned and

approached.

Imagination – informed and appropriately fluent – can move beyond and between the limitations of separate images or models. But imagination is liable, on the one hand, to stray into fantasies and illusions. And, on the other, it tends to be limited by habits, assumptions and received interpretations. What is needed is open-minded, informed imagination, continually taking account of reality through a range approaches. These may include direct study of tissues and casts, imaging, critical use of published information and interactive experiments in the limited but adaptable context of physical or computational models.

2. Methods available

This section summarizes some approaches to cardiovascular imaging and modeling, and offers hints towards more inclusive appreciation of the living cardiovascular system.

2.1. Cardiovascular Imaging

The semi-invasive trans-esophageal approach gives improved ultrasonic access to more posterior parts of the heart. In recent years 3-dimensional ultrasound techniques have been developed involving translation or rotation of a 2-D scanning plane, but access tends to be restricted, as with conventional echocardiography.

Cardiovascular Magnetic Resonance Imaging

Magnetic resonance (MRI) is relatively expensive and complex, but has the advantages of non-invasiveness, safety, unrestricted access, and unrivaled versatility [Bogaert et al., 2000; Manning and Pennell, 2001].

All imaging techniques (MRI, x-ray, ultrasound, etc.) require an energy source, interaction of the energy with body tissue, and reception of energy coming out again to form an image. In MRI, the energy source is a radio transmitter, the tissue interaction involves resonance between radio signal and oscillations, in the magnetic field, of spinning protons that constitute the nuclei of hydrogen in body water or fat. The receiver is a radio aerial, picking up signal that has been re-emitted by energized protons. What is unique about magnetic resonance compared with other imaging techniques is the degree to which interactions at tissue level – nuclear magnetic resonance – can be controlled and manipulated by magnetic gradients. Protons are effectively ‘played’ – energized by radio pulses and tuned and re-tuned by magnetic gradients. Different imaging sequences, which consist of sequences of radio pulse and magnetic gradient switches, result in different contrast between tissues. They may also be used to encode velocities of flow in different directions. This is the basis of the versatility of magnetic resonance. Magnetic gradients are applied with respect to x, y and z coordinates, and MRI is inherently 3-dimensional, allowing resolution of voxels in 3-dimensional space. Imaging is usually carried out in 2-dimensional planes however, with typical in-plane voxel dimensions of 1 or 2mm, and a slice thickness of 5 mm or more. Resolution in the time dimension is achieved by gating at a series of different delays from the R-wave of the ECG. Sequential images can be played back as a cine loop which represents an averaged cardiac cycle, typically acquired over several heartbeats during a single breath-hold. This can give very clear images of the heart and vessels, with wide fields of view, but with a slice thickness of 5mm or more, spatial resolution is not necessarily as good as it may appear, and is rarely as good as that provided by computed x-ray tomography.

One of the great strengths of cardiovascular MRI compared with other modalities is acquisition of velocity data in any chosen direction, in or through a chosen plane. This gives the potential to acquire ‘comprehensive’ flow data, i.e. all three directional components of velocity for points distributed in 3-dimensional space and the dimension of time [Firmin et al., 1993]. At present, however, constraints of hardware, software and available time usually limit cine velocity acquisitions to 1 or 2 directions of velocity in or through the two dimensions of a plane. Several planes may be imaged to build up information on a volume [Kilner et al., 1993 and 2000; Walker et al., 1996]. This type of velocity data can be

correlated with cardiovascular boundaries detected by other magnetic resonance imaging techniques, and used as a basis for computational modeling of flow through heart chambers or large vessels [Saber et al., 2001].

For delineation of 3-dimensional vascular geometry, magnetic resonance angiography can be performed following injection in a vein of the contrast agent Gadolinium. This gives fairly good 3-D spatial resolution, but generally without cardiac gating, during a breath-hold of about 10 seconds.

Magnetic resonance hardware and software continues to be developed, and there is great potential for further refinement. MRI is already the most comprehensive and versatile modality for cardiovascular imaging and flow measurement, both in clinical diagnosis and as a basis for cardiovascular modeling.

2.2. Cardiovascular Modeling

The greatest challenges facing those who attempt to model aspects of cardiovascular flow are probably complexity of *form* and complexity of *compliance* of vascular walls. Vascular compliance is variable, non-linear and non-isotropic. Vessels have a mixture of circularly, longitudinally and irregularly orientated fibers of elastin, plus less-elastic fibers of collagen which help to limit over–stretching of a vessel as wall tension rises relative to pressure as diameter increases. In addition, arteries have smooth muscle fibers that modify elasticity in response to autonomic and other biochemical signals.

Blood vessels have branching, tree-like structures, dividing and re-dividing until diameters of less than 100^{th} of a millimeter are reached in the capillary beds. Increase in numbers of branches peripherally is so great that, in spite of extreme diminution in size, summed cross sectional areas increase about 100-fold from great vessels to micro-vessels. This goes with decrease in velocities of flow from center to periphery [Caro et al., 1978].

Centrally, flow through cavities of the heart traces sinuous paths, with changes of direction at atrial, ventricular and arterial levels, and quasi-helical twists to the outflow tracts and great arteries. These turns and twists have significance for dynamics of flow, especially in the exercising state, when it would be unrealistic to model flow in one chamber or great vessel in isolation from those immediately up- and down-stream [Kilner et al., 1997 and 2000]. In the heart itself, the blood-muscle boundary is indented and fragmented by trabeculations consisting of separate but interlinked muscle bundles that may help to optimize combinations of contractility and compliance of the muscular wall. The myocardium as a whole is composed of muscle fibres with different, more or less oblique orientations in different layers.

Variable viscosity of blood, a non-newtonian fluid, also contributes to the difficulty of accurate modeling, but perhaps less than do the complexities of geometry, compliance and contractility when large-scale cardiovascular flows are under consideration.

Physical Flow Models

Combinations of form, flow, compliance (and contractility) found in the cardiovascular system cannot be simulated closely in models. Form alone can be copied through a process of casting from post-mortem tissues, if available, for example using wax or silicone rubber [Kilner et al. 1988]. But although it is relatively easy to cast the forms of blood spaces as solid objects, it is much more difficult to re-create the hollow tubes of vascular branches. Segments of hollow walls may be cast in silicone rubber around a wax or rubber cast of the lumen, but their compliance depends on properties of the rubber and its thickness. Attempts may be made to include fibers, but I do not think that close approximation to arterial wall geometry *and* compliance has ever been achieved in physical models.

Unrealistic compliance would be relatively unimportant if flows were continuous, but compliance significantly effects pressure-flow relationships in pulsatile flow.

For a study of flow through a simple pulsatile cavity, I have used a pneumatically contained elastic membrane in circuit of otherwise incompliant polythene tubing [de Leval et al. 1988]. The model was used only to explore the effect of pulsatility on flows and pressures in this setting, and conclusions could only be drawn cautiously in relation to limitations of the model.

Open-channel flow models are worth exploring even though they can never give close representations of flow in fully enclosed blood vessels. It is technically easy to manipulate and visualize patterns of flow in open channels, which can be made in malleable materials such as wax or clay. A suspension of fine metal flakes can be used for flow visualization, and contours of the free surface may give some insight into differences of pressure beneath the surface. Much can be learned about wave propagation, flow separation and flow instability through interactive modeling in open channels. Surface gravity waves propagate and interact in ways that loosely simulate pressure wave propagation in elastic vessels – but the approximation is not close. Also, multi-directional flows in the half-cylinder of an open channel may loosely simulate those in one half of a tubular vessel, although the approximation fails where axes of vessels and branches have non-planar geometry. Although open–channels fail to simulate vascular dynamics, their suitability for interactive, easily viewed experiment makes them invaluable aids to exploring principles of flow dynamics in relation to variable geometry. Experience gained is relevant to interpretation of appearances on flow images and design of other types of flow model.

Computational Fluid Dynamic Modeling

I do not have direct experience of computational flow modeling, but have collaborated with others in the field [Migliavacca et al., 1997 and 1999; Saber et al., 2001]. My impression is that computational simulation of vascular geometry is as challenging as its physical counterparts, and simulation of interactions between fluid and compliant boundaries remains extremely difficult by computation. The great advantage of computation, however, is that methods are readily stored and transferred as software, and computation lends itself to interactive manipulation of selected parameters. Parameters such as velocity, pressure and shear may be mapped across the volume of virtual flow. A further, increasingly relevant advantage is that geometrical information available from magnetic resonance and other imaging techniques can be used fairly directly for determination of the geometry of containing boundaries, although accuracy leaves much to be desired, mainly due to limitations of spatio-temporal resolution.

We should not be deceived by apparent sophistication of computational fluid dynamics in attempted simulations of in vivo flow. The inaccuracies of simulated geometry, compliance and, in the case of cardiac cavities, contractility remains significant. As with simplified physical models described above, I see computational modeling as a valuable means of exploring and separating out *principles* of flow-structure interaction that may be relevant to the living system. Modeling still falls a long way short of simulating the complexity, flexibility and interactive responsiveness of living cardiovascular systems. In life dynamics of flow through the heart and vessels change radically from resting to exercising states – a fact rarely considered in relation to computational simulations.

2.3. Complementary Approaches to Cardiovascular Structure

We live in times of ever increasing specialisation. For this reason, it is important to make efforts to broaden perspectives and explore alternative approaches. I will outline two kinds of resource, which complement more familiar approaches to cardiovascular research. Each allows direct use of the senses – tactile and visual – on aspects of cardiovascular structure, but inevitably not in the living circulatory system. Then I will list some basic methods that may foster more comprehensive appreciation of the cardiovascular system.

Fresh Animal Tissues

A number of years ago, when preparing to work with physical flow models, I bought and

handled fresh animal hearts-and-lungs from a local meat supplier. I also experimented with incorporation of fresh vessel segments (caval vein, pulmonary artery and aorta) in simple pulsatile flow models. These tissues are of little commercial value to meat traders, but unfortunately, with precautions against possible spread of infective disease, fresh animal cardiovascular tissues may be less easy to obtain now.

Handling fresh tissue gives insight into the varied structure and elastic properties of veins, atrial and ventricular cavities, heart valves, pulmonary arteries, aorta and arterial branches. It is striking how elasticity and strength of each tissue is adapted to the range of pressures and stresses it supports in vivo. The non-linear compliance of vascular walls, both longitudinal and circumferential, can be judged by stretching with the fingertips. The delicate compliance and collapsibility of caval veins, normally functioning with low, sometimes negative transmural pressures, contrasts with the elastic resilience and circular cross section of the pulmonary artery and aorta.

Cardiovascular Casts

For a number of decades post mortem casts of cardiovascular blood spaces have been prepared using injectable, solidifying, extractable materials such as resin [Tompsett 1970; McMinn and Hutchings, 1985], silicone rubber [Kilner et al., 1988] or ‘microfil’ gel for microvascular casts [Williams and Warwick, 1980]. There is a superb collection of colored resin casts of vascular trees of human organs and organ systems in the anatomical museum of the Royal College of Surgeons in London. Well-prepared three-dimensional casts give unique insight into the complexity of cardiovascular form. Different kinds of cast should be considered in relation to one another, for example arterial and venous, and casts that exclude and include very small branches. Larger branches may only be visible when smaller branches have been removed from a cast, so dense can be the fine branches towards the microvessels.

Suggestions Towards an Inclusive, Imaginative Approach to the Cardiovascular System:

- Practice careful, unbiased, inclusive observation. As far as possible, observation should begin with direct sensory perception, unaided by instruments. The living cardiovascular system is largely inaccessible, however. Fresh post-mortem tissues and vascular casts provide non-living substitutes, allowing selected aspects of structure and form to be studied directly.

- Efforts should be made to withhold interpretation or explanation while gathering more observations and information on different aspects of the cardiovascular system.

- It is worth being alert to the observations of others, who may notice what you do not.

- Where instruments (imaging equipment, blood pressure monitors, ECG traces, microscopes, etc) are used, it is important to be aware of their mode of action, their limitations, and the ways in which they select or alter appearances. A microscope or microscopic image, for example, gives false impressions of massiveness and distance, which should be countered by efforts to appreciate the actual smallness of what is seen.

- Attention should be paid to the wider context (organism, environment) as well as to the details that contribute to phenomena.

- Attention should be paid to processes and change in the dimension of time [Hildebrandt 1991; Hidebrandt et al., 1998], as well as in space.

- Do not necessarily trust what you read or are taught. Do not even trust what you see, which tends to be biased by what you expect to see. Repeatedly question whether another point of view or interpretation is also feasible.

- As you enrich your experience through several observational and imaging approaches,

allow your imagination – informed and appropriately fluid – to move among the phenomena. New kinds of understanding may arise which can show up the limitations of previously held interpretations.

- Creative engagement is a potent way of testing understanding. This is where modeling – physical or computational – has its place. Relationships and influences of one variable on another can be explored, within the acknowledged limits of a model. Understanding can applied back to *in vivo* information, and further investigations or experiments devised.

- Another kind of creative engagement is drawing, from image data, the forms and flow paths of the cardiovascular system. [Kilner et al., 1993; Kilner et al., 2000].

3. Result – a Brief Description of the Living Cardiovascular System

Such a richly varied fluid system cannot be captured in words or images alone – appropriate fluency of thought is needed to begin to appreciate the dynamic beauty of the circulatory system.

As you read this, your blood is streaming inwards and outwards - converging in veins from all parts of your body, turning through the entwined but separate flow paths of right and left heart, and branching out again through arteries to the microscopically fine capillary webs of the lungs and other organs.

Observation of vascular and micro-vascular casts allows appreciation of the division and sub-division of vascular branches, down to the delicate webs of capillaries that permeate most of the volume of the body. These filament-like micro-vessels have diameters approaching one tenth of those of a human hair. They accommodate red blood cells (each less than one hundredth of a millimeter in diameter) only in single-file, and with compliant deformation. Capillary webs in different organs (lung, kidney, liver, muscle etc.) have varied spatial forms. Capillaries in the lungs, for example, have the form of a net so dense that there is more net than hole – i.e. a thin membrane of blood effectively seeps round each alveolus, its bounding endothelial surfaces linked by tiny columns of endothelium that form the holes of the net. Capillaries of a renal glomerulus are also densely packed in a tuft, whereas those of the renal tubules extend in linear filaments [Williams and Warwick; 1980]. Each organ or tissue has characteristic capillary morphologies, which are associated with different metabolic and functional roles. They vary in compliance, resistance to flow and responsiveness to biochemical change. The pulmonary vascular bed, for example, generally has about one fifth of the resistance of all the systemic vascular beds combined. This is reflected in low pulmonary artery pressures relative to those of systemic arteries, despite similar outputs from right and left ventricle.

Each of many billions of capillaries of the body is in fluid continuity, via arterial branches upstream, and venous branches downstream, with the entwined streams of the left and right heart. Arterial and venous branches of each organ or limb usually run side-by side, so that venous and arterial trees penetrate the same volume, their branches adjacent and counter-flowing. Organs may also be penetrated by additional vascular trees, for example the portal venous and biliary trees of the liver, the bronchial trees of the lungs, the tubules of the kidneys, and delicate lymphatic branches through most tissues of the body.

Components of living systems, more than those of mechanical or computational systems, are interactive and mutually responsive. The heart – generally thought of rather simply as a pump propelling blood through vascular resistance – is responsive to and dependent on returning streams in a number of ways. These include the responsiveness of myocardial fibres to initial stretch, according to the Frank-Starling principle [Noble, 1978], and responsiveness to circulating substances such as adrenaline. Heart rhythm and contractility are modulated by sympathetic and parasympathetic nerve activity via various feedback pathways and myocardial contractility depends on exchanges of nutrients and gases via coronary blood flow. Flows of left and right ventricles interact with one another through

displacements of the septum, especially when it is relaxed during ventricular filling.

Thanks to its confluent situation, central to circulatory branches of the body and lungs, the heart unifies the diversity of our organism. Blood filling the right atrium with each beat includes cells that have passed through capillary beds in all parts of the body. Similarly, blood ejected from the left ventricle is destined for arterial and microvascular branches throughout the volume of the body. Different individual blood cells will take different paths and different periods of time (from about 0.3 to about 6 seconds) to reach and pass through capillary beds. Periods of venous return can be longer and even more variable. This means that the particular gathering of blood cells in the heart at one moment will never come together again – there will always be thorough mixing and re-mixing through circulatory dispersions and confluences.

A single red cell, with a life span of about 3 months, will trace more than 100,000 systemic and pulmonary journeys, probably never by exactly the same route twice. It will gradually trace paths to and from the heart, to and from all parts of the body and lungs. The circulatory system is a system of continual transport, mixing and exchange.

In summary, blood circulation and heart maintain unity in diversity, and continuity through continual change. The heart is responsive and active, sounding and reliably serving the diversity of our organism. The seeping of blood through billions of varied, microscopically fine capillary branches and, at the same time, the flows and counter-flows in branches of arteries and veins, and the sinuous streams swirling through the curvatures of the heart - these are awesome in their complexity, unity and beauty of form. This fluent masterwork moves in each one of us, and continues to move, reliably, but ever changing, day and night, life-long.

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