

# Biofluid mechanics: quo vadis?

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## Background

Medical and Biological Engineering and Science (MBES) integrate physical, mathematical and life sciences and engineering principles for the study of biology, medicine and health systems and for the application of technology to improve health and quality of life. It creates knowledge from the molecular to organ system levels, develops materials, devices, systems, information, technology and health care management, and methods for assessment and evaluation of technology, for the prevention, diagnosis and treatment of disease, for health care delivery and for patient care and rehabilitation (*definition according to EAMBES, the European alliance for Medical and Biological Engineering and Sciences, 2003*).

Biofluid mechanics refers to the application of fluid mechanics to biological systems. When applied to human systems, the aim of the research can be focused on insight in the biofluid mechanical problem (basic research also contributing to the progress of fluid mechanics) aimed at the prevention, diagnosis and treatment of diseases in animals and humans.

An integrated methodology frequently makes use of the combination of a numerical (in numero), experimental (in vitro), animal (in animal) and patient data (in vivo model).

In this biological century biofluid mechanics is undergoing a marvelous evolution with tremendous opportunities due to an enormous progress in associated areas as biomedical imaging and signal processing, computational fluid dynamics, cellular and subcellular mechanics, mechanotransduction, genomics, bioartificial organs, regenerative medicine, etc ...

## Multiscale modeling integrating biology

In the past, attention was paid to basic fluid mechanical approach at macro scale in idealized 2D rigid vascular wall models with no attention at all to the biology (flow separation, secondary flows,..). Later, more realistic 3D models were studied mainly experimentally. Nowadays we are participating to the development of patient-specific multi scale models scaling fluid mechanics down to the biological cellular and subcellular level to answer questions as:

- what is the frequency and the direction of forces acting on endothelial cells in disturbed flow?
- what is the impact of the endothelial glycocalyx interface between blood and vessel wall on the transmission of fluid shear stress?

This opens a renewed clinical interest in vascular biomechanics. The study of blood flow in major blood vessels includes nowadays disturbed flow visualization with shear stress calculation and gene expression (mechanotransduction), e.g. visualization of shear stress related gene expression and shear stress related inflammation in plaque formation. This leads to biofluid mechanics at microscale level: modelling flows and transport in microstructures to integrate molecular dynamics to understand the interaction between mechanical stimuli and biological response.

Biofluid mechanics at nanoscale level deals with the phenomenology and description of the flow of fluids (gas, liquids) around and inside nanoscale systems and has a lot of potential.

Molecular biology evolves in an environment that is mainly water. It is undoubtedly important for near-wall flow dynamics (e.g. blood-foreign material interaction), design of fluid immersed nanodevices (nanosensors) and complex fluid flows in MEMs devices (Micro-Electro-Mechanical Systems) which consists of the integration of mechanical elements, sensors, actuators, and electronics on a common silicon substrate through microfabrication technology. While the electronics are fabricated using integrated circuit (IC) process sequences, the micromechanical components are fabricated using compatible "micromachining" processes that selectively etch away parts of the silicon wafer or add new structural layers to form the mechanical and electromechanical devices. This is another rapidly growing field for the design of microfluid components such as needles, pumps, valves and mixers. Their study includes two-phase flows containing bubbles, particles or polymers. Therefore the length scale is of the order of cells, large molecules or bead dimensions.

### **Image based computational fluid dynamics integrating biomedical imaging and signal processing**

Starting from clinical images and data coming from Magnetic Resonance Angiography, computer tomography (CT), functional angiography, positron emission tomography (PET), or single photon emission computed tomography (SPECT), combined with computational fluid dynamics (CFD), the blood flow fields and according biomechanical parameters are obtained in human subjects.

Although most of the published models assume a rigid wall, Newtonian and fully developed flow, they yield potentially clinically relevant results. Question remains of course how accurate the models must be for patient-specific models and evidence based studies. Today we are able to characterize the in vivo distribution of haemodynamic variables and relate them to in vivo or post mortem biological measurements. Fluid-structure interaction algorithms are developed for vulnerable plaque detection and aneurysm assessment in vessels and blood-wall interaction in diastolic and systolic ventricular dysfunction.

Future research efforts will lead to blood-wall interactive simulations of non-Newtonian turbulent flow in order to predict events, to design the tools necessary for longitudinal evidence based (multi-center) studies which requires reproducibility of the image based CFD protocols, to realize virtual imaging and simulation-based medical planning (patient imaging, preoperative modeling, intervention planning, physiological simulation and validation) in order to answer critical clinical questions as "When to treat?" and "How to treat?"

For patient-specific models an accurate way of getting the appropriate boundary conditions remains an issue to be solved. And how will we translate these boundary conditions to biological stimulus variables?

Validation of these image based models will result in a standard approach of analytical solutions, benchmark numerical models and experimental models.

### **Biotransport modeling supporting the development of regenerative medicine**

Literature survey clearly indicates an evolution from purely biofluid mechanics towards biotransport modeling including fluid mechanics (momentum transport), mass transport and sometimes thermodynamics (heat transport).

Due to the semi-permeable nature of the vascular endothelium to plasma solubles, there is a flow dependent concentration polarization of low-density lipoproteins leading to the genesis and development of vascular diseases such as atherosclerosis, intimal hyperplasia, ... It is recognized that wall mechanics and mass transport play an important role in normal and pathologic vascular remodeling.

Biotransport modeling is already longer a standard procedure in artificial organ design such as oxygenators, artificial kidneys and nowadays to artificial livers and pancreas. Biotransport modeling remains important in the evolution of artificial organ treatment towards regenerative medicine and tissue engineering. Examples are the flow dynamics and transport phenomena in vascular access, grafts, valves, biodegradable coated stents, bioreactors,...

The possibility to compute shear stress histories of platelets along individual paths across or in artificial organ devices opens the possibility to assess clotting potential already during design process of a new device prior to production and implantation rather than post factum.

### **Basic fluid mechanics**

Basic biofluid mechanics remain important: not only laminar and turbulent flow but new algorithms for pulsatile transitional flow often found in the presence of high grade stenoses resulting from atherosclerosis. We should not forget to mention the importance of the many other application areas including ocular to pulmonary gas- and fluid dynamics (air flow in large airways), urethral flow haemodynamics (collapsible tube modeling) , placental blood flow and cell rheology, both experimental and numerical

### **Biomedical engineering sciences**

These new evolutions in biomedical signal processing, imaging, biofluid mechanics, molecular biology and imaging, genomics, tissue engineering, biomaterials, regenerative medicine must stimulate a better communication with medical doctors and biologists, and strengthen intensive collaboration in multidisciplinary teams.

Appropriate education programs at bachelor, master and PhD level are a crucial step in this process including the development of a lifelong learning platform.

The final objective of this research is to improve patient treatment requiring continuous attention for how to translate biofluid mechanics research results into clinical practice. It is clear that these ambitious objectives need a well balanced multi-disciplinary team in the first place, but also international, well communicating multi-scale teams. This does not mean immediate mega-teams.

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