Hybrid and Multiscale Modelling

In the last few years research aimed at modelling phenomena of interest in biology and medicine has been developing in response to two main needs: on the one hand, there is a requirement to link more strongly mathematical modelling, visualisation tools and experimental validation, and on the other hand, there is a need to take into account phenomena occurring at different spatial and/or temporal scales.

Working in a multiscale framework is an almost unconsciously standard procedure in biology and medicine. In fact, in order to understand and describe the behaviour of any biological phenomena, researchers in the Life Sciences naturally tend to go to the smallest scale possible, because it is known, for instance, that the behaviour of a cell and the interactions it has with its environment depend on interactions between its internal chemistry, genetic information, such as gene expression, and on the activation of particular signalling pathways.

Study of the interplay between the genomic, proteomic and tissueomic level has made evident the need to deal with the complexity of the phenomena governing the behavior of any biological tissue considering and linking all levels of description. In fact, one can identify

- A molecular scale referring to the structure of proteins, genomic content and gen expression;
- A sub-cellular scale referring to phenomena taking place within the cell or at the cell membrane, e.g. signal transduction and protein cascades, expression or internalisation of receptors;
- A cellular scale referring to the behavior of the single cell, e.g., motion, adhesion, intravasation and extravasation from blood vessels;
- An inter-cellular scale referring to interactions between cells of the same or different populations, e.g. proliferative, inhibitive and destructive interactions, aggregation and disaggregation behaviors;
- A supra-cellular scale referring to those phenomena which are typical of continuum systems, e.g. diffusion and transport of nutrients and chemical factors, mechanical responses, interactions with external tissues.

Even if one is interested only in macroscopic phenomena, such as heart or lung physiology, cancer or other diseases, it is important to take into account the fact that in a given environment cells interact with other cells, of the same or of different type, and with other structures, such as the extracellular matrix, fluids and diffusing chemicals. The final result of this interaction is eventually decided at the sub-cellular scale, e.g., protein cascade activation, which turns out to be driven by the genetic characteristics of the cell and by its particular gene expression.

It can be observed that the modelling frameworks used in the literature to describe a single phenomenon are not uniquely defined and each approach has its advantages and disadvantages. It is also interesting to note that the number of details taken into account by the mathematical models proposed in the literature is increasing because of the strengthening of multidisciplinary interactions with the bio-medical community. However, at present these models typically operate at a particular scale.

Another consequence of the development of stronger multidisciplinary collaborations is that the time is now ripe

- to link, in a horizontal fashion, different modeling frameworks operating at a the same scale, e.g. individual-based models and partial differential equations, building hybrid models that combine and exploit the advantages brought by the different frameworks, and
- to link in a vertical fashion mathematical models operating at different scales, e.g. Boolean networks in cellular automata models, building nested models that can be used to transfer information between different spatial scales.

The challenge now is to describe biological process not using a single-scale view but in a multi-scale landscape; we believe that this approach will produce the key to unlock the function of complex tissues based on their genetic and cellular composition.

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