Methodological Bridges for Multi-Level Systems

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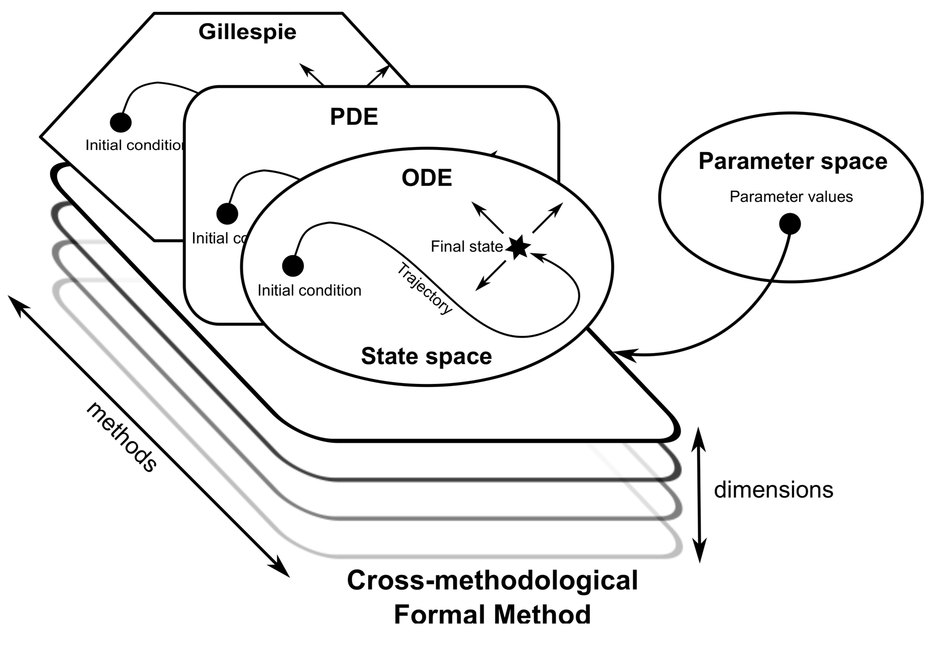
The Methodological Bridges

*"All models are wrong, but some are useful." **George Box**, statistician*

Nowdays since modeling is growing of importance, this sentence would reflect many things: the continuous improvement of developing new models in all scientific fields, the different level of abstractions that a model could express and our difficulties in modelling multiscale dynamical systems. If the scientific progress relies on asking the right questions, we observe that different modelling methodologies often suggest slightly different questions and provide similar or different answers. In the figure on the right, a point in parameter space, given by a set of parameter values, defines a dynamics on the state space. If the system is prepared in an initial condition, then the dynamics typically lead to an attractor, pictured here as a star.

We believe that a better understanding of the compositional framework of different modelling will bring easiness in making sense of large amount of heterogenesous data gathered on varison scales and also in robust parameter estimation and reverse engineering properties of various types of networks and parameters relationship. We found that when the system has a multiscale structure, formal methods help in guiding the exploration across dimensionality. In particular we report that Shape Calculus can effectively interface with a wide range of methodologies for example: Hybrid Automata, Stochastic Simulations (implemented as Gillespie algorithm or software Agent) and Model Checking, Bayesian inference and Model Checking, ODE (Ordinary Differential Equation) and PDE. We can imagine Shape Calculus as "high order" set of levers that pull the low order procedures implemented. Here we investigate the emerging behavior of connecting the Shape high levers (the tissue, the social network) with the low lever types of gear-bevel, spur-lever, helical gear constituents, etc (the cells, the individuals).



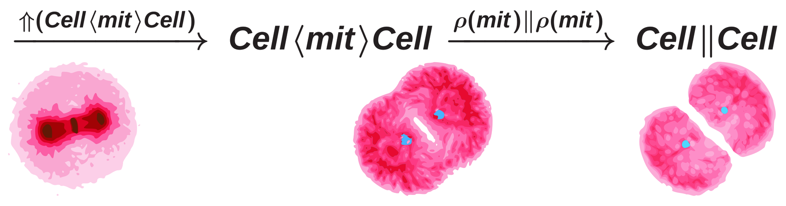
Multi-Method Multi-Level approach

The Shape Calculus: a versatile "bridge" modeling paradigm

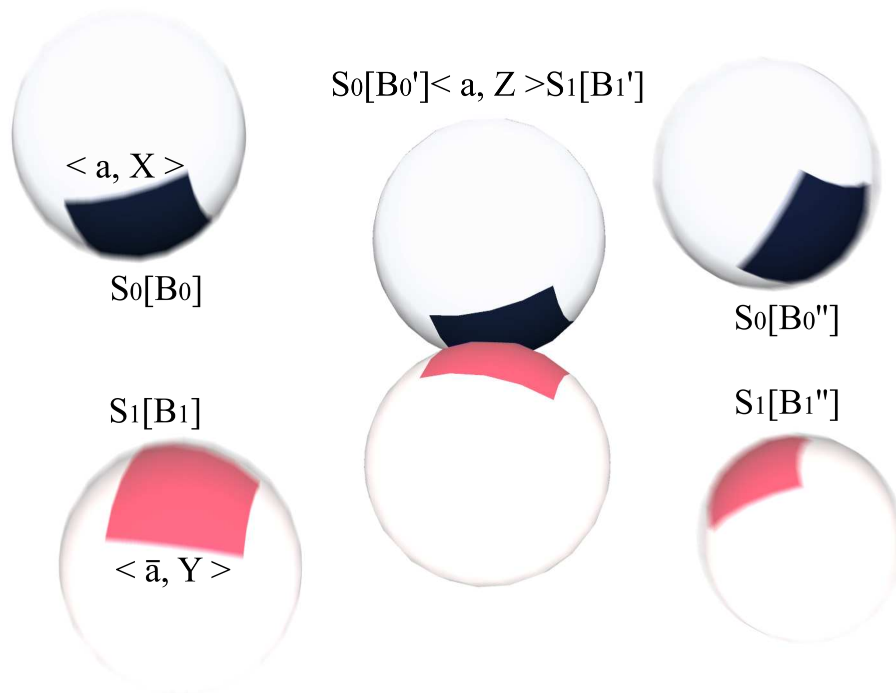
The Shape Calculus [1] is a bio-inspired spatial process calculus for describing 3D-processes moving, colliding and interacting in a 3D-dimensional space. A 3D-process is characterized by a 3D shape ***S***, collecting physical and spatial information (geometry, mass, position, velocity), and by a timed behaviour ***B*** encapsulated inside the shape: ***S*[*B*]**.
Shapes move according to their velocities that are determined by a general motion law - for instance as in a force field or Brownian motion - and by the collisions occurring among shapes. In the case of inelastic collisions, objects can bind and become a compound new object with a new shape and possibly a different behaviour. Established bonds can also be broken by performing a split operation.

$$Cell \stackrel{def}{=} S_{cell}[DNA + \rho(mit).DNA + \Uparrow (Cell\langle mit\rangle Cell)]$$

$$Cell \xrightarrow{\Uparrow(Cell\langle mit\rangle Cell)} Cell\langle mit\rangle Cell \xrightarrow{\rho(mit)\|\rho(mit)} Cell\|Cell$$



Mitosis in the Shape Calculus



Binding and splitting of two 3D processes, $\mathbf{S_0[B_0]}$ and $\mathbf{S_1[B_1]}$.

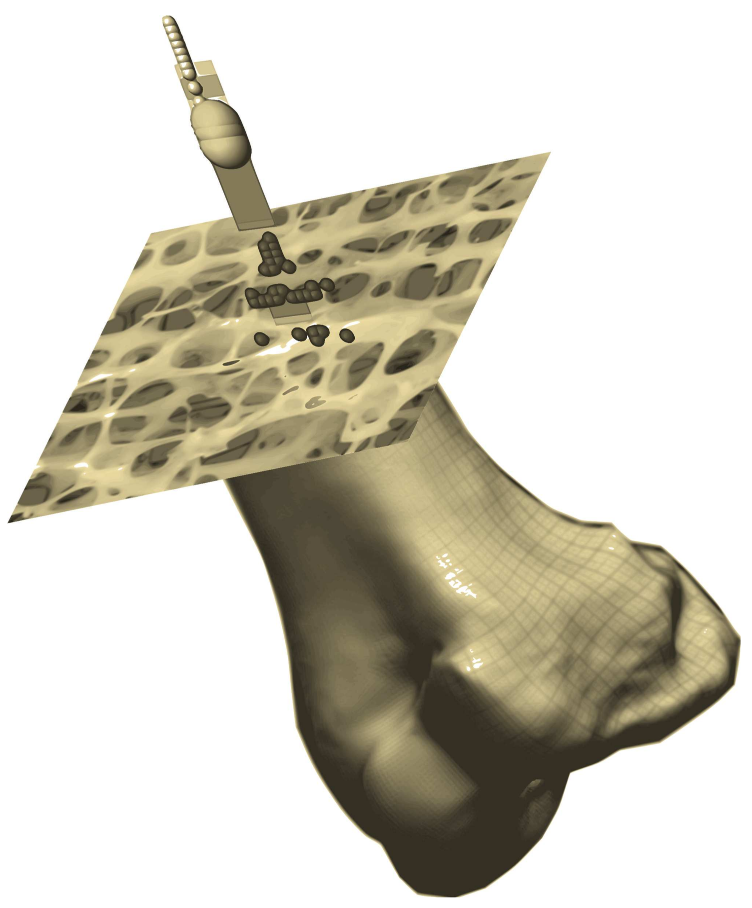
The composition of compatible 3D processes is modeled in a process-algebraic fashion, that is, by communicating on complementary channels.
The examples below describe how simple is to encode a cellular mitosis and a reversible reaction in the Shape Calculus, thus demonstrating the versatility of the language; indeed it is simple and rich enough to express biochemical systems, signalling mechanisms, cellular and multicellular scenarios, as in the case of Bone Remodeling. Moreover, the Shape Calculus seems promising in the modeling of higher-level systems such as socio-economical dynamics or infectious disease processes; the application of a process algebraic language for such domains is an unexplored scientific challenge: we believe that our framework can be suitable to describe a wide range of complex systems, regardless their spatial and temporal scale.

$$A \stackrel{def}{=} S_A[\langle r\rangle\rho(r)] \quad B \stackrel{def}{=} S_B[\langle r\rangle\rho(r)] \qquad (A + B \rightleftharpoons AB)$$

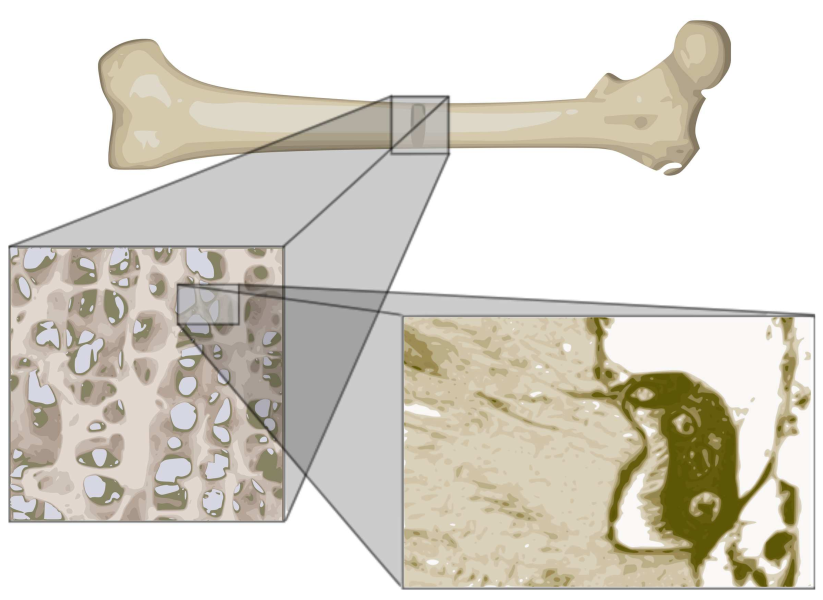
$$A\|B \xrightarrow{\langle r\rangle\|\langle r\rangle} A\langle r\rangle B \xrightarrow{\rho(r)\|\rho(r)} A\|B$$
$$A + B \rightarrow AB \rightarrow A + B$$

Reversible reaction in the Shape Calculus

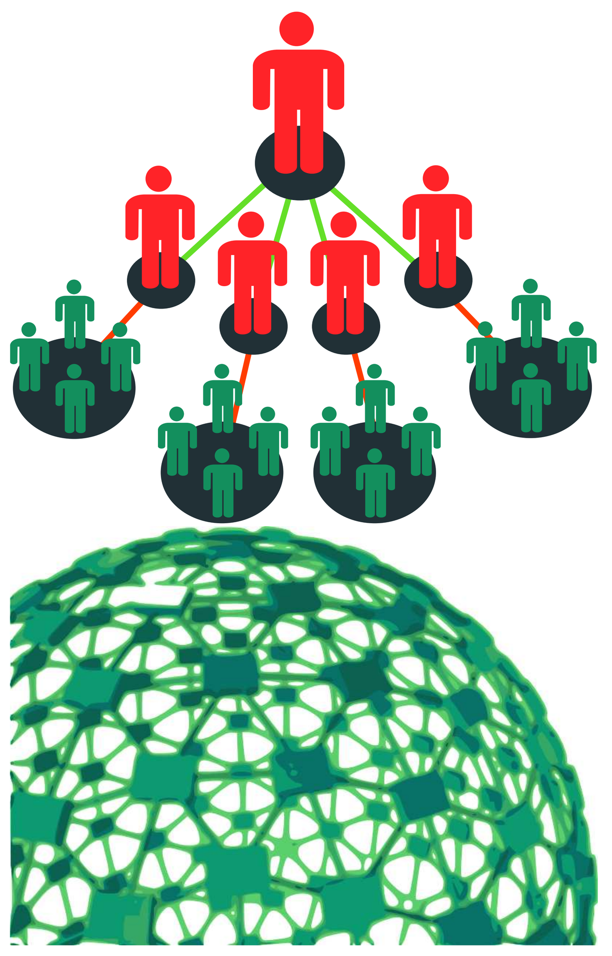
Translational medicine: application to bone remodeling



In the process of Bone Remodeling (BR), old bone is continuously replaced by new tissue; this ensures that the mechanical integrity of the bone is maintained and, in healthy conditions, there are no global changes in the morphology. However, pathological conditions can alter the equilibrium between bone resorption and bone formation; osteoporosis is an example of negative remodeling: the resorption process prevails on the formation one and this reduces bone density, so increasing the risk of spontaneous fractures. Hence, the definition of faithful models for BR has an eminent social and clinical relevance in the prediction of bone diseases.
The bone remodeling involves osteocytes as mechanosensors, and the Basic Multi-cellular Units (BMUs) formed by the osteoclasts (that destroy old bone) and osteoblasts (that build new one). Tissue and whole body metabolism implement fine regulative mechanism acting on the within cell signalling network. Bone Remodeling is a multiscale phenomenon, since macroscopic (tissue) and microscopic (cellular) levels are closely interdependent [2]. The key observation is that cells do not vary continuously and deterministically. They vary stochastically and discretely. A stochastic modeling approach may also provide a better fit to the experimental data which have also a noise component. The multiscale nature of the process is rendered through the combination of a low level stochastic approach with a high level algebraic approach, by addressing emergence of and interactions between scales. It is important to note the analogy between the high scale bone tissue and low scale molecules and cells with respect to the Shape Calculus and the its low level implementation. The BMU represents the emerging behavior of the collective action of osteoclasts and osteoblasts and it is the primary building block of the tissue.



Modeling socio economic infrastructure: the green agenda



The green agenda is currently a very pressing topic worldwide. Without doubt this will be a dominant issue for mankind in the coming decades. This concern is driven by a number of factors, but particularly by diminishing of resources to support the ever-growing population and energy hungry technological advancements of the last century. From the perspective of resource consumption, the strategy adopted by modern economies is to assume an over-provisioning of resources to support economic growth, while at the same time ignoring proper plans to recycle/re-use these resources. One good example of this is the energy consumption required to support Internet infrastructures. To date world Internet infrastructure is know to consume 2%-10% of total power consumption. Decision making is often distributed, ad hoc, and made by individuals and institutions that do not normally interact. For these reasons, better design and simulation of the green energy and related infrastructure management scenarios are needed to improve decision making in this environment. The analysis of the multiscale behaviour of the energy context complex social economic system could be modeled interfacing the stochastic-multiagent behavior of the individuals [3] with the infrastructure constraint dynamic implemented in process algebra.

Key references

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