SEMANTIC INSIGHT AND BEHAVIOUR OF THE COMPUTATIONAL BONE CELL POPULATION MODELS

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Background

Bone mechanobiology develops computational models in order to address and better understand mechanotransduction - the molecular mechanisms by which bone cells sense and respond to mechanical signals. Today's high-quality and high-throughput experimentation techniques in molecular biology are the basis for an increasing number of bio-models with growing size and complexity. This necessitates computer support for the overall modelling task. Computer-aided modelling has to be based on a formal semantic description of bio-models. But, even if computational bio-models themselves are represented precisely in terms of mathematical expressions their full meaning is not yet formally specified and only described in natural language. For example, the common mathematical constraint of non-zero division sometimes does not have an adequate interpretation of real biological condition.

A Bio-Mathematical-model has a dual interpretation, referred as intrinsic and extrinsic meaning in [1]: The mathematical expression bears meaning by itself without referring to the biological reality. It can be interpreted, analyzed, and used in computational simulations without knowing what it represents. However, a bio-model is more than a pure syntactical formal expression: it describes a piece of biological reality. The processes included in the model should be significantly precise with all aspects (inputs I, outcomes O, time T, resources R, controls C and preconditions P, *Fig.1*), to be amenable to mathematical formalization. A functional bio-model establishes a mapping between these two conceptual sides.

Results

Equations of bone turnover balance between bone resorption and formation together with time changes of bone resorbing and forming cells numbers form the mathematical model of system of ordinary differential equations (ODEs). Depends on the representative volume of interest these equations describe the process of bone remodelling inside one bone multicellular unit (BMU) or compartment (BMC). The level of complexity depends on number of cell lineages involved in signalling processes and the number of parameters that describe biochemical changes in mechanotransduction of the signals. Two models are presented, compared and discussed. The first model comprises of the system of coupled ODEs with power-law nonlinearity terms that describe autocrine and paracrine signalling of the cell lineages inside BMU [2, 3, 4]. The second contains the cooperative binding Hill`s

equation terms that describe decoy-receptor linking processes of released molecules inside BMC (e.g. [5]). The former is simpler, more elegant and intuitive, however, still has the ability to deliberate about the involved parameters. The second model is more detailed and complex with an increased number of equations and parameters. In both models, the multi-parametric analysis gives the opportunity to decide, which one of the parameters is more responsive regarding of the purpose of the model, for instance as it is effectiveness of osteoclast autocrine signalling g_{cc} presented in [2].
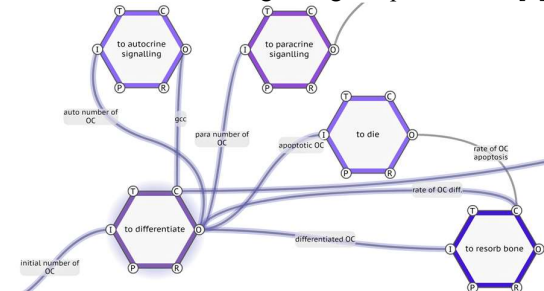

Figure 1: Functional model of osteoclasts activities inside BMU correspondent to the equation from [2, 3].

Conclusions

Functional models are efforts to thwart the ambiguities of written formulas and mathematical solutions and its semantic limits to describe biological reality. A formal semantic description of bio-models would not only be useful in corresponding computer-assisted application scenarios, but also would support biologists to access models, their use and their behaviour as well as the underlying assumptions and decisions. A formal functional description of the involved aspects and their upstream and downstream functions allow presenting relevant information about a model to both biologists and mathematicians in a familiar way.

Keywords

Functional mode of bone cell activities, system of ordinary differential equations, mechanotransduction, and nonlinear multi-parametric analysis

References

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Acknowledgements