Computing Life: Blue-print modelling and domino approach in design principle studies of Reactive Oxygen Species management

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One of the goals of systems biology is to understand how biological function absent from macromolecules in isolation, emerges when they are components in a system. Millions of interactions in the living organism make the system too complex to be handled intuitively in a human brain or on the back of an envelope and require a computer replica of reality. A computer replica of the whole human body will ultimately lead to the Virtual Human model which is now anticipated for personalized medicine.

Here we discuss the application of two techniques which may be useful in building the Virtual Human model: *a domino* approach (building the model by adding modules incrementally, like domino tiles) and blueprint modelling (a generic "blueprint" can be parameterized for a particular instantiation). Both *domino* approach and *blueprint* modelling may be performed hand in hand with design principle studies aiming to identify how certain design features are responsible for a certain biological function. On the one hand, when using the domino approach, one can analyze the functional role of each domino module and check which new emergent properties are gained with the addition of an extra module. On the other hand, one can check which emergent properties are affected by a certain parameter set, e.g. attributed to healthy or diseased cell instantiations.

As an example of design principles study accompanied by blueprint modelling and domino approach, we have built a dynamic ODE-based Reactive Oxygen Species (ROS) management model. ROS management is associated with obesity, cancer, Parkinson's Disease (PD) and other systems biology diseases, which result from a persistent perturbation of the healthy functioning of intracellular and paracellular networks; by implication, each disease is caused by multiple malfunctions at various positions in the network. The converse implication is that different diseases may share the same molecular processes. Our model offers insight into the structure of the system of ROS management and allows the simulation of the disease-specific systemic response to oxidative stress and it can be used in the development of personalized medicine approaches.