MULTISCALE SELF-ORGANIZATION FOR BIOLOGICAL SIGNALING IN CELL-TO-CELL INTERACTION

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ABSTRACT

The study of biological signaling coupled with the problem of multiscale representation and modeling of signal emitter and receiver. The method of additional particles for modeling of self-assembly in such supra-molecular multilevel systems was suggested. The solution for the description and qualitative exploration of living system hierarchical organization and self-assembly processes was developed. Employing well-known effective particles principle for supra-level properties description, we elaborate a theoretical framework that make possible the multiscale biological modeling. We demonstrate that the qualitative nature of the hierarchical organization that described in a manner of multilevel system with a help of developed additional particles approach. We provide a discussion of biological measures and the nature of biological signals. Signaling in this processes are tell by self-organization procedures. The theory of biological signals at collective multilevel hierarchical organization that can form the basis of the description of the internal structures and relative biological measures is proposed. We discuss new theoretical approaches to understand the measurement problems, biological functions and signaling.

Keywords: biological signals, biological measures, self-assembly, multiscale pattern model, coarse-grained modeling.

INTRODUCTION INTO THE PROBLEM

The description of biological interaction requiring adequate quantitative measures. Popular methods of molecular dynamics and chemical kinetics did not fit our needs in detailed description of the biosignaling essence. We are supposing that biological signal transduction tightly connected with processes of self-organizing consistency in emitter and receiver. Therefore biological signaling system requiring multiscale modeling [1]. However there was no trusted theoretical framework for multiscale sub-cell modeling as well there were no efficient computational methods for that purpose. There is coarse-grained approach for supramolecular modeling [2] that can be developed. We tried to investigate the simple method which would allow us to catch physical mechanisms of reciprocal self-consistency of model emitter and receiver of biological signal. This could be imagine as massive conformational changes in several levels of organization.

We assumed that such method should be built up around the bond concept. Self-assembly processes in multilevel systems are related with formation of complexes. In one hand we need to find simplified mechanical analogs for modeled objects, in other hand we need to find adequate models of complex formation engaged with emergent appearing of new properties.

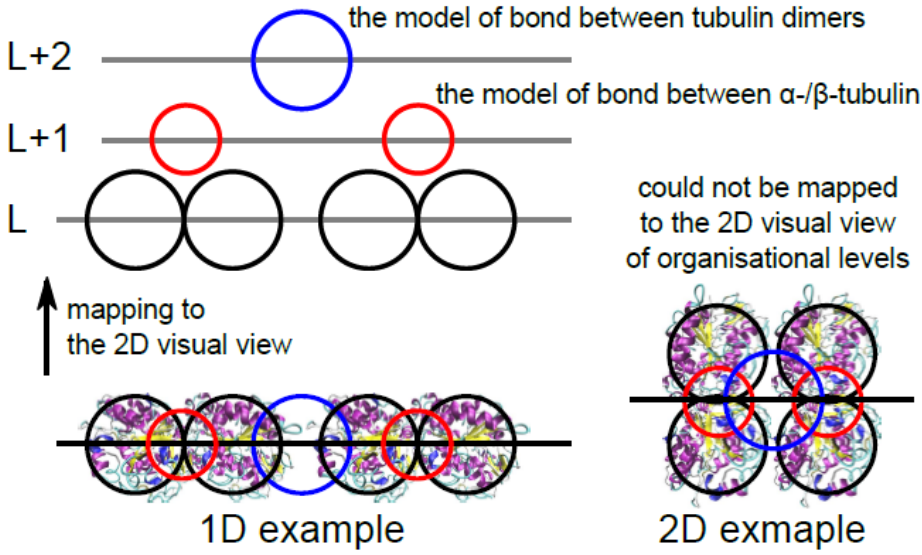

Fig. 1. Object of organization is appearing when the distance between parental objects is less some threshold value

THE SOLUTION

The scale-invariant method of additional particles for modeling bonds in self-assembly models and the theoretical frameworks for modeling multilevel systems were suggested. The concept is based on the idea that model system can be represented by multilevel analog with links described as separate objects (Fig. 1).

In this paradigm the formation and breaking of complexes is describing by the multilevel derivative from the Langevin equation (Fig. 2). We are calling it "reconstruction equation", because it describes constriction as well as destruction processes. This equation can be used for computation of system state evolution. Variable amount of additional particles representing bonds and new properties of complexes. Effective particles are emerging according to fixed local preconditions and forming potential for further system evolution (Fig. 3).

$$m_j^i \frac{d^2 q_j^i}{dt^2} = \sum_{k \neq i} F_j^L(q_j^i, q_j^k) + \sum_{k \notin D_j^i} F_j^{L+1}(q_j^i, q_{j+1}^k)\mathcal{T}_{j+1}^k + \sum_{k \notin P_j^i} F_j^{L-1}(q_j^i, q_{j-1}^k)\mathcal{T}_{j-1}^k +$$
$$+ \sum_{k \in P_j^i} F_j^P(q_j^i, q_{j-1}^k)\mathcal{T}_{j-1}^k + \sum_{k \in D_j^i} F_j^D(q_j^i, q_{j+1}^k)\mathcal{T}_{j+1}^k - \gamma_j^i \dot{q}_j^i + \eta_j^i(t),$$

$$\mathcal{T}_j^i = \theta\left(\sum_{m,n \neq m, D_{j-1}^n \cup D_{j-1}^m = \varnothing} \sqcap\left(\frac{q_{j-1}^n - q_{j-1}^m}{2(r_{j-1}^n + r_{j-1}^m)}\right)\right)$$

Fig. 2. The equation of multi-level self-organization. $\mathcal{T}$— is a trigger function for switching of potentials

This equation uses the idea that particles after interaction changing their configuration. This conformational changes led to irreversible potential energy changes and interaction with other particles is also changing. All this consequences is describing by additional particle without need in rebuilding initial particles potentials (Fig. 4). This concept was quite different from popular effective potentials method, that is why it should been go through the series of verification procedures.

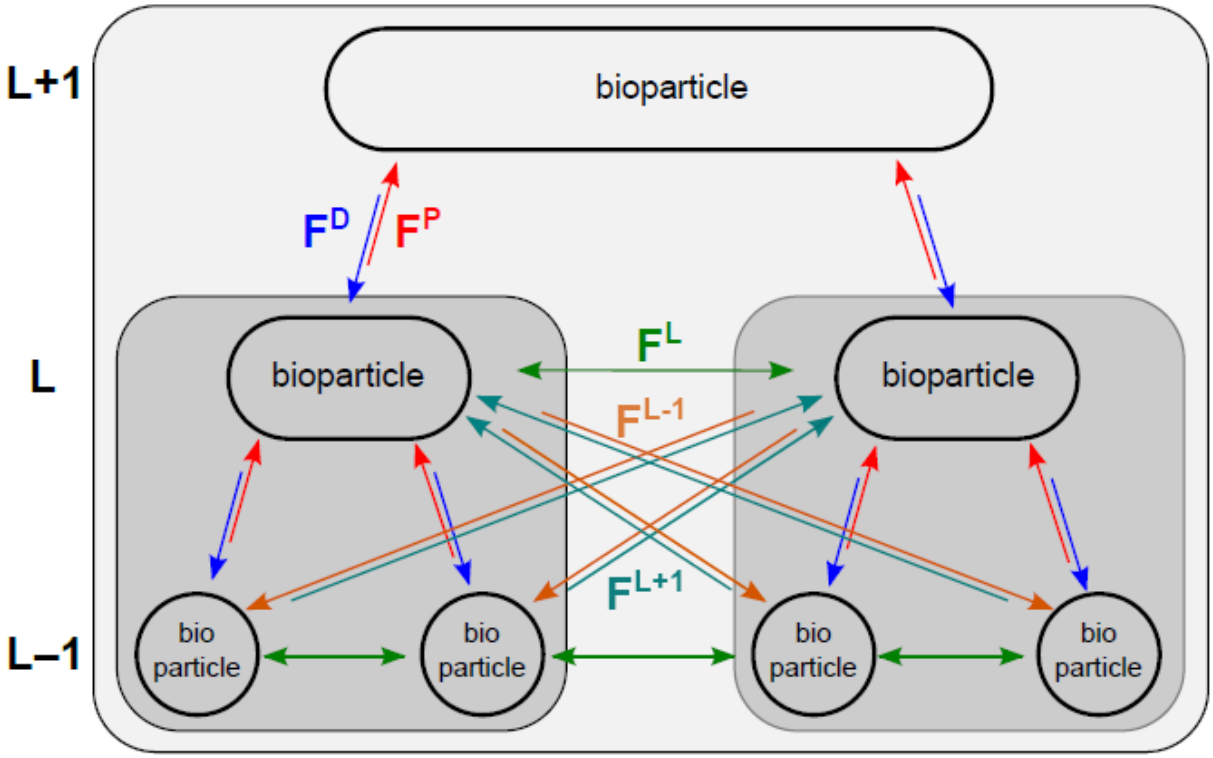

Fig. 3. Five-forces approach for describing of multi-level systems

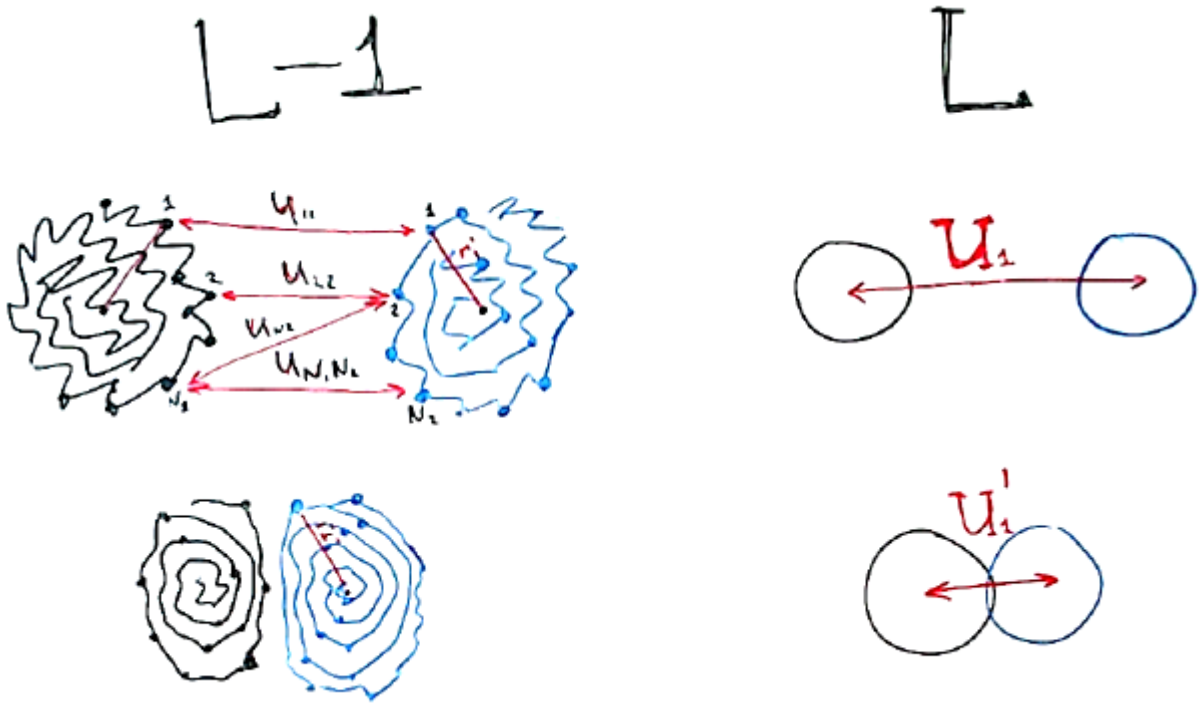

Fig. 4. The parameters that are hidden from the used mechanical analogy, lead to the changes of the potentials between model particles during the bonding process

For porpoise of the framework demonstration the artificial multilevel systems were generated with simple rules of properties succession from one level organization to another. The evolution of model multilevel systems were studied using Runge-Kutta-Merson numerical method in a specially developed computer application (http://levels.molpit.com). It was shown that reconstruction equations allows to study various stable periodic patterns, the dynamics of multilevel systems and the energy transfer through the levels of organization

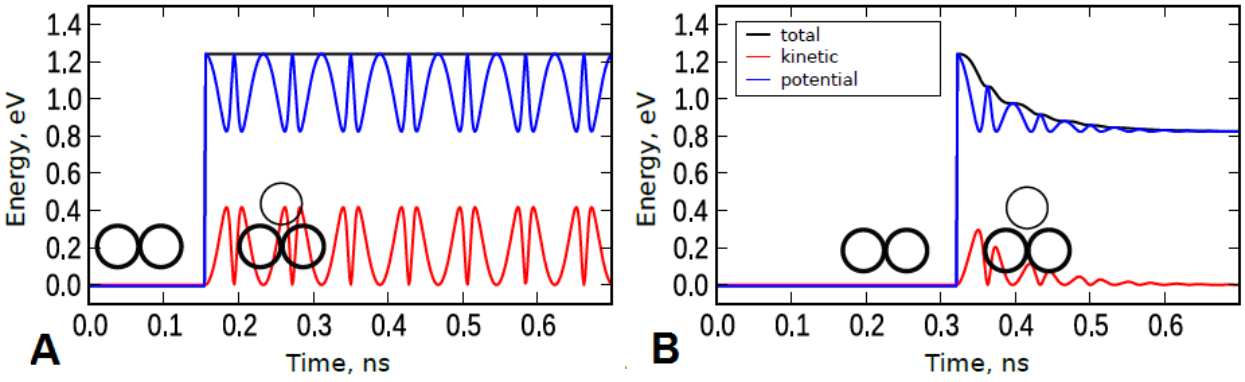

Fig. 5. The energy is skipping with appearing of new object and oscillate or decay in the case of dissipation

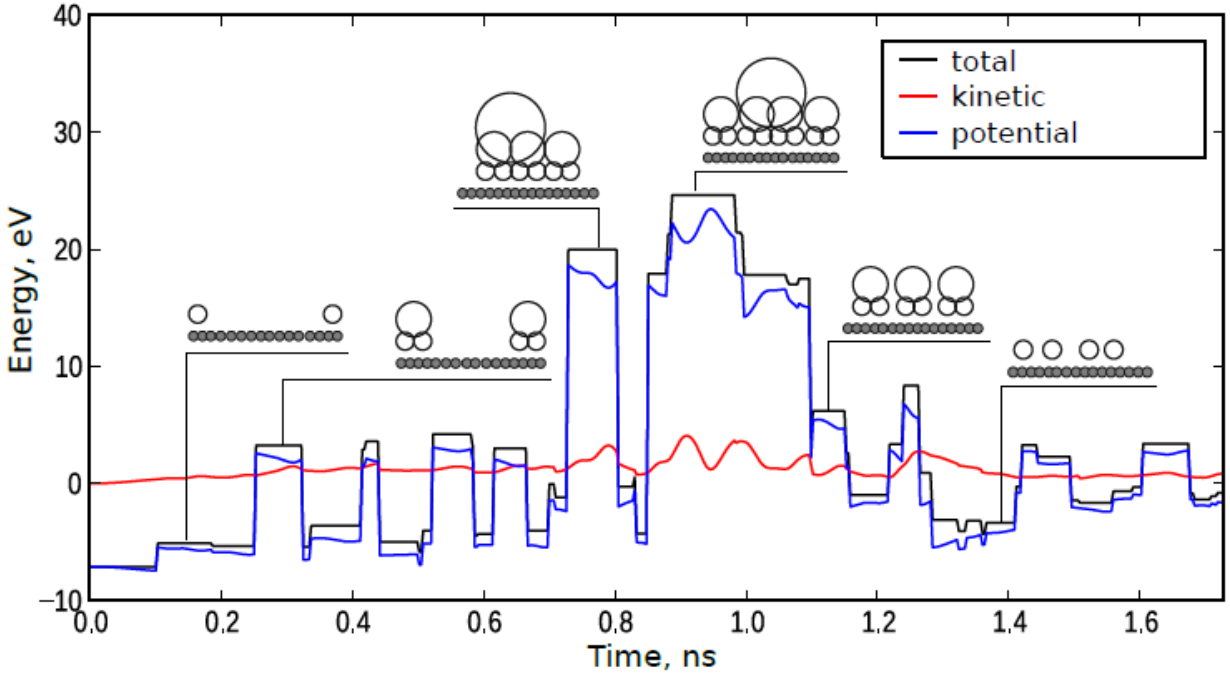

Fig. 6. The total energy dynamics in the case of multi-level self-assembly

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In the molecular dynamics and various shape-based coarse-grain models [2] the effective potentials approach is used to parametrize formation and breaking of bonds. However there are some contraindications like entropic forces (depletion interaction and hydrophobic forces) and various mesoscopic electronic effects on the supra-molecular level that are challenging for the search of the other bonds approximations. On the higher levels of organization the configuration of sub-levels can be dramatically changed during the bonding process what will make the analogy of effective potential even less credible.

CONCLUSION

The method of additional particles was introduced for multiscale modeling of biological systems. The method of additional particles easier taking into account side effects for other particles in the system from the bond formation such us charge redistribution or conformational change. Suggested approach for complex formation can be used in multiscale theoretical frameworks such as coarse-grain models in a couple with effective potentials to increase accuracy of computations. The application for exploring of multi-level systems was developed (http://levels.molpit.com). This allows as to describe biosignaling on the series of model emitters and receivers.

REFERENCES

[1] Pave A. Biological and ecological systems hierarchical organisation // Hierarchy in Natural and Social Sciences / ed. Pumain D. Berlin/Heidelberg: Springer-Verlag, 2006. Vol. 3. P. 39-70.

[2] Arkhipov A., Freddolino P.L., Schulten K. Stability Dynamics of Virus Capsids Described by Coarse-Grained Modeling // Structure. 2006. Vol. 14, N° 12. P. 1767-1777.