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Multiscale modeling of biological systems

Modeling phenomena in biology often requires the inclusion of processes occurring at different spatial and temporal scales. There is an urgent and challenging need to describe biological systems utilizing a multiscale landscape and not just a single scale view. To this end, theories from Mathematics and Physics can provide tools for the modeling and analysis of multiscale phenomena. In this talk, we present a theoretical multiscale framework inspired from Physics, the *Dynamic Density Functional Theory*, which we apply to derive a modeling approach for biological systems that is consistent across the scales.

Our starting point is to model the spatio-temporal evolution of a multi-cellular system by means of the stochastic Langevin equations. In this approach, each cell moves as the result of a balance of forces exerted among the surrounding cells and by the cell microenvironment. A random contribution arises from the local exploration of the neighborhood by the cells.

Methods from statistical physics can be used to derive the corresponding generalized Fokker-Planck equation, which gives the spatio-temporal evolution of the probability distribution of finding the cells of the system at specific locations in the domain.

An interesting level of description consists in assuming the scalar density field as the relevant variable for describing the dynamics of the system. We show how to derive the corresponding *functional* Fokker-Planck equation, which gives the spatio-temporal evolution of the probability that the cells adopt a particular density profile. At this level of description, we show how to include cell proliferation and apoptosis as a stochastic birth-death process in our framework.

Finally, we present the derivation of a *deterministic* macroscopic equation that describes the spatio-temporal evolution of the cell density, including cell movement as a result of a balance of forces, and cell proliferation and death. In this equation, the dynamics of the cell density are regulated by a free energy functional that accounts for interactions among cells and with the microenvironment.

This Dynamic Density Functional Theory is applied to simple interacting multicellular systems. We show how microscopic interactions at the cellular level (*e.g.*, cell-cell adhesion and repulsion) generate correlation terms that contribute to the corresponding macroscopic description at the tissue level. We illustrate our approach for well-established mean-field approximations such as Keller-Segel- and Fisher-Kolmogorov-like models.