Singular perturbations leading to averaging principles in models originating from biology and medicine. Description for general public.

In modelling complex biological phenomena one often needs to take into account the fact that some component processes may be faster than others. For example, in modelling a shoal of fish that some parts of the day spend at the seabed and other parts of the day – just below the surface, and so change survival and growth conditions, one needs to remember that these changes are matters of hours while equally important ageing processes take months and years. As a result, a differential equation one needs to deal with may be of the form

$$u' = Au + \varepsilon^{-1} Bu. \tag{1}$$

The dynamics of a solution u of this equation depends on two operators, A and B, describing two – often competing – forces, and the small parameter ε reflects the fact that B is 'faster'. In some cases the time scales differ so much that a sensible approximation is obtained by letting $\varepsilon \to 0$. Such cases are customarily referred to as singular perturbations (the 'original' equation $u' = Au$ is perturbed by B, but the perturbation is singular since the influence of B is infinitely times larger than that of A). Mathematical analysis of singular perturbations is rather non-trivial: the limit equation is usually quite different from those approximating it (for example, hyperbolic equations may approximate a parabolic equation), while retaining traces of influence of both A and B. The question of convergence of solutions is also rather complex: typically, the solutions converge 'in a regular way' for quite special initial data, taken from a subspace of the underlying Banach space; outside of this subspace they may converge in a weaker sense.

The project is aimed at analysing two models involving singular perturbations. These models originate from contemporary biology and medicine. In the first of them, we consider a chaotic motion of particles in a thin layer between two very similar surfaces and are interested in the form of the equation describing the limit movement, as the distance between these surfaces tends to 0. Intuitively, the limit equation should describe a movement on a surface analogous to the boundaries. For example, in modelling signal transmission in B lymphocytes one should take into account that the radius of the nucleus of these cells is quite large (larger than 0.9 of the radius of the cell) so that the signal-transmitting kinases move in a very thin layer between the nucleus and the cell's membrane, which may be thought of as a sphere. The fact that the layer is so thin strengthens the interactions between diffusing kinases and receptors on the cells' membrane, and has important biological implications.

This idea can be formally expressed as a convergence theorem concerning solutions of approximating equations; this convergence becomes of singular perturbation type once we note that decreasing the distance between the surfaces forming the boundary is tantamount to fixing the distance while increasing the speed of diffusion in one direction (perpendicular to the surface). It is worth stressing that reaction diffusion equations involved here are usually supplemented by boundary conditions describing loss or inflow of particles of interest at the boundary of the region (for example, if kinases are activated at the cell's membrane, we observe inflow of active kinases from that direction; if we are interested in the dynamics of inactive kinases, however, we will observe their loss at the boundary). Clearly, the limit equation should also feature terms responsible for such loss or inflow, but they cannot be a part of a boundary condition, since there are no boundary conditions in the limit. One of the mathematical challenges is to describe analytically the mechanism of transferring information contained in boundary conditions to the limit equation.

The other model the project is devoted to comes from medicine, and is concerned with two types of mutations: 'drivers' and 'passengers', that are crucial in early stages of cancer development. The unfrequent 'drivers' lead to rapid increase of selective advantage of mutated cells, while numerous 'passengers' gradually decrease this advantage. We propose a model of a population of individuals where, besides random changes in fitness, selective forces play an important role: this is an equation of the form (1) where A describes mutation and B describes selection. In cancerous populations mutated cells take over by eliminating less fit cells, and a master equation for such population can be obtained by letting $\varepsilon \to 0$ in (1). If the majority of cells is healthy, selective forces are of smaller importance than mutations, and a proper approximation is obtained by letting $\varepsilon \to 0$ after exchanging the roles of A and B in (1).