This project has arisen from my curiosity as why biological processes happen the way they do, what determines the rates of these processes and the life-time of biological entities; how to model biological, living systems? These are extraordinary complex questions and I have no illusion that they might not be fully answered by many generations to come. However, even a tiny step forward can cause a substantial breakthrough in our knowledge and in the development of new biotechnological applications. For instance, developing reliable tools for modelling cellular processes can help to optimize the *in vivo* methods for production of many important enzymes and other molecules for medicine and biotechnology, while saving the money of business and tax-payers on expensive experiments.

This proposal is a first step towards such modelling, and a humble attempt to expand our knowledge and provide a better understanding of diffusion in a crowded, jelly-like environment of the interior of biological cells, which are the basic elements, the atoms of all known lifeforms on Earth. My primary interest is the diffusion of macromolecules (such as proteins, enzymes, *etc.*) in equilibrium, but also out of equilibrium, as very recent experiments demonstrate that diffusion inside active and non-active cells can differ dramatically. The focus of this project is on the dependence of diffusion on the size and shape of macromolecules, and how the basic processes of cell metabolism, such as metabolic fluxes and chemical reactions, affect it.

I will also pay a considerable attention to metabolites, smaller molecules (such as glucose, sucrose, vitamins, *etc.*) that are transformed in various metabolic pathways inside cells. Diffusion of these molecules has been practically forgotten by the biophysical community, but it is the key to understanding the rates of many cellular processes. The ultimate goal is to predict the transport properties of metabolites from computer simulations, and to connect them to mulstiscale approaches for reaction-diffusion processes in a cellular environment.

This study will be conducted mainly by using computer simulations, but a tight collaboration with my experimental colleagues is also planned. This is important in order to validate the models and approaches used, but even more so to set a solid ground for our understanding of diffusion as the foundation for further work. Indeed, my long-term goals go far beyond the objectives of this project. I aim ultimately at developing a reliable spatially-resolved whole-cell simulation framework, which would help us answer many technologically and biophysically relevant questions. Metabolic transport and macromolecular diffusion are two essential ingredients of this framework, and their clear understanding is absolutely crucial, without which any progress in this direction will not be possible.