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COMPUTATION OF CANCER CELLS STEADY STATE THROUGH CHEMICAL REACTION NETWORKS FOR KINETIC PARAMETERS ESTIMATION

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Most cellular functions are regulated by complex networks of chemical reactions involving loads of proteins and many cancer diseases arise due to the effects of one or multiple mutations that alter the behavior of the network by enhancing or supressing the activity of specific proteins of the network.
From a mathematical viewpoint, Chemical Reaction Networks (CRNs) can be modelled like systems of autonomous ordinary differential equations, whose steady state solutions yield the cell's proteins concentrations [1] [2]. Finding such states is a key step for studying the global effects due to each mutation and may help to determine which drugs to administer in order to balance mutations' effect and bring cells back to the physiological state.

Steady states of cell's proteins are usually computed by simulating the system's dynamical evolution in time [3], but, since this is a vary time-consuming process, here a different method is proposed. It consists in recasting the steady state computation problem as a root-finding one: to solve the latter, the system's equilibrium points are computed by means of an algorithm that combines the Newton method and the gradient descent approach. Considered that proteins concentrations must have positive or, at most, null values, a suitable operator at the end of every iterative step is applied for assuring compliance with the non-negativity constraints.

The CRN used to conduct the research is the one associated to colorectal cancer cells. Such CRN and the kinetic parameters therein have been manually defined starting from literature data; however, to make such a model actually usable, an automatic technique needs to be developed in order to build CRNs associated to different cell types. To this end, it's necessary to estimate the kinetic parameters from measurements of some of the species concentrations, that results in an ill-posed inverse problem where the number of unknowns is typically much higher than the quantity of available data. Having a fast and robust method for solving the corresponding forward problem is a good starting point for dealing with the inverse one and, therefore, figuring out how to build new CRNs.

References

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