11th Conference on Dynamical Systems Applied
to Biology and Natural Sciences DSABNS 2020
Trento, Italy, February 4-7, 2020

VALIDATION OF A DYNAMIC SYSTEM MODEL FOR THE COLON–RECTAL CANCER CELLS VIA CHEMICAL REACTION NETWORKS

Sara Sommariva*[1], Mara Scussolini[1],
Giacomo Caviglia[1], Silvia Ravera[2],
Lorenzo Tortolina[3], Nicoletta Castagnino[3],
Silvio Parodi[3] and Michele Piana[1,4]

[1]Dipartimento di Matematica, Università di Genova, Italy

[2]Dipartimento di medicina sperimentale, Università di Genova, Italy

[3]Dipartimento di medicina interna, Università di Genova, Italy

[4]CNR–SPIN, Genova, Italy

sommariva@dima.unige.it (*corresponding author),
scussolini@dima.unige.it, caviglia@dima.unige.it,
silvia.ravera@gmail.com, nicoletta.castagnino@gmail.com,
silvio.parodi@unige.it, piana@dima.unige.it

Each cell function is regulated by a complex signaling network that translates extracellular signals into cellular responses and whose alteration underline diseases as cancer [1].

From a mathematical perspective, this process can be modelled through a chemical reaction network (CRN) [2], i.e. through a graph whose nodes are the involved chemical species and the edges are the chemical reactions. By applying mass action kinetics, the concentration dynamics of the species in a CRN gives rise to a polynomial system of ordinary differential equations (ODEs).

Here we study and validate the CNR for the G0-G1-S transition of colon-rectal cancer cells presented by Tortolina and colleagues [3], involving 419 chemical species and 850 chemical reactions. In particular, we study the corresponding system of ODEs, by characterizing moiety conservation laws, asymptotic steady states, and numerical solutions. We then simulate the steady state of a physiological cell and quantify its alteration due to various combinations of loss and gain of function mutations. We validate our model by comparing our results with those in the literature on the effect of each mutation.

Our study represents the first step of a mathematical tool for the design of targeted drugs.

References

[1] Barabási, A. L. & Oltvai, Z. N. (2004). *Network biology: understanding the cells functional organization*. Nature Reviews Genetics, 5(2):101. https://doi.org/10.1038/nrg1272.

 ISBN: 978-989-98750-7-4

[2] Feinberg, M. (1987). *Chemical reaction network structure and the stability of complex isothermal reactorsI. The deficiency zero and deficiency one theorems.* Chemical Engineering Science, 42(10), 2229-2268. https://doi.org/10.1016/0009-2509(87)80099-4

[3] Tortolina, L., Duffy, D. J., Maffei, M., Castagnino, N. & others. (2015). *Advances in dynamic modeling of colorectal cancer signaling network regions, a path toward targeted therapies*. Oncotarget 6.7:5041. https://doi.org/10.18632/oncotarget.3238.

 ISBN: 978-989-98750-7-4