Analysis of the complex system "TE-TA-P" [telomeres-telomerase-proliferation] coupled to experimental data in cancer cells.

Despite the difficulty for analyzing the physiopathological mechanisms which are involved, the practical importance of biological oscillations justifies the development of their study because they condition the response to an external stimulation depending on the time when it is applied to the system. The Te-TA-P network includes 3 oscillating parameters : - length of telomeres (chromosome endings) - telomerase activity (telomere repair)- cell proliferation rate. The Te-TA-P system is paradigmatic among oscillatory biological systems, because it is a key both for normal tissular development (characterized by progressive cell senescence due to definitive telomere erosion), and for long-term survival of stem cells and tumor cells (characterized by telomere repair which allows unlimited proliferative capacity). The maintenance of the system TE-TA-P at equilibrium is linked to the cancerous character of the cells. One can foresee that pushing the cells out of this equilibrium by light impulsions on a component of the system will durably change the proliferation dynamics. Our hypothesis is that such bifurcation of the dynamics, incompatible with persistent high proliferation, will induce the slow-down of mitoses and/or increase apoptosis, resulting in a negative balance of tumor cell growth.

The purpose of our experimental work on tumor cultured cells is 1) to analyse the interactions of the 3 variables in the Te-TA-P network by simultaneous quantification in long time series, 2) to modelize the metabolic loops that link them in order to predict the fluctuations, and finally 3) to control the activity of this system by external forcing.

This approach of the cell proliferation dynamics already brought us important results. It bears important applications on practical problems such as tumor regression and intermittent resistance to anticancer drugs.