

CELL PROLIFERATION, CIRCADIAN RHYTHM, TUMOUR GROWTH AND CANCER CHRONOTHERAPEUTICS

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ABSTRACT. Cell proliferation in health and disease, particularly cancer, is never a question involving a single isolated cell, but rather a problem to be considered at the level of cell populations. For this reason, physiologically structured partial differential equations modelling the cell division cycle in proliferating cell populations have been designed. The structure variables used are not space, but age in the cell cycle or in one of its phases, cell size, content in DNA or specific proteins (cyclins). Physiological cell proliferation control, that is disrupted in cancer, relies in particular on molecular circadian clocks (one is present in each nucleated cell), for which models, and models of their control on the cell division cycle, have also been developed. Another type of control on cell proliferation is exerted by anticancer drugs, that have effects on both healthy and cancer cells, and these effects are again dependent on circadian clocks. Hence an optimal control problem: destroying cancer cells with minimal damage to healthy cell populations, taking into account circadian influences. This can be tackled and partly solved by taking advantage of differences, known though not completely understood, between healthy and cancer cells with respect to the effects of drugs at different times of the 24-hour span. This is the object of cancer chronotherapeutics, in use in the clinic, for which modelling approaches will be presented.

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