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seminar series

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Cell cycle regulation by systems-level feedback controls

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Thursday, 16:00 – 17:00

Seminar room 132, pavilion A11
University campus Bohunice

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Cell cycle progression in eukaryotes is controlled by a seemingly universal protein interaction network composed of protein kinases and phosphatases, transcription factors, ubiquitin-conjugating enzymes, and stoichiometric inhibitors. These molecular interactions embody a dynamical system that (when all is well) oscillates once per cell cycle. When genomic integrity is in jeopardy, however, the oscillation ceases immediately at a checkpoint until the problem is resolved. Negative feedback loops are fundamental for the oscillation, whereby a cell cycle regulator down-regulates another one that acts earlier in the sequence and is responsible for its activation. I will argue that bistable ('toggle') switches are also important design principles of eukaryotic cell cycle control networks. A bistable switch arises from positive or double-negative feedback loops, and it is characterized by two alternative steady states separated by two distinct thresholds. The two qualitatively different states correspond to two successive phases of the cell cycle. Bistable cell cycle switches provide a conceptual framework for irreversibility of cell cycle transitions and underlie the G1/S and G2/M transitions as well as the Start/Restriction Point and mitotic exit. The meta/anaphase transition, guarded by the Spindle Assembly Checkpoint (SAC), is also characterized by a 'toggle' switch. A few representative cell cycle switches will be illustrated by experiments and computational modelling.

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