

Spontaneous synchronisation and the cell cycle

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The cell cycle is the series of events that take place in a cell leading to DNA replication and production of two daughter cells [1]. The cycle includes processes that detect and repair genetic damage, and prevent uncontrolled cell division [2]. It has been suggested that a network of cyclin-dependent kinases (Cdks) drives progression along the phases of the mammalian cell cycle, and that this network engages in sustained oscillations which correspond to ordered, sequential activation of the cyclin/Cdk complexes that control the successive phases of the cell cycle [3]. Other studies have shown that a Cdk-autonomous network of transcription factors is sufficient to produce steady-state oscillations in gene expression [4].

Description of the driving force for the cell cycle in terms of sustained or steady-state oscillations is reminiscent of descriptions of biological, physical and mechanical systems that have been shown to exhibit spontaneous synchronised, collective behaviour. Examples from biology include fireflies, heart muscles, sleep cycles and brain waves [5]. In some cases spontaneous synchronisation has been identified even if the mechanism of coupling between individual participants is not obvious. We suggest that, in a similar way, it may be possible for the cell cycles of neighbouring cells to become spontaneously synchronised, if and when suitable conditions exist, e.g., in the presence of defects or disease. We are not proposing that spontaneous synchronisation of cycles between neighbouring cells is necessarily common or permanent. Rather, we suggest that temporary islands or “domains” of cells with synchronised cell cycles can form and exhibit collective behaviour for some time, before disappearing. Spontaneous synchronisation is more likely when a number of neighbouring cells are at similar points in their cycles, i.e., the cycles have similar phases. Spontaneous synchronisation is also made more likely by the presence of defects in membranes between neighbouring cells [6].

During the lifetime of a domain, the cycle of an individual cell would be entrained by the cycles of neighbouring cells. Rather than each cell cycling at a rate that is suitable for its own circumstances, the cells that are members of the domain would cycle collectively at some averaged rate.

The G1/S and G2/M checkpoints in the cell cycle are critical in enabling the repair or elimination of cells with damaged DNA, before they produce mutant daughter cells. Checkpoints either stall the cell cycle until repairs are made or, if repairs cannot be made, target the cell for destruction via apoptosis [2]. We suggest that a cell with faulty DNA whose cycle is synchronised with those of surrounding healthy cells may be dragged past the checkpoints even if, in isolation, it would be stalled to allow repair or marking for apoptosis. In this case a faulty cell that is cycling collectively with its neighbours would be

able to produce flawed daughters, whereas an identical cell that is cycling independently of its neighbours would not.

Coupled progression of neighbouring cell cycles could also have the opposite effect, forcing individual cells to cycle more slowly than they would in isolation, thereby slowing creation of new cells for repair or growth.

Boundaries between domains of synchronised cell cycles would be of interest in their own right: they could exhibit motions and pinning analogous to those of magnetic domain boundaries. Coupling behaviour within domains could cause excitations analogous to, e.g., phonons or magnons [7].

Experimental work would look to find spontaneous synchronisation between cell cycles of neighbouring cells, identify a mechanism for coupling, understand the consequences of synchronisation and, ultimately, engineer coupling.

References:

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- 6) http://en.wikipedia.org/wiki/Cell_membrane
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