Contribution ID: **63** Type: **Oral Presentation**

Continuum mathematical models for cell migration incorporating cell cycle dynamics

Wednesday, 11 July 2018 16:00 (20 minutes)

Fluorescent ubiquitination-based cell cycle indicator, also known as FUCCI, allows the visualisation of the G1 and S/G2/M cell cycle phases of individual cells. FUCCI consists of two fluorescent probes, so that cells in the G1 phase fluoresce red and cells in the S/G2/M phase fluoresce green. FUCCI reveals real-time information about cell cycle dynamics of individual cells, and can be used to explore how the cell cycle relates to the location of individual cells, local cell density, and different cellular microenvironments. In particular, FUCCI is used in experimental studies examining cell migration, such as malignant invasion and wound healing. Here we present new mathematical models which can describe cell migration and cell cycle dynamics as indicated by FUCCI. The *fundamental* model describes the two cell cycle phases, G1 and S/G2/M, which FUCCI directly labels. The *extended* model includes a third phase, early S, which FUCCI indirectly labels. We present experimental data from scratch assays using FUCCI-transduced melanoma cells, and show that the predictions of spatial and temporal patterns of cell density in the experiments can be described by the fundamental model. We obtain numerical solutions of both the fundamental and extended models, which can take the form of travelling waves. These solutions are mathematically interesting because they are a combination of moving wavefronts and moving pulses. We derive and confirm a simple analytical expression for the minimum wave speed, as well as exploring how the wave speed depends on the spatial decay rate of the initial condition.

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Session Classification: In-host, cell cycle & differentiation

Track Classification: Biochemistry and Cell Biology