Thursday, July 26th, 14:00 **Room: T.B.A.**

MINISYMPOSIUM

COLLECTIVE MIGRATION IN INTERACTING CELL SYSTEMS

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Minisymposium Keywords: collective cell migration, mathematical model, wound healing, organogenesis, development

Collective migration is an emergent phenomenon observed in systems consisting of moving and locally interacting agents. In particular, collective cell migration plays a crucial role in multi-cellular organisms during development, but also in patho-physiological situations. In the minisymposium examples are presented including wound healing, and development of epithelia and the lateral line.

We address two main topics: first, new data-based methods used for reverse-engineering interactions between units from their trajectories, and, secondly, the characterisation of unifying principles behind the diverse manifestations of collective migration in interacting cell systems on the basis of mathematical models. We will focus on multiscale analysis of the mathematical models for collective migration which allows to predict behaviours on one scale, e.g. the scale of the population, from known behaviour on other scales, e.g. the individual interaction scale. Models include cellular automata, cellular Potts model and partial differential equations [1, 2].

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THE ROLE OF PERSISTENCY IN SINGLE AND COLLECTIVE CELL MIGRATION

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Joint work with Haralampos Hatzikirou (Helmholtz Center for Infection Reserarch), Rainer Klages (Queen Mary University of London) and Andreas Deutsch (Technische Universität Dresden)

Keywords: Cellular automata, Alignment interactions, Persistency.

Cellular automata (CA) are discrete time, space, and state models which are extensively used for modeling biological phenomena. CA are "on-lattice" models with low computational demands. In particular, lattice-gas cellular automata (LGCA) have been introduced as models of single and collective cell migration. We introduce a method to obtain lattice-gas cellular automaton interaction rules from physically-motivated "off-lattice" Langevin equation models for migrating cells. In particular, we consider Langevin equations related to single cell movement (movement of cells independent of each other) and collective cell migration (movement influenced by cell-cell interactions). First, we derive rules for pairwise nematic alignment interaction [3]. This kind of alignment has been observed in biological systems such as swarms of amoebae and myxobacteria. Nematic alignment drives cells to align either front-to-front or back-to-front. Under appropriate assumptions, we have derived the LGCA transition probability rule from the steady-state distribution of the off-lattice Fokker-Planck equation. Furthermore, using an analogous procedure, we derive rules for single-cell persistent movement [4]. In this model, single cells move superdiffusively at short times, while at long times appearing normally diffusive. Finally, we combine both rules to model persistent cells with cell-cell nematic alignment interactions. We show that, at high cell densities, the competition between persistency and alignment interactions results in an order transition from global nematic alignment at low persistency values, to local nematic alignment at high persistency values.

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INFLUENCE OF GROUP DECISIONS ON COLLECTIVE CELL MIGRATION

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Joint work with Jacopo Di Russo, Dimitri Probst, Ulrich S. Schwarz, Tamal Das and Joachim P. Spatz (MPI for Medical Research Forschung)

Keywords: Collective cell migration, Directional guidance, Decision making, Wound healing.

Collective migration is a central event involving coordinated movement of several individuals. One of the critical events during collective migration is the emergence of leading individuals, who provide directional guidance for the group movement. While on the move, animals select their leaders by a collective decision making process, which require active participation of the followers. On the contrary, the prevalent view on collective cell migration, especially in the context of epithelial cells during wound healing, assumes a hierarchical leader-follower organization and belittles the contribution of follower cells in choosing or regulating the leaders. We report and analyse distinct phases of collective migration during wound closure and demonstrate how cellular-level shared decision-making process and collective mechanical dynamics influence selection, regulation and kinematics of leader cells in these phases. We demonstrate that emergence of leader depends on the dynamics of the follower cells and is spatially limited by the length-scale of collective force transduction. Once formed, the leader becomes the puller and guide the followers by a force mediated mechanism [5]. The territory of a leader can extend only to the length up-to which cells can pull on their neighbors. These findings provide a novel mechanobiological-insight into the hierarchy in cell collectives during epithelial wound healing.

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COLLECTIVE EFFECTS OF CELL MOTILITY WITHIN STRATIFIED EPITHELIA

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Keywords: Epithelium, Cell migration, Mechanical stress.

Cell motility within a stratified (multi-layered) epithelium, like radial intercalation during epiboly of frog embryos [6], is driven by mechanical stresses between the cells. External forces, often used to drive cell motility in theoretical models, are inadequate due to the lack of a rigid scaffold surrounding the cells [7]. Thus we consider a mechanism that involves shear forces acting between adjacent cells, and moving one cell forward requires the adjacent cells pulled backward. We show that the collective effect of such a behavior yields tissue deformations that strongly depend on the volume fraction of motile cells: low and high volume fractions yield opposite cell displacements and bending moments within the tissue.

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NON-LOCAL HYBRID MODEL FOR COLLECTIVE CELL MIGRATION DURING ZEBRAFISH POSTERIOR LATERAL LINE DEVELOPMENT

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Keywords: Lateral line development, Collective migration, Organogenesis, Hybrid model.

The morphogenesis of zebrafish posterior lateral line (pLL) constitutes an interesting system widely used to study cell collective migration and reorganization. From a biological point of view, it indeed provides an example of in vivo organogenesis process that has the potential to be easily observed as, following fertilization, zebrafish embryos are in fact transparent and characterized by a rapid development. From a modelling point of view, it constitutes an interesting challenge as physiological pLL formation results from several interconnected phenomena regulating the organization of a small group of cells constituting pLL primordium, and their collective migration along the body of the animal. In this respect, we propose a hybrid model where cells are represented as discrete entities, while a continuous approach is employed at the molecular level. Proper rules are defined to implement the cell phenotypic transitions [8] that trigger and regulate cell collective migration driving the directional motion of pLL primordium and the formation (and deposition) of mechanosensory proto-organs with rosette-like structure. Moreover, the model is able to take into account cell proliferation (and consequent cell reorganization) occurring during pLL development. Numerical simulations show the potential of the proposed approach to qualitatively reproduce the biological experiments as, for instance, some of those presented in [9, 10].

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