**2959-Pos**

**The Morphological Signatures Related to Heterogeneous Motility of Cancer Cells Under Constraints**

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Cancer cell metastasis is a leading cause of cancer-related death. However, little is known about the biophysical signature of individual tumor cells and their heterogeneous invasion abilities through pores of the dense extracellular matrix. Using multi-staged serial invasion microchannel (MUSIC) devices, where there are serial constrictions to sample individual cell invasion dynamics, we investigate the morphological signatures of subpopulations of heterogeneous MDA-MB-231 breast cancer cells during invasion through confined constriction channels and determine the relationship with cell speed, with a focus on distinguishing between fast and slow groups. We further determine the effects of different confinement geometries. The microfluidic devices are fabricated using soft-lithography. MDA-MB-231 cells are loaded into the inlet reservoir of a device by external pressure. The cells are carried by the fluid flow into the micro-channel (19μm W*6.8μm H) and become stuck at the entrance of the first constricted region (7μm W*6.8μm H)) of each channel. The inlet is then washed and the pressure is balanced. A confocal microscope (Leica TCS SP8) is used to image the spontaneous migration of the cells. Acquired images are processed by custom macro (ImageJ) and Matlab scripts. We find a significantly higher speed in the subpopulation with the highest rate of length change compared to the subpopulation with the lowest rate. This suggests that rapid cell shape oscillations are characteristic of the fastest subpopulation. In addition, we quantify other morphological signatures of cancer cells associated with high motility. We find that the formation of a distinct wide protrusion(s) at the anterior is a key characteristic of the fastest cell subpopulations in all channel geometries.

**2960-Pos**

**Topographical Guidance of Highly Motile Amoeboid Cell Migration**

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Cells encounter a wide variety of physical and chemical cues when navigating their native environments. Recently, anisotropically distributed topographic features, much smaller than the cell size, were shown to direct cell migration, a processes named topotaxis. To complement these results, we explored the possibility of long-range topographical guidance, generated by physical objects of cell size and larger. Such guidance is especially relevant for cells that navigate entire tissues, have minimal adhesion to their micro-environment and being highly motile, like patrolling leukocytes during immune response and amoeboid sarcoma cell migration during metastasis. For such highly motile amoeboid cell migration, we show that long-range topotaxis is generated by anisotropic distributions of physical objects of cell size and larger. This form of topotaxis emerges as a physical effect from a combination of the asymmetry of the cell environment and the inherent stochasticity of cell motion. By modeling cell movement through a crowded environment, as a jump process between different spacings, we show that random movement in a field of large physical objects must result in topotaxis. In addition, we explore the role of persistence during topotaxis by active-particle simulations and the role of adhesion and volume exclusion by a cellular-potts modelling. Finally, our measurements show that long-range topographic guidance is conserved during chemotaxis, and moreover, the two guidance cues, topotaxis and chemotaxis, abide to linear summation, guiding the cell in the direction of both external cues combined. While in vivo studies mostly focus on chemotaxis alone, as topographical guidance is conserved for multi-cue micro-environments, it is an additional deciding factor in in vivo cell migration. Finally, topotaxis offers an independent way to steer cells, which can be exploited as a tool for in vitro applications, like cell sorting, lab on chip diagnosis and tissue engineering.

**2961-Pos**

**High Hydrostatic Pressure Induces Vigorous Flagellar Beating In*Chlamydomonas* Non-Motilemutants Lacking the Central Apparatus**

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The beating of eukaryotic flagella (also called cilia) depends on the sliding movements between microtubules powered by dynein. In cilia/flagella of most organisms, microtubule sliding is regulated by the internal structure of cilia comprising the central pair of microtubules (CP) and radial spokes (RS). *Chlamydomonasparalyzed-flagella* (*pf*) mutants lacking CP or RS are non-motile under physiological conditions. Using high-pressure microscopy [1,2], here, we show that high hydrostatic pressure induces vigorous flagellar beating in *pf* mutants. The beating pattern at 40 MPa was similar to that of wild type at atmospheric pressure. This is the first in vivo observation of beating in CP/RS-lacking cilia/flagella. Demembranated axonemes of these mutants also display beating upon addition of ATP at high pressure; therefore, pressure must induce beating by directly acting on the axoneme. Mutant flagella lacking outer arm dynein (OAD) together with the CP or RS do not display beating at high pressure, suggesting the involvement of OAD activity in pressure-induction of beating. This is similar to the previous results, at which the demembranated *pf* mutant axonemes could be activated in vitro in the presence of ATP plus salts or organic compounds [3]. In addition, at 80 MPa, flagella underwent an asymmetric-to-symmetric waveform conversion, similar to the one triggered by an increase in intra-flagella $Ca^{2+}$ concentration during cell's response to strong light. Thus, high hydrolytic pressure seems to increase intra-flagella $Ca^{2+}$ concentration, in addition to inducing flagellar beating in the *pf* mutants.

[1] Nishiyama M. & Arai Y. 2017. *Methods Mol Biol.***1593**, 175-184.
[2] Nishiyama M. 2017. *Biophys Chem.***231**, 71-78.
[3] Yagi T. & Kamiya R. 2000. *Cell Motil Cytoskeleton*. 46, 190-199.

**2962-Pos**

**Collective Synchronization of Contractile Forces in Tumor Spheroids**

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Contractile forces that tumor spheroids exert on 3D collagen matrices can be computed from the matrix deformations surrounding the spheroids, whereby their spherical geometry can be exploited to greatly simplify the computation. In particular, we find a scale-invariant relationship between spheroid radius and matrix deformation amplitude that allows us to derive a look-up table of spheroid contractility as a function of the radially decaying matrix deformations. For spheroids with low contractility, matrix deformations decay with increasing distance to the spheroid center according to a power law with an exponent of −2, as expected for a linear elastic material. With increasing contractile forces, the deformations close to the spheroid decay more slowly, with a power law exponent of −0.2 near the spheroid surface, indicating long-range force transmission due to the stiffening of collagen fibers. Far from the spheroid surface, the deformations again decay with radius according to an exponent of −2. This holds true also for non-spherical tumoroids and histoids so that deviations from spherical geometry do not pose a problem for our method. With this method, we investigate primary breast cancer tumor spheroids derived from patient biopsies and observe forces that are substantially greater compared to forces of breast cancer cell lines. Contractile forces increase linearly with spheroid radius, indicating that mostly cells at the outer surface contribute to collective forces. Furthermore, we observe periodic force fluctuations in primary luminal B tumor spheroids, indicating collective synchronization of traction generation across the entire spheroid.

**2963-Pos**

**Modeling Co-Evolution of Mechanically Heterogeneous Cell Populations**

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Biological tissues are commonly heterogeneous with many different cellular phenotypes populating them. This heterogeneity can be witnessed in the different biomechanical properties of cells such as differences in cell stiffness, cell-cell adhesion and cell contractility. These differences in cell mechanotype can manifest themselves as varying rates of proliferation, migration and apoptosis. Here we simulate the coevolution of co-cultures of mechanically different cells to understand how heterogeneity in the cellular mechanotype influences cell-cell interactions and overall tissue dynamics. The key features of our simulations are the incorporation of mechanosensitive cell death and division rates, and fate dependent changes in cell mechanotype to accurately capture the effects of these on tissue function and dynamics. When the simulations are run without cell death and division, the simulated fate of the tissue aligns with the predictions of the SPV model and the differential adhesion hypothesis in terms of the extent of mixing or de-mixing and self-organization of the different cell types. However, the introduction of cell death and division into the model provides contrasting results such that there is – 1) fluidization of previously jammed epithelial tissue, 2) de-mixing of epithelial and mesenchymal-like cells even though the overall tissue is fluid, and 3) mixing of cells types