Collective cell motion in endothelial monolayers

A. Szabó[1,5,6], R. Ünnep[1], E. Méhes[1], W.O. Twal[2], W.S. Argraves[2], Y. Cao[3], A. Czirók[1,4]

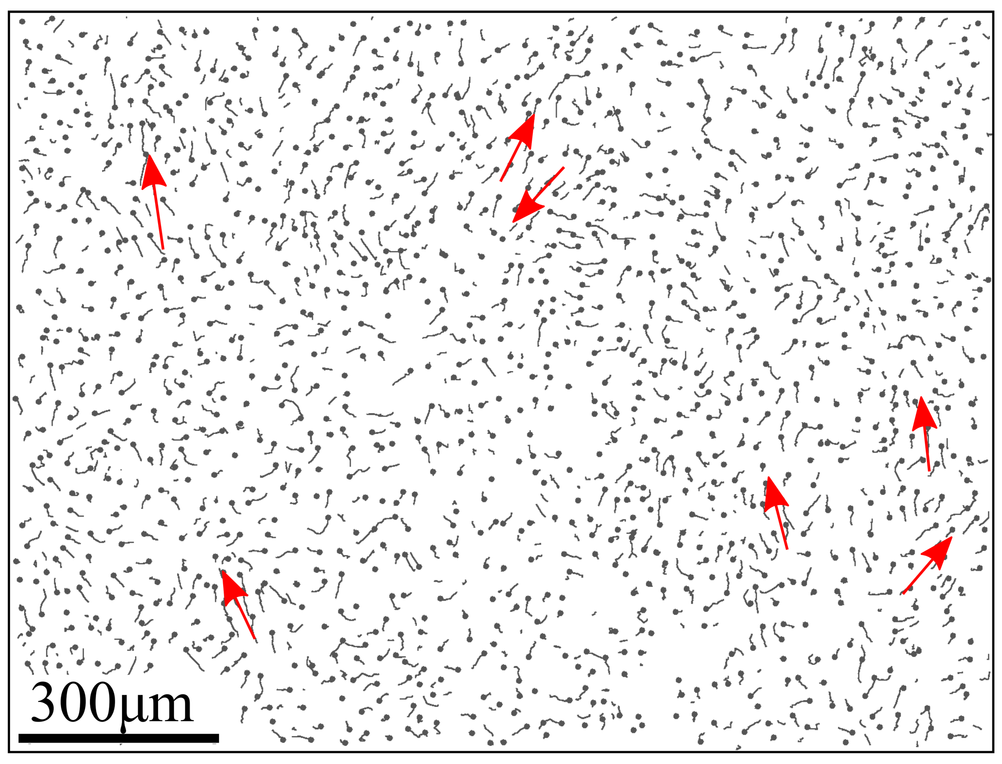
[1]Eötvös University, Budapest, Hungary [2]Medical University of South Carolina, Charleston, SC, USA
[3]Karolinska Institute, Stockholm, Sweden [4]University of Kansas Medical Center, Kansas City, KS, USA
[5]Centrum Wiskunde en Informatica, Amsterdam, The Netherlands [6]NISB, NCSB

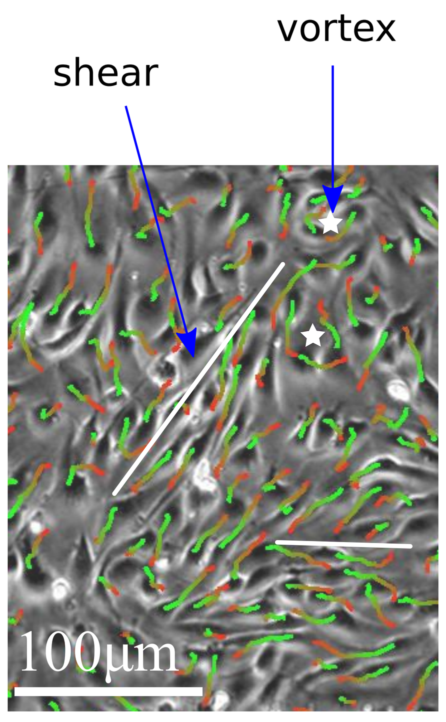
Abstract

Random collective motion in monolayer cultures of endothelial cells is observed and described using statistical methods. Trajectory analysis reveal vortices and neighboring cell streams in opposing direction creating shear lines between cells. To understand the observed behavior, we implement active cell motility in the cellular Potts model using a compass-like cell polarity approach. For spontaneous directed motility we assume a positive feedback between cell displacements and cell polarity. The model behavior is compatible with the experimental results: both the speed and persistence of cell motion decrease in monolayer cultures, transient cell chains move together as groups, and velocity correlations extend over several cell diameters.

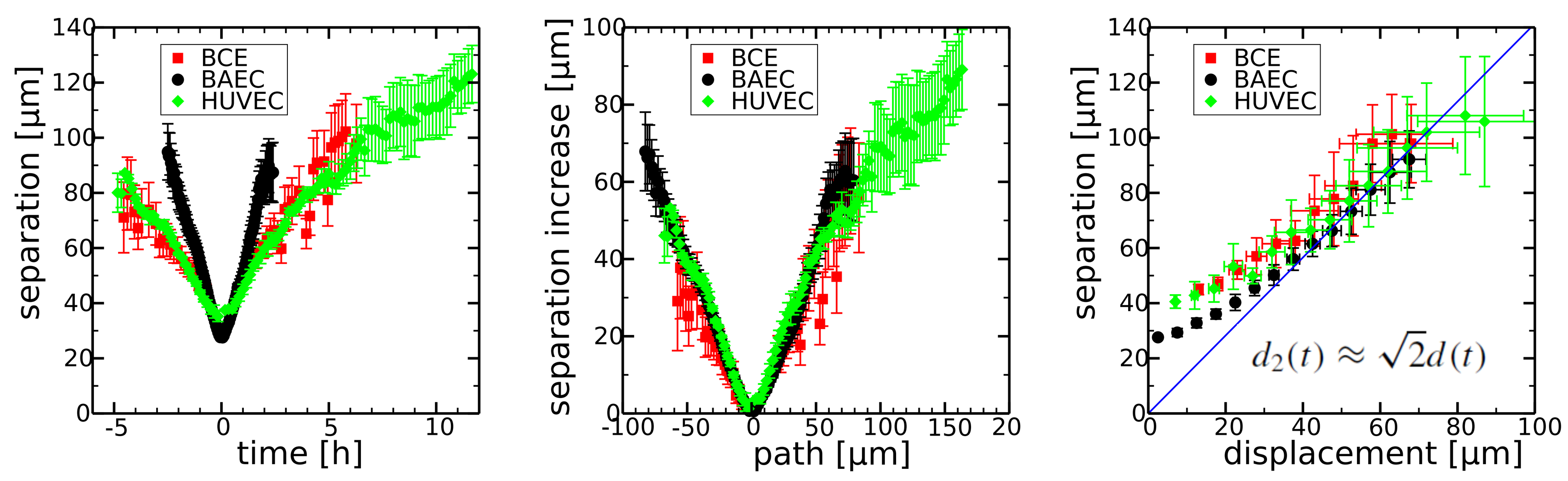
Endothelial cells form streams in vitro

Trajectories of Bovine Aortic Endothelial Cells (BAEC) on Matrigel reveal groups of cells moving in streams, creating vortices. Neighboring streams often move in opposite direction





Cell movement is essentially independent

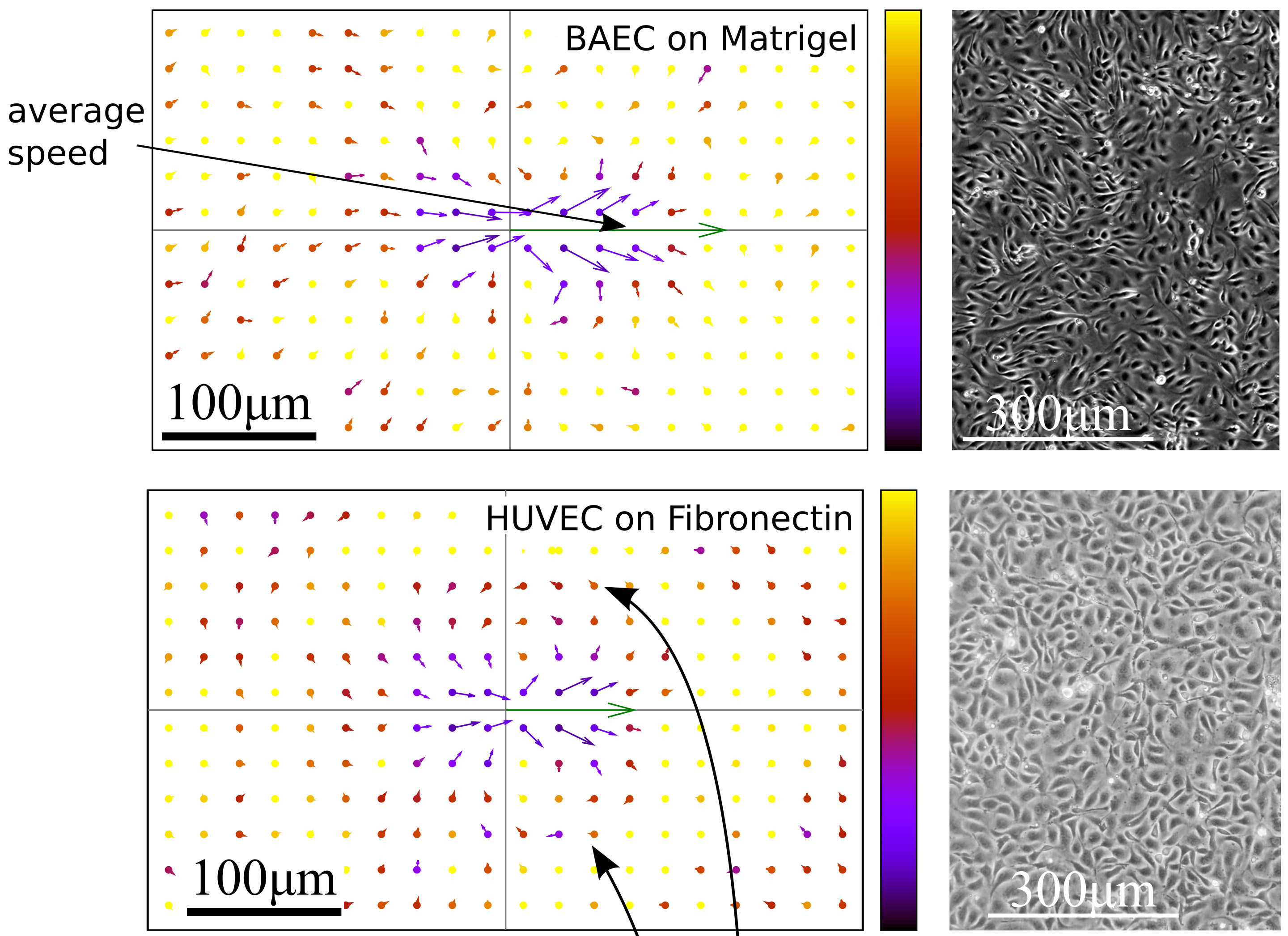


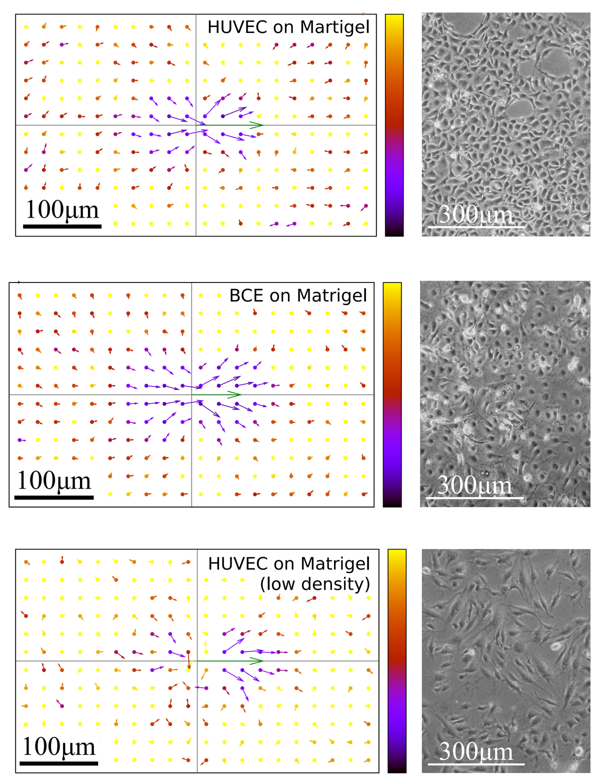
$$d_2^2(t) = \langle (X_i(t) - X_j(t))^2 \rangle_{(i,j)}$$

$$d_2^2(t) \approx \langle [(X_i(t) - X_i(t_0)) - (X_j(t) - X_j(t_0))]^2 \rangle = 2d^2(t) - 2\langle (X_i(t) - X_i(t_0))(X_j(t) - X_j(t_0)) \rangle$$

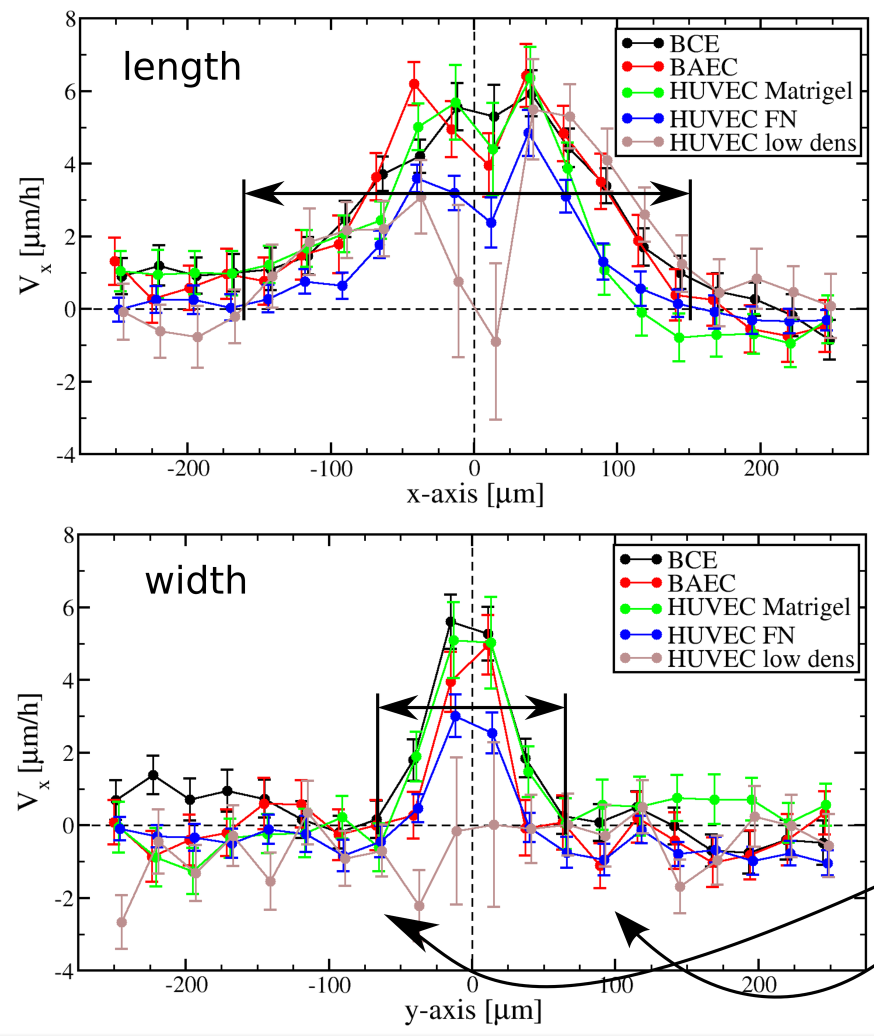
Averaging vector fields around moving cells

The average flow field around moving cells is a measure sensitive to the local cell movement patterns. For a given configuration of cell positions and velocities, this procedure assigns reference systems co-aligned with the movement of each cell and averages the velocity vectors observed at similar locations (e.g. immediately in front, behind, left and right). The vectors of the flow field diminish in a hypothetical ensemble of statistically independent cells, as they are averages of independent random vectors. The value of SEM relative to the vectors is depicted in color showing SEM=0 with black and SEM equal to the length of the vector with yellow.



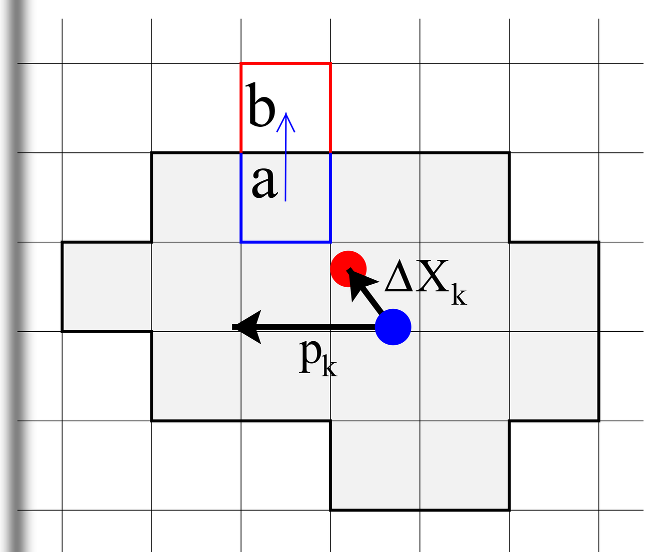


Streams are elongated



Neighboring streams often move in opposite directions

A self-propelled cellular Potts model



We hypothesize that the observed streaming behaviour is a consequence of cells moving in the direction of an intrinsic polarity vector which is reinforced by successive cell motion. The hypothesis was tested using the cellular Potts model. The cellular Potts model is augmented by a persistent cell polarity term through increasing the Potts energy with a polarisation term:

$$\ln p(a \to b) = \min[0, -\Delta u(a \to b) + w(a \to b)]$$

$$u = \sum_{\langle x,x' \rangle} J_{\sigma(x),\sigma(x')} + \lambda \sum_{i=1}^{N} \delta A_i^2$$

adhesion and volume constraint

$$w(a \to b) = P \sum_{k=\sigma(a),\sigma(b)} \frac{\Delta X_k(a \to b) p_k}{|p_k|}$$

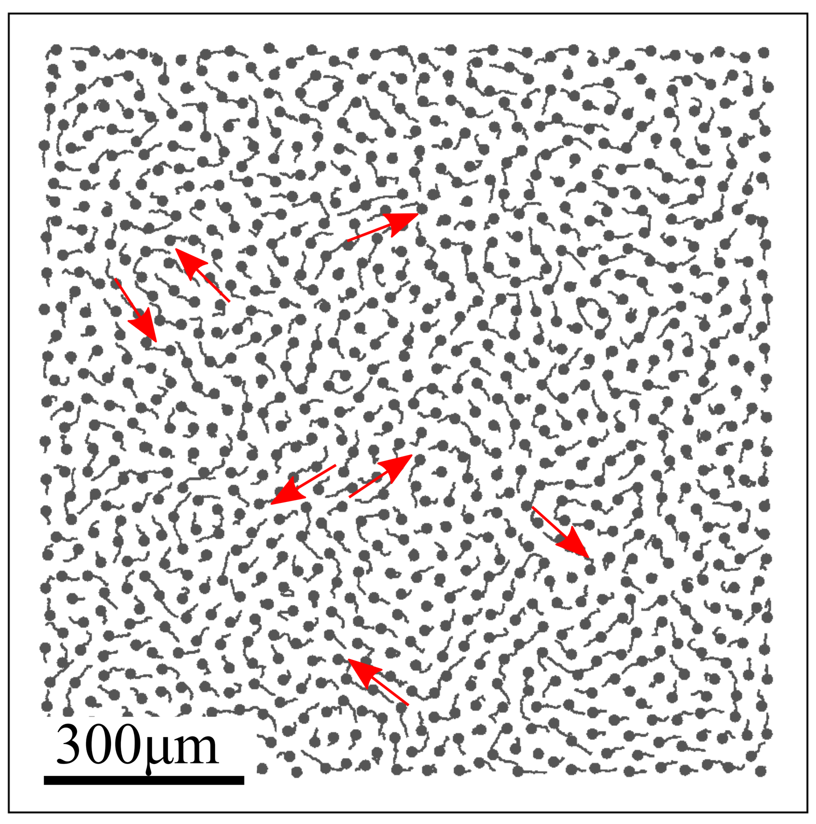
probability of movement enhanced in the direction of the polarity vector

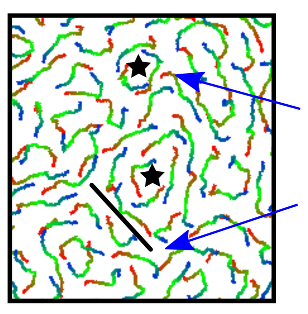
$$\Delta p_k = -r p_k + \Delta X_k$$

polarity is updated with cell displacements

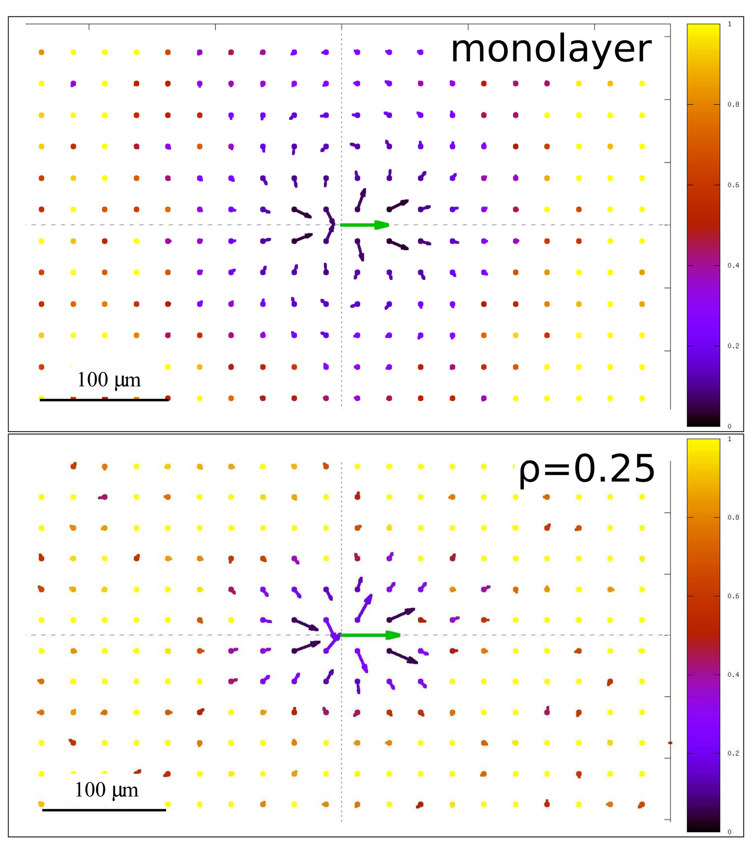
The model reproduces the observed collective behavior:

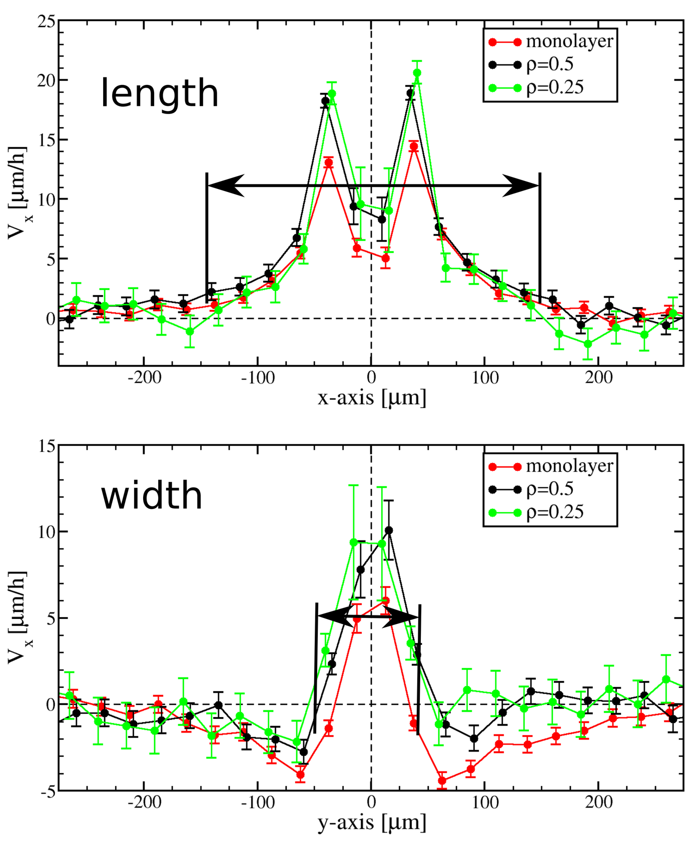
- elongated streams form at random positions
- neighboring streams often move in opposite directions, creating shear lines and vortices
- at low density the streams are still apparent, but shear is reduced





Streams in the model





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Netherlands Consortium for Systems Biology
CWI Centrum Wiskunde & Informatica
NETHERLANDS INSTITUTE FOR SYSTEMS BIOLOGY