Motility Dashboard

Summary of the metrics you can get

Motility assays are vital tools for measuring the movement of cells. In a single-cell random motility assay, cells move independently of one another due to their dispersed state. As Livecyte tracks cells individually, the motility of every cell can be automatically measured throughout the entirety of an assay.

Livecyte's Motility Dashboard includes measurements of speed; mean velocity, instantaneous velocity, and track speed, and metrics describing the direction and directness of movement; confinement, displacement, and directionality.

Applications where it would be useful

The main areas of study of single cell motility are cancer biology, immunology, development, and wound healing (although the latter two fields are more closely concerned with collective motility, see Wound Healing Dashboard).

Cells will move in response to external stimuli such as chemoattractants (the process of which is called chemotaxis), geometrical constraints, or, in absence of any external signals, cells will simply search the surrounding space. Cells involved in the immune response will often increase in motility upon exposure to molecular changes, for example macrophages exhibit increased speed when activated by LPS to enable them to quickly migrate to and target the source.

Stimuli intrinsic to the cell physiology can also impact cell mobility. For example, editing of genes such as Rock1, Rock2 or RhoA can amplify or suppress motility pathways in cells and lead to changes in cell speed, confinement, and displacement. The phenomena of epidermal-mesenchymal transition, where differentiated cells lose their polarity and become more mobile mesenchymal stem cells, is another example of this.

Speed Metrics

Use in biology:

Speed metrics are used widely in cell biology in areas such as oncology and immunology. Faster cells indicate an increase in invasiveness of cancer cells as they have an increased likelihood of breaking away from a primary tumour and metastasising around the body. Activated immune response cells such as macrophages show an increase in cell speed.

Instantaneous Velocity - The velocity of each cell in a population from one frame to the next at every time point, plotted into a distribution chart. This is quantified by measuring how far each cell moves between each frame. Each cell contributes one data point to the plot in each frame. In a data set with a high number of track breaks, this metric provides a simple sanity check to ensure that any double counted tracks in the track speed plot are not skewing the distribution.

Track speed - The speed of every cell track in a population as measured by the total distance travelled divided by time. This is plotted in a distribution chart.

Mean Velocity - A line graph of the mean instantaneous velocity of all cells at each frame over time.

How are cells moving?

Observing the nature of the movement of cells can elucidate key cellular behaviours and movement patterns such as how far they have migrated from their origin, how direct or meandering their movement is, and whether the movement of the cells is isotropic or anisotropic. This is key in the study of chemotaxis, neurology, cancer, and development. We may observe these metrics when considering neuronal migration during development, movement of cancer cells leading to metastasis, and the persistence of migration in cells when exposed to chemoattractants.

Displacement - A spider graph showing the positions of 50 cell tracks. The tracks chosen random from all those longer than the median track length of the whole assay. They are then cropped to that median cell track length (to maintain comparison validity) and plotted on an X-Y Axis, with each track starting in the centre of the plot.

This gives a visual representation of cell movement patterns. Studying displacement is important in development, for example imaging the migration of neurons along radial glia and in response to chemical signals.

Directionality - A rose plot of the angular direction of the instantaneous velocity vector of each cell between each frame. Higher bars indicate more movements, showing a bias in motion towards that direction. The direction of the bar corresponds to the direction of motion in the image – i.e. the bar pointing straight up corresponds to cells moving straight up in the image.

More directionally persistent, anisotropic movement in cancer cells lead to cells invading further and metastasising earlier. Cells in absence of external stimuli often move in an isotropic, random motion. Directionality is also relevant in our wound healing dashboard, when considering collective migration into a wound.

Confinement Ratio - A measure of how directly or indirectly a cell moves. A low confinement ratio means a cell is less confined to its straight path and meanders more. A high confinement means cell motion is more confined and moves more directly to its eventual destination.

Confinement ratio is calculated by dividing displacement (distance cell has travelled from its origin) by pathlength (total distance travelled). This gives a metric known as Meandering Index (MI). MI is then multiplied by the square root of the track lifetime (in hrs) to give the Confinement Ratio.

The values of confinement ratio are relative within a single experiment, larger values corresponding to more direct motion.

Confinement can tell us the strength of a chemoattractant. More attractive compounds will cause cells to move more directly with a higher confinement ratio. For example in inflammation leukocytes move towards area of inflammation guided by increasing concentrations of inflammatory chemokines. Chemokines which cause cells to migrate in a more confined manner are more attractive than those where cells move more indirectly towards the source.

Publication Example

Frame FM *et al*. Assessing the Advantages, Limitations and Potential of Human Primary Prostate Epithelial Cells as a Pre-Clinical Model for Prostate Cancer Research. Advances in Experimental Medicine and Biology; Vol 1164, 109-118. (2019). doi: 10.1007/978-3-030-22254-3_9

Frame *et al* studied the effects of docetaxel, a chemotherapeutic agent, on primary prostate cancer cells. They observed a dose dependent reduction in instantaneous velocity and analysed single cell motility and displacement, identifying a cell with a drug resistant phenotype which continued to move upon failing mitosis instead of undergoing apoptosis.