Slides, videos, links and more:
https://github.com/physicell-training/02-How-to-nanoHUB

Lesson 08.01: Motility Training

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PhysiCell Project

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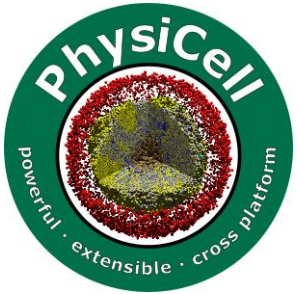
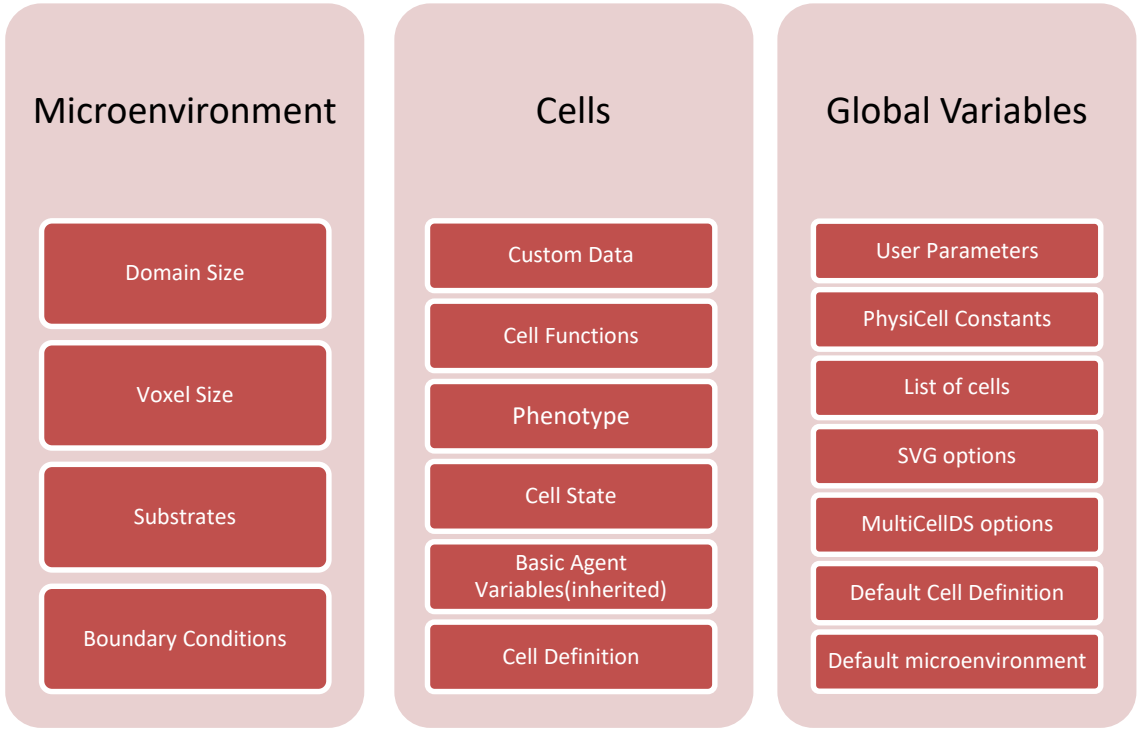
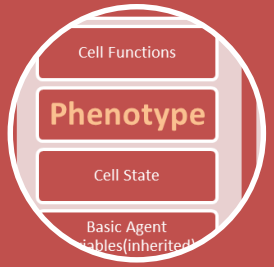


Context


Microenvironment
Domain Size
Voxel Size
Substrates
Boundary Conditions
Cells
Custom Data
Cell Functions
Phenotype
Cell State
Basic Agent Variables(inherited)
Cell Definition
Global Variables
User Parameters
PhysiCell Constants
List of cells
SVG options
MultiCellDS options
Default Cell Definition
Default microenvironment

Context

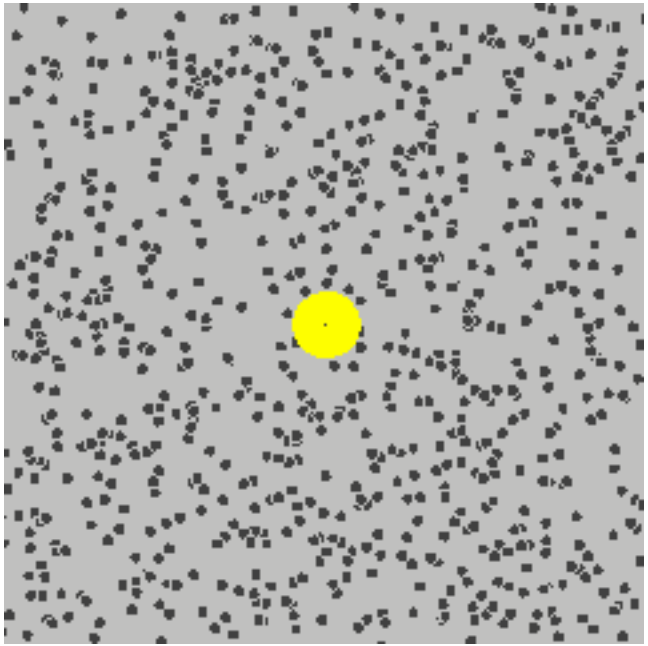


Phenotype

- Motility
- Cell Cycle
- Death
- Mechanics
- Geometry
- Molecular
- Volume

Background

- Cells move through motility.
- Mathematically modeled as a biased Random walk.
- No bias : Brownian Motion
  - Cells move randomly due to their collisions
    - Yellow Particle
- With bias : Random Biased Motion
  - Cells select movement directions according to some rules
    - e.g Chemotaxis



"Brownian Motion and Random Walks." *MIT*, web.mit.edu/8.334/www/grades/projects/projects17/OscarMickelin/brownian.html.

Mathematics: Variables and Definitions

- **Migration speed:** Migration speed is the speed at which the cells move in μm/min.
- **Migration bias direction:** Preferred migration direction
- **Migration bias:** Impacts the direction that a cell moves.
  - 0 ➔ Random Walk
  - 1 ➔ Deterministic Motion along migration bias direction
- **(Mean) persistence time:** The mean duration in minutes that a cell moves in its current direction before choosing a new motility vector to follow.

Mathematics: Models

- How is motility direction chosen and determines the bias direction?

$$\mathbf{d}_{\text{mot}} = \frac{b\,\mathbf{d}_{\text{bias}} + (1-b)\boldsymbol{\xi}}{||b\,\mathbf{d}_{\text{bias}} + (1-b)\boldsymbol{\xi}||}$$

Where;
$\mathbf{d}_{\text{mot}}$: direction of the motility
b: the level of bias in motility (migration bias)
$\boldsymbol{\xi}$: random unit vector of length 1,
$\mathbf{d}_{\text{bias}}$: direction of the bias

- How is the motility velocity computed?

$$\mathbf{v}_{\text{mot}} = s_{\text{mot}}\mathbf{d}_{\text{mot}}$$

Where;
s_{mot}: migration speed

- How often do cells change motility direction?

  Persistence Time

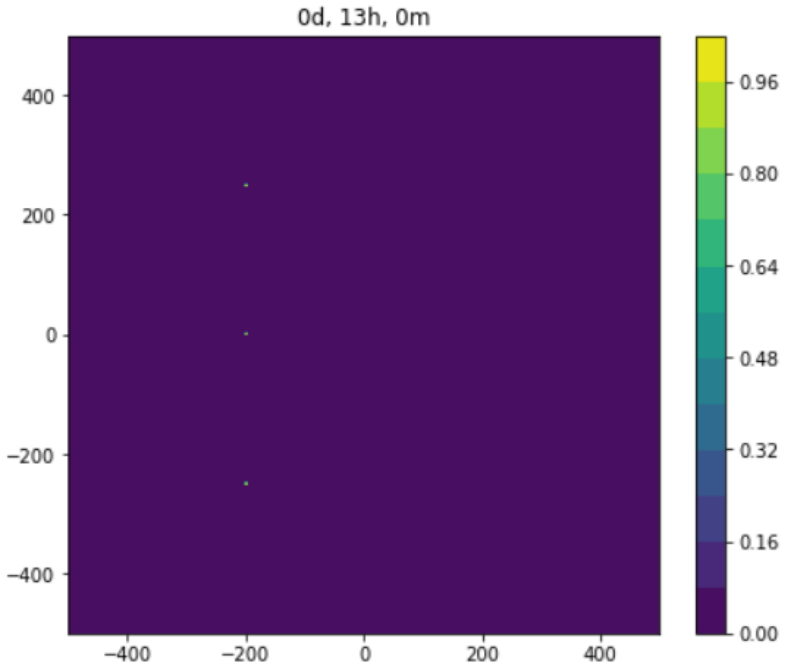
Demonstration

- Demo on NanoHUB:
  https://nanohub.org/tools/trmotility

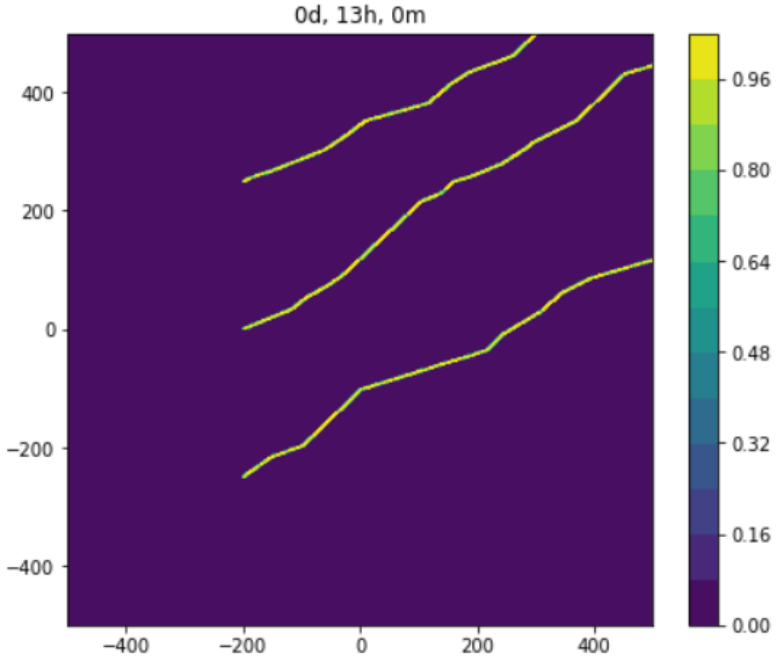
- How to use NanoHUB:

https://github.com/physicell-training/02-How-to-nanoHUB

Expected Results (is_motile)

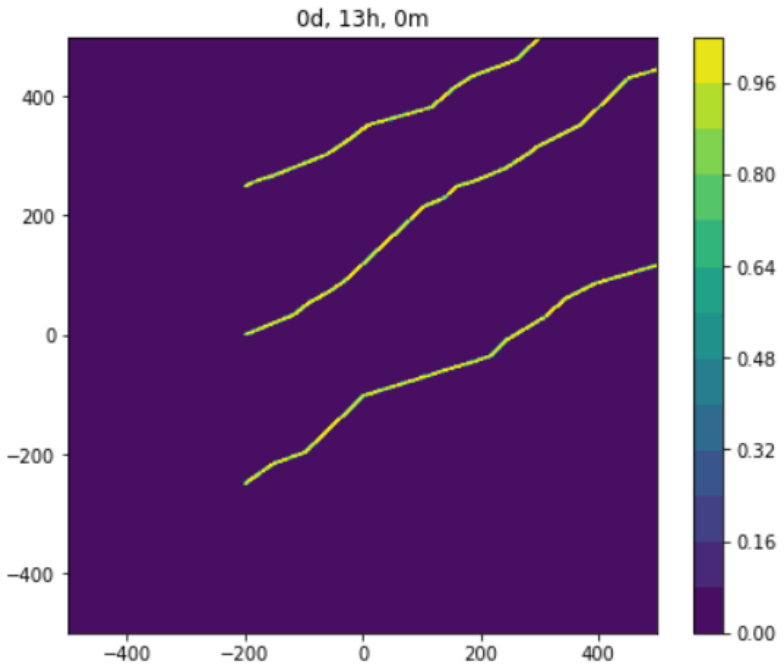


is_motile = False

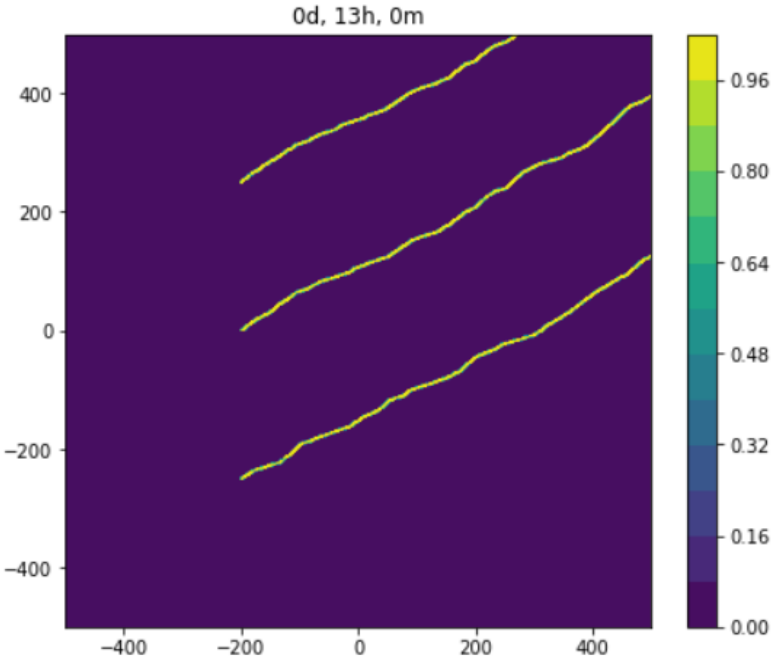


is_motile = True

Expected Results (Persistence_time)

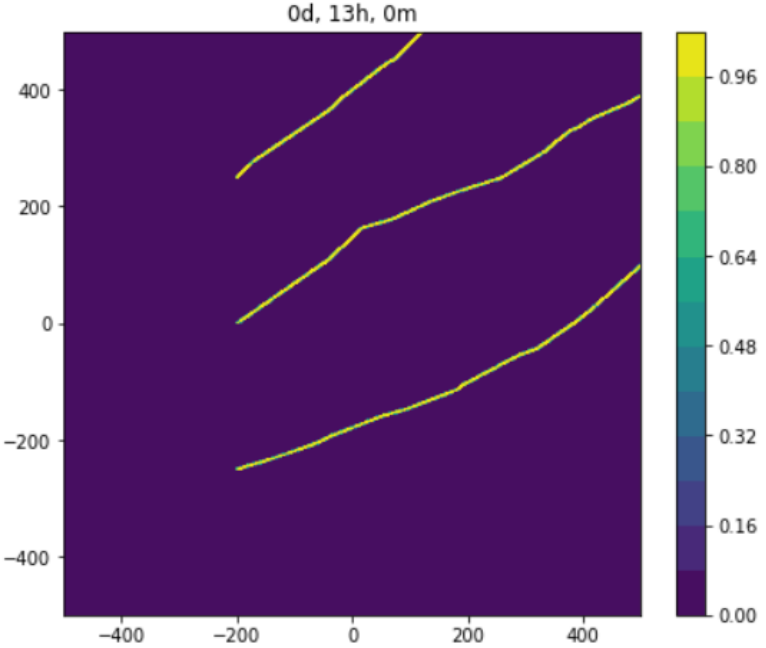


persistence_time = 30 min

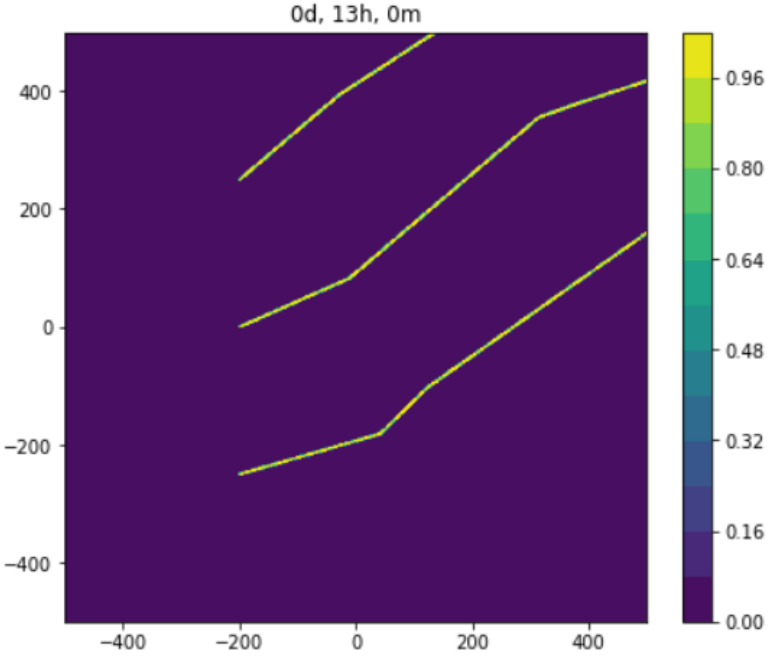


persistence_time = 5 min

Expected Results (migration_speed)

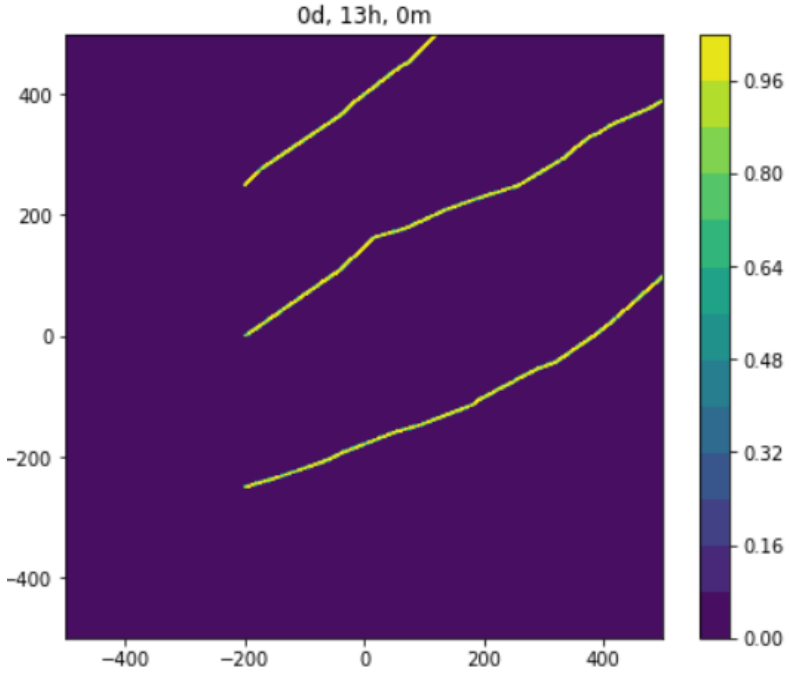


Migration_speed = 2 micron/min^{-1}

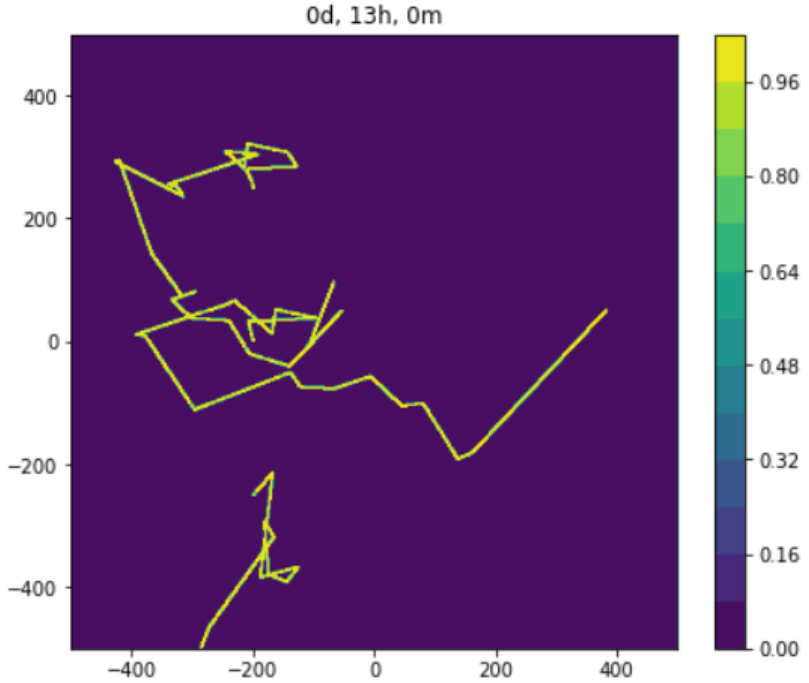


Migration_speed = 10 micron/min^{-1}

Expected Results (migration_bias)

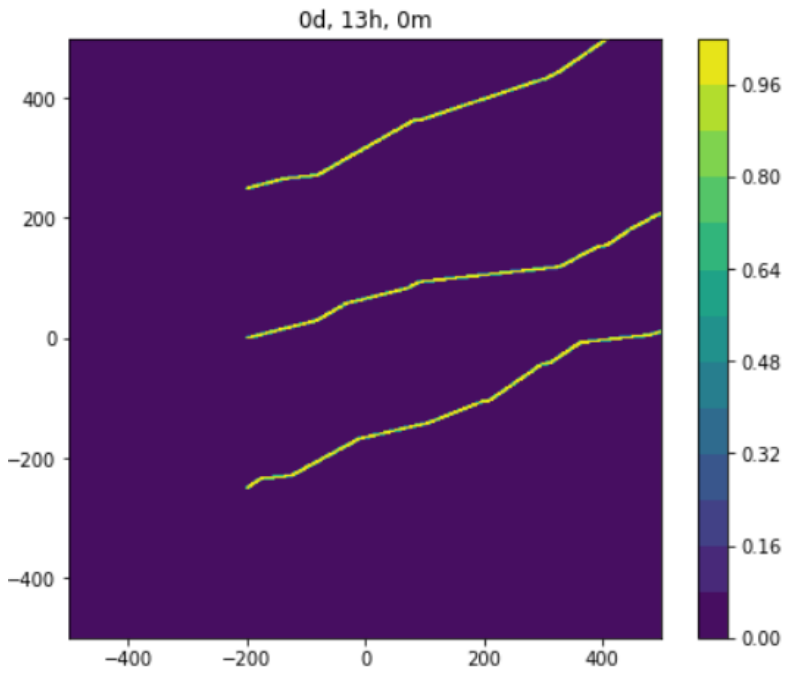


Migration_bias = 0.8

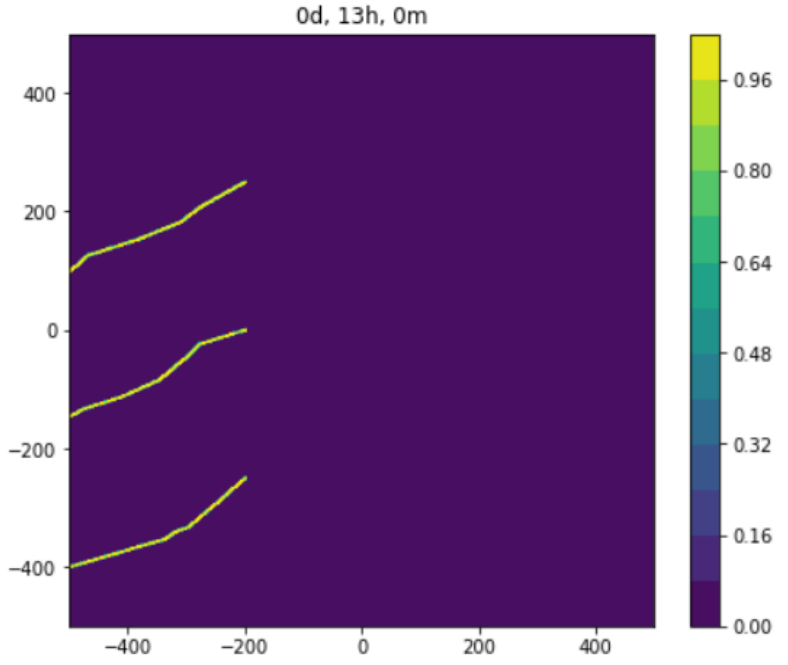


Migration_bias = 0.2

Expected Results (bias_migration_angle)



Migration_bias_angle = 20



Migration_bias_angle = 210

Class structure: Data

Key parameters in phenotype.motility

- `bool is_motile;`
  - Set to true if cell is / can actively migrate
- `double persistence_time;`
  - mean time to keep going in one direction before resampling for a new direction.
- `double migration_speed;`
  - migration speed along chosen direction, in absence of all other adhesive / repulsive forces
- `std::vector<double> migration_bias_direction;`
  - random motility is biased in this direction (e.g., chemotaxis)
- `double migration_bias;`
  - how biased is motility
  - if 0, completely random. if 1, deterministic along the bias vector
- `bool restrict_to_2D;`
  - Set to true if you want to guarantee 2D motion
- `std::vector<double> motility_vector;`
  - direction of migration

Example

custom.cpp

```
Cell* pCell= create_cell();
pCell->phenotype.motility.is_motile= true;
pCell->phenotype.motility.migration_speed= 1.0;
pCell->phenotype.motility.migration.persistence_time= 20;
pCell->phenotype.motility.restrict_to_2D = true;
pCell->phenotype.motility.migration_bias= 0.8;
std::vector<double> temp = { 0.1 , 0.2, 0.0 };
normalize( temp );// makes it's length 1
pCell->phenotype.motility.migration_bias_direction= temp;
```

Example

custom.cpp

```
Cell* pCell= create_cell();
pCell->phenotype.motility.is_motile= parameters.bools( "is_motile" );
pCell->phenotype.motility.migration_speed= parameters.doubles( "migration_speed" );
pCell->phenotype.motility.migration.persistence_time= parameters.doubles("persistence_time")
pCell->phenotype.motility.restrict_to_2D = true;
pCell->phenotype.motility.migration_bias= parameters.doubles( "migration_bias" );
std::vector<double> temp = { 0.1 , 0.2, 0.0 };
normalize( temp );// makes it's length 1
pCell->phenotype.motility.migration_bias_direction= temp;
```

PhysiCell_settings.xml

```
<is_motile type="bool" units="none" description="true if cells are motile">True</is_motile>
<migration_speed type="double" units="micron/min" description="migration speed">1.0</
migration_speed>
<persistence_time type="double" units="min" description="mean persistence time">1.0</
persistence_time>
<migration_bias type="double" units="none" description="migration bias parameter">0.8</
migration_bias>
```

Next steps

Super fast: Please proceed to any Lesson 08.x or 09
Link: https://github.com/physicell-training/08.02-phenotype-mechanics

Intermediate: Please proceed to 08.02 (Motility)
Link: https://github.com/physicell-training/08.02-phenotype-mechanics

Full training: Please proceed to 08.02 (Motility)
Link: https://github.com/physicell-training/08.02-phenotype-mechanics

More materials: https://github.com/physicell-training/master-list

Credits

Lesson Planning: Paul Macklin

Slides: Kali Konstantinopoulos*, Mary Chen*, Furkan Kurtoglu

Recording: Drew Willis

Post-production: Paul Macklin, Drew Willis*, Kali Konstantinopoulos*

Microapps: Furkan Kurtoglu, Paul Macklin

* denotes undergraduate researcher

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- Breast Cancer Research Foundation
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- National Cancer Institute (U01CA232137)
- National Science Foundation (1720625)

Training materials:

* Administrative supplement to NCI U01CA232137 (Year 2)