Role of intercellular adhesion in cell migration : A cellular potts model perspective

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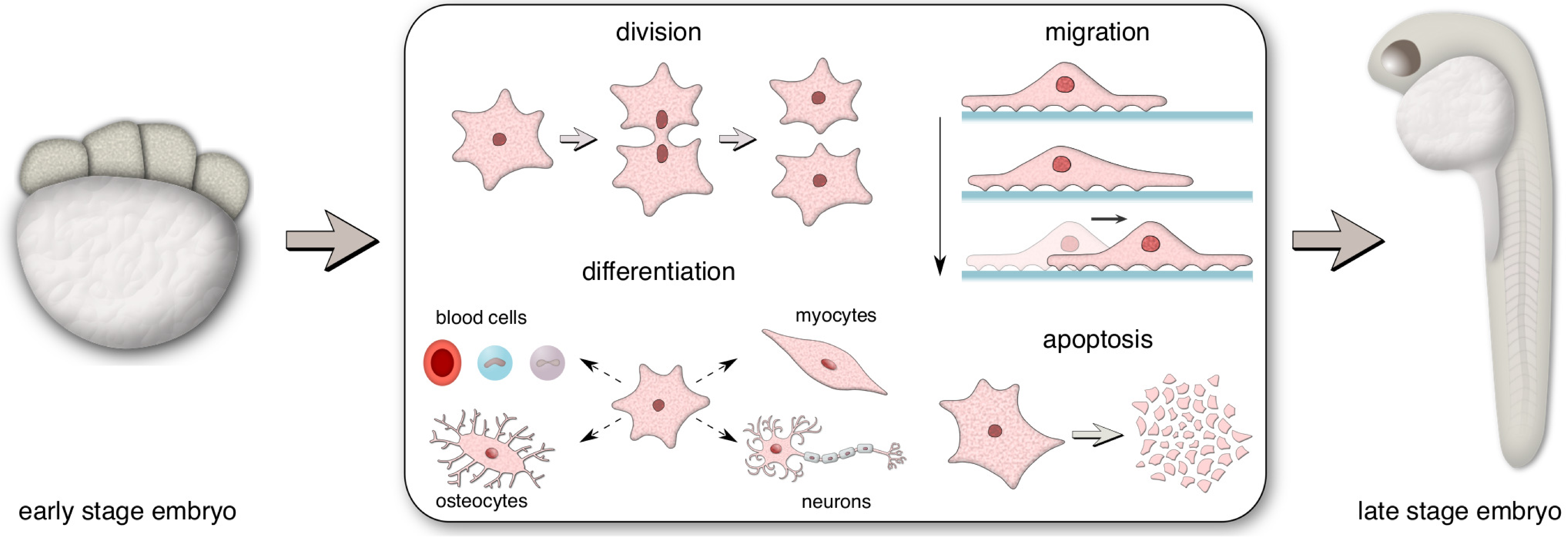
May 13, 2024

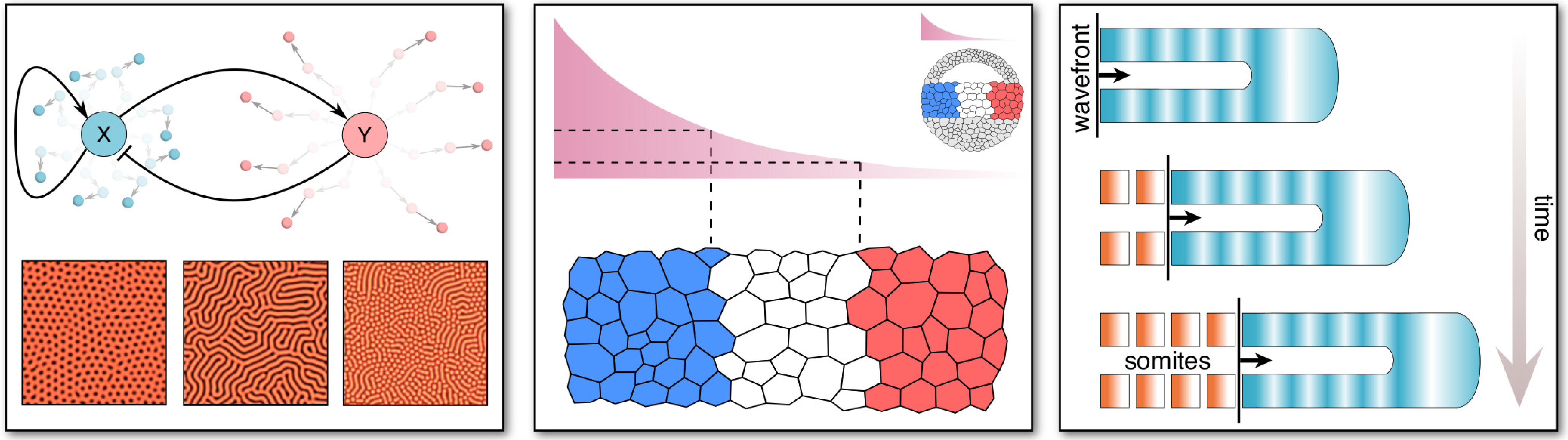
Extavour Lab

Tools that shape the embryo



Drawn by Shakti Menon

Ways to pattern an embryo

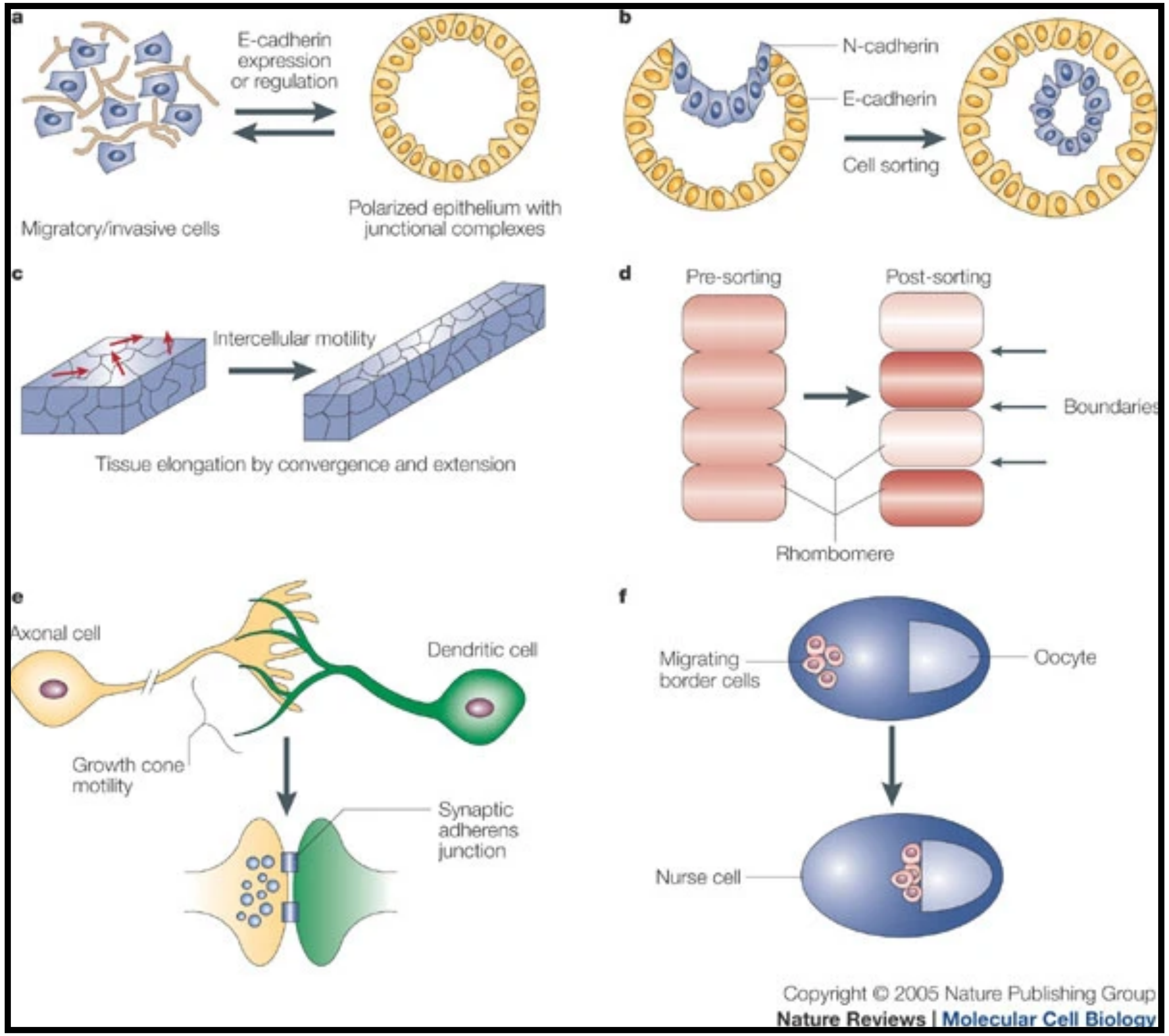


Turing mechanism
French flag model
Clock and wavefront

Symmetry breaking is at the heart of all pattern formation. Biology employs various ways to break spatial symmetry.

Drawn by Shakti Menon

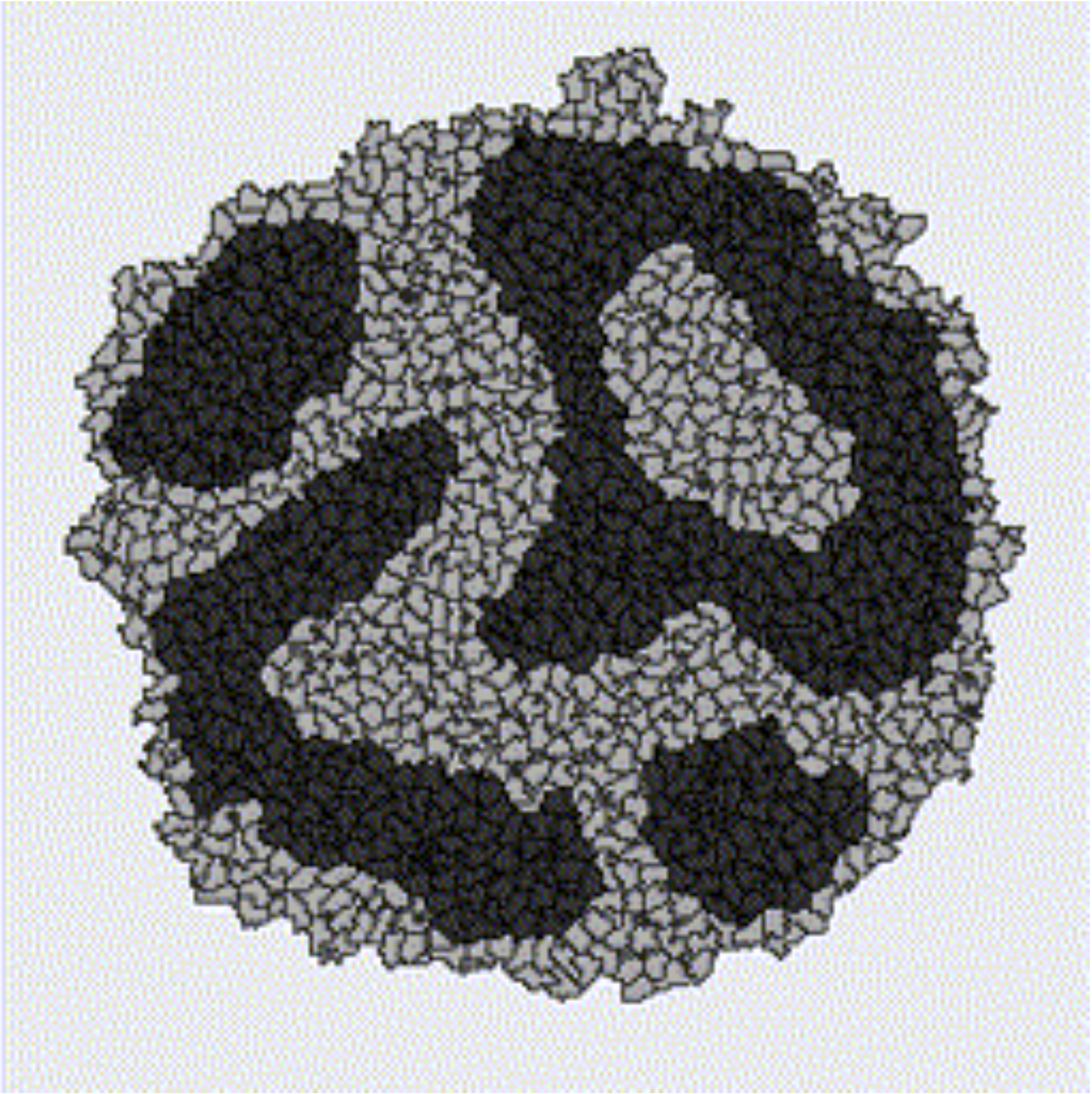
Cell adhesion - morphogenesis



Cadherin regulation during morphogenesis.
Source : Gumbiner *Nat Rev Mol Cell Biol 2005*

Differential adhesion - Cellular Potts Model

- Can different cell types sort into homogenous domains due to differential adhesion between cell types ?
- Graner and Glazier in 1992 tested the differential adhesion driven cell sorting hypothesis computationally
- Inspired by Potts Model, a generalization of Ising model in statistical mechanics

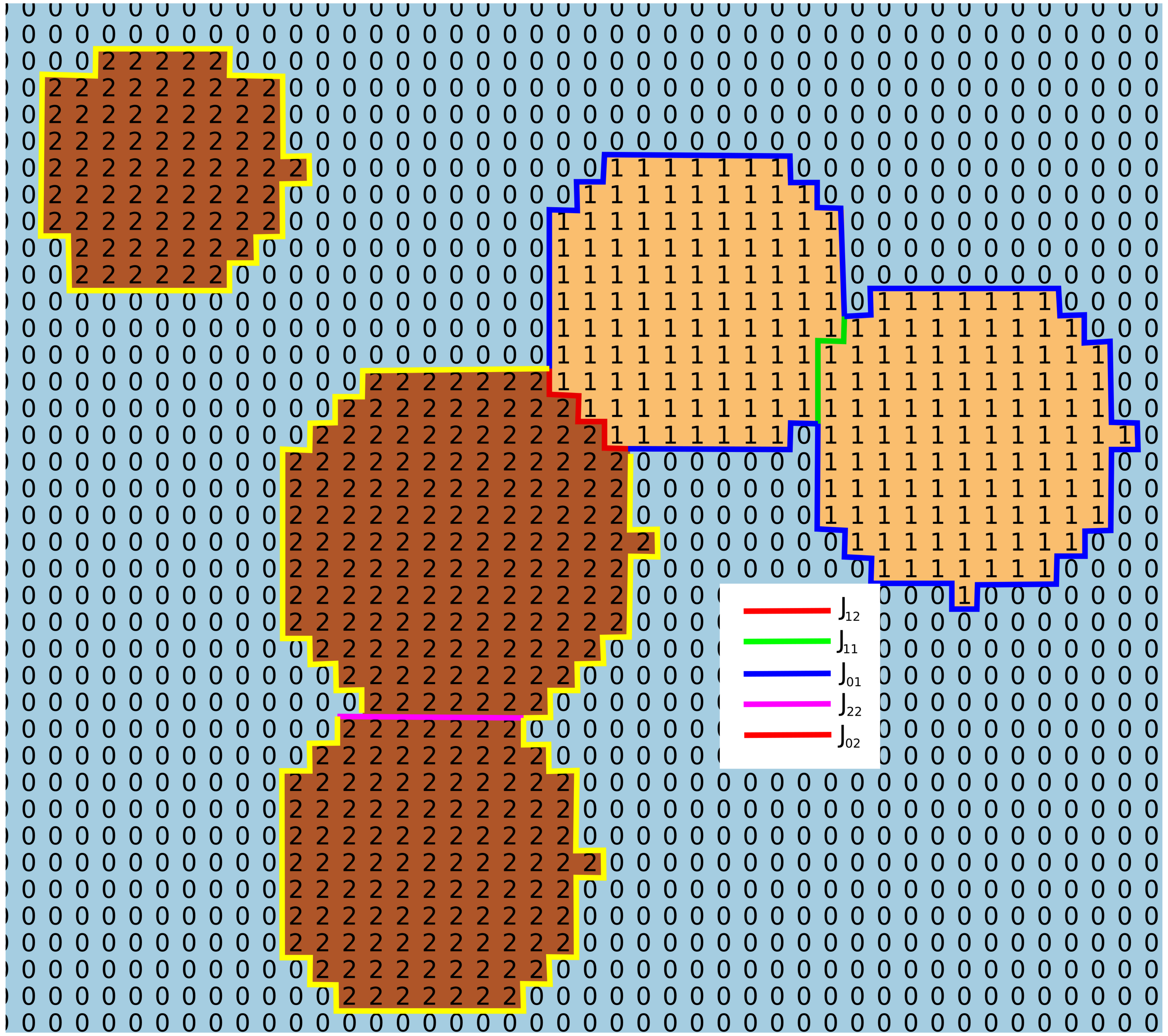


https://artistoo.net/

Graner and Glazier, PRL 1992

Pixel flip

- Cells are spatially contiguous collection of pixels
- The background in which the cells exist is referred to as the medium. Medium is treated as a cell which isn't constraint by the spatial contiguity requirement
- Pick a pixel that has at least one neighbor which belongs to a different cell
- Compute the energy difference if the pixel were to flip to its neighbor's state
- If the energy difference is negative flip or else flip with a probability p_{flip}
- The pixel flip is accepted iff it doesn't violate the spatial contiguity of a cell

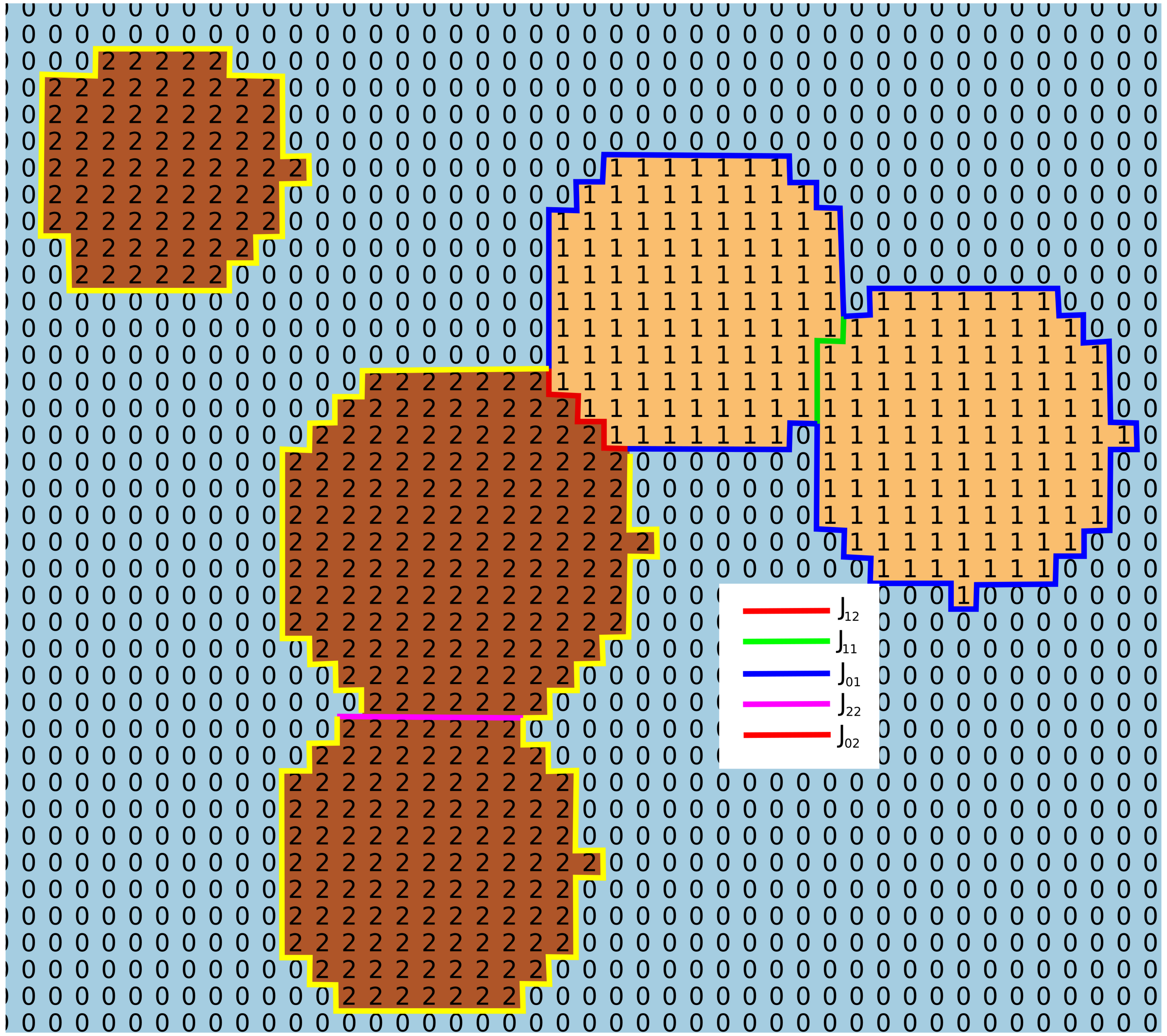


5 cells and the medium

Energy function

$$\boxed{E = \sum_{i,j} J(\tau(\sigma_i), \tau(\sigma_j))(1 - \delta(\sigma_i, \sigma_j)) + \lambda_V \sum_{\sigma_i} (V(\sigma_i - V_0(\sigma_i))^2}$$

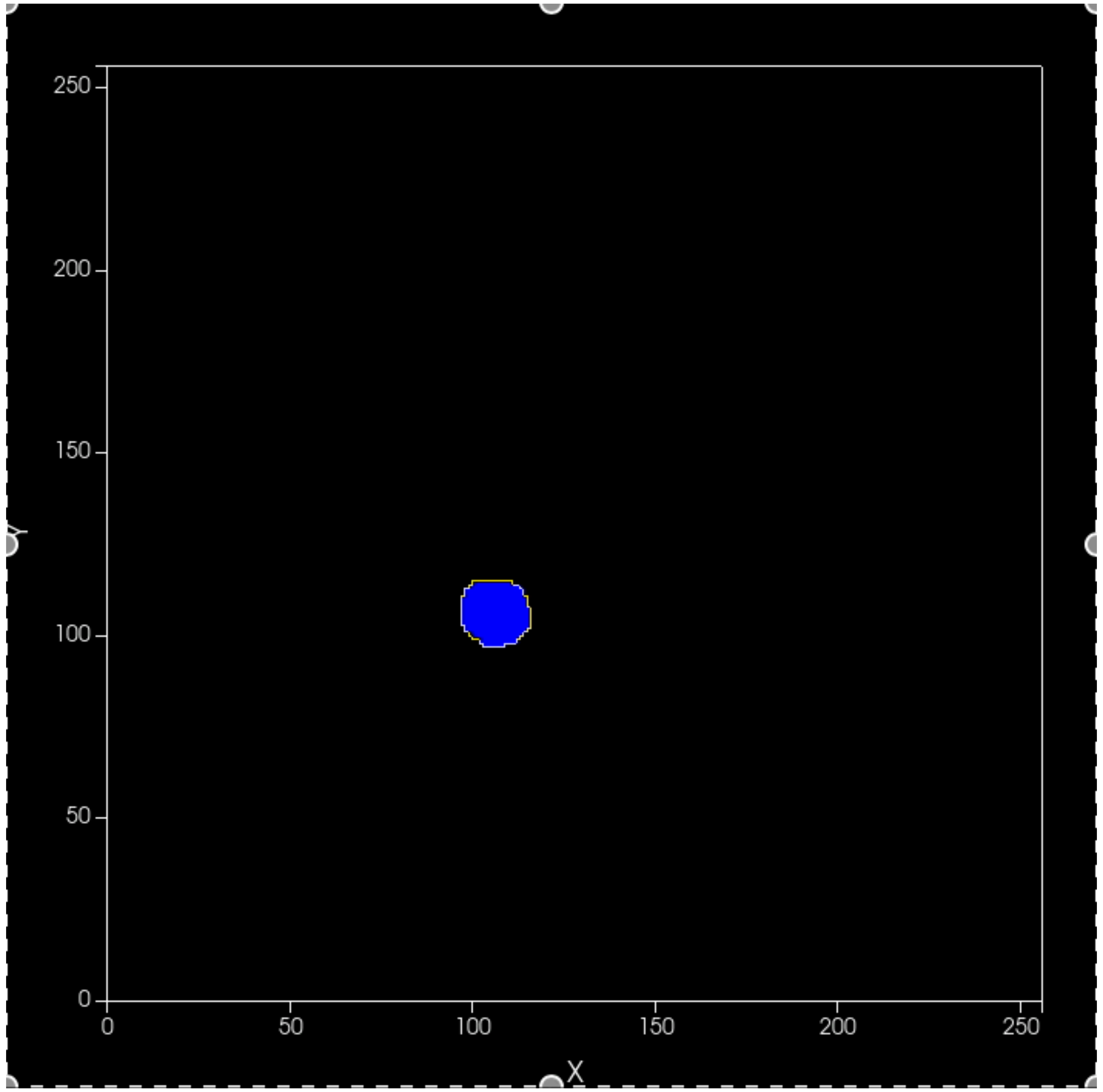
- There is an energy cost associated with pairwise interaction between pixels belonging to different cells (σ_i & σ_j)
- The cost is dependent on the cell type ($\tau(\sigma_i)$ & $\tau(\sigma_j)$)
- The energy cost is given by the symmetric matrix **J** of dimension k x k where k is the number of cell types (including the medium)



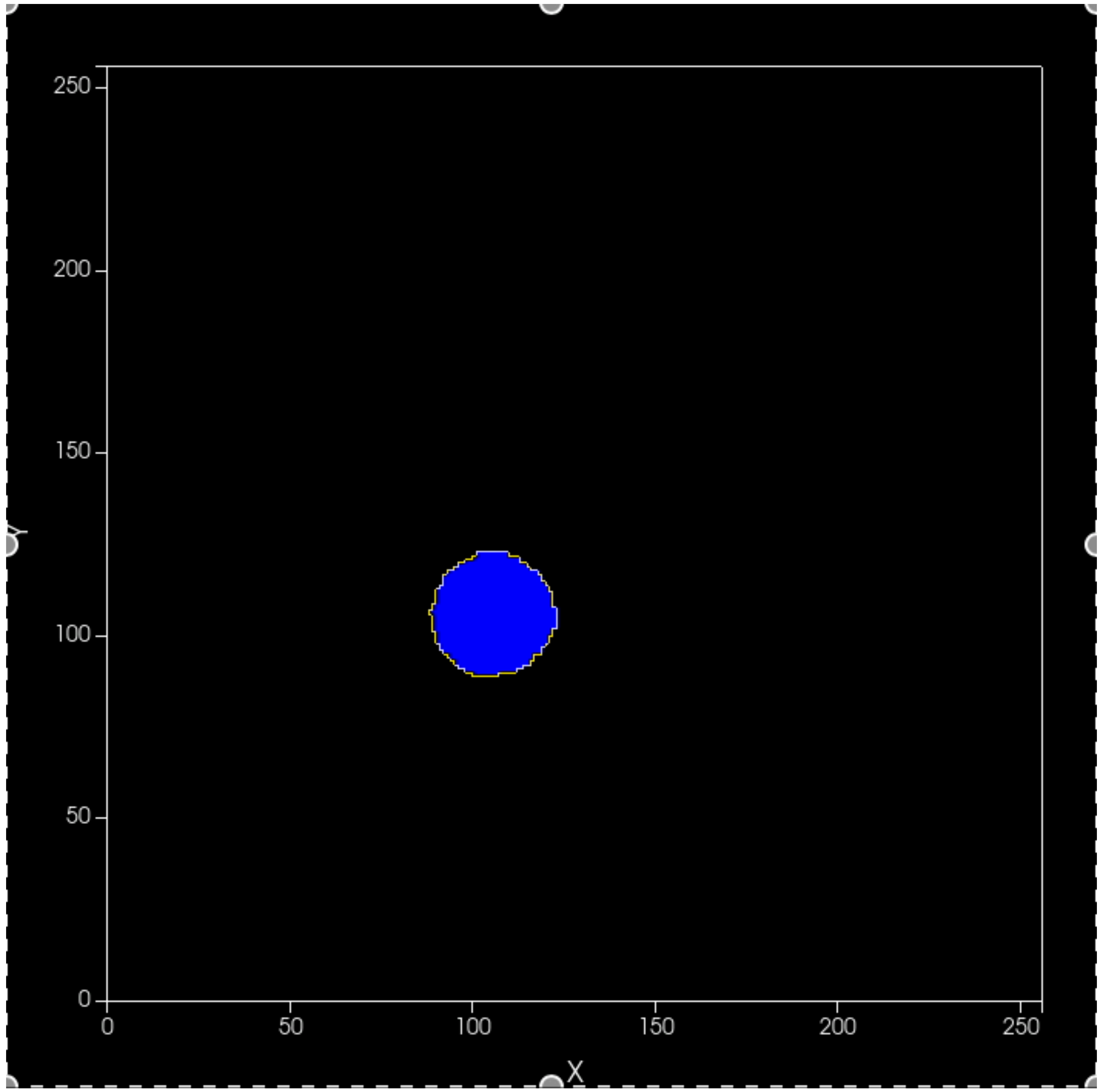
Schematic illustrating the interaction between different cells

Volume constraint

$$\lambda_V \sum_{\sigma_i} (V(\sigma_i - V_0(\sigma_i))^2$$



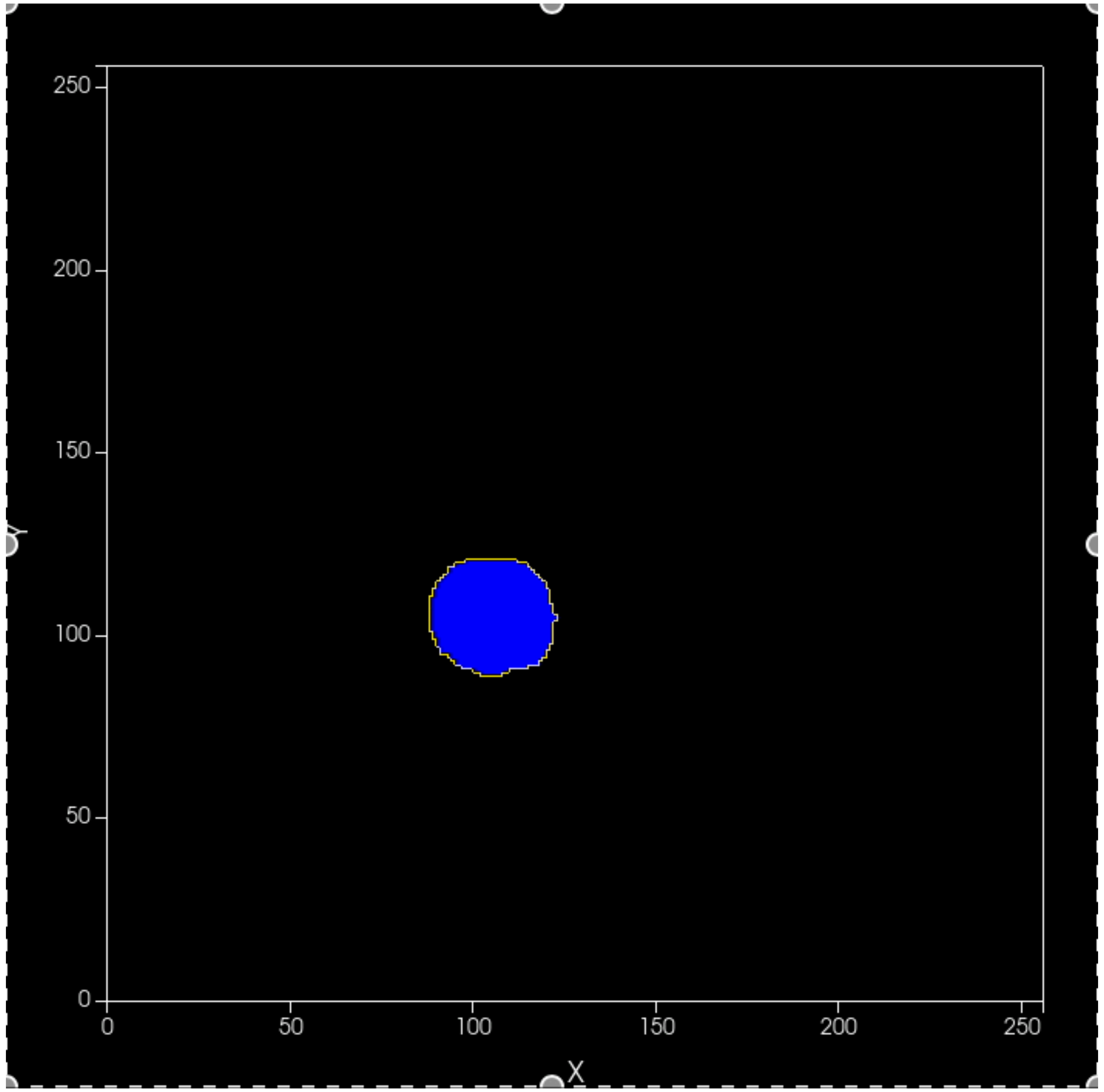
$\lambda_V = 0.01$



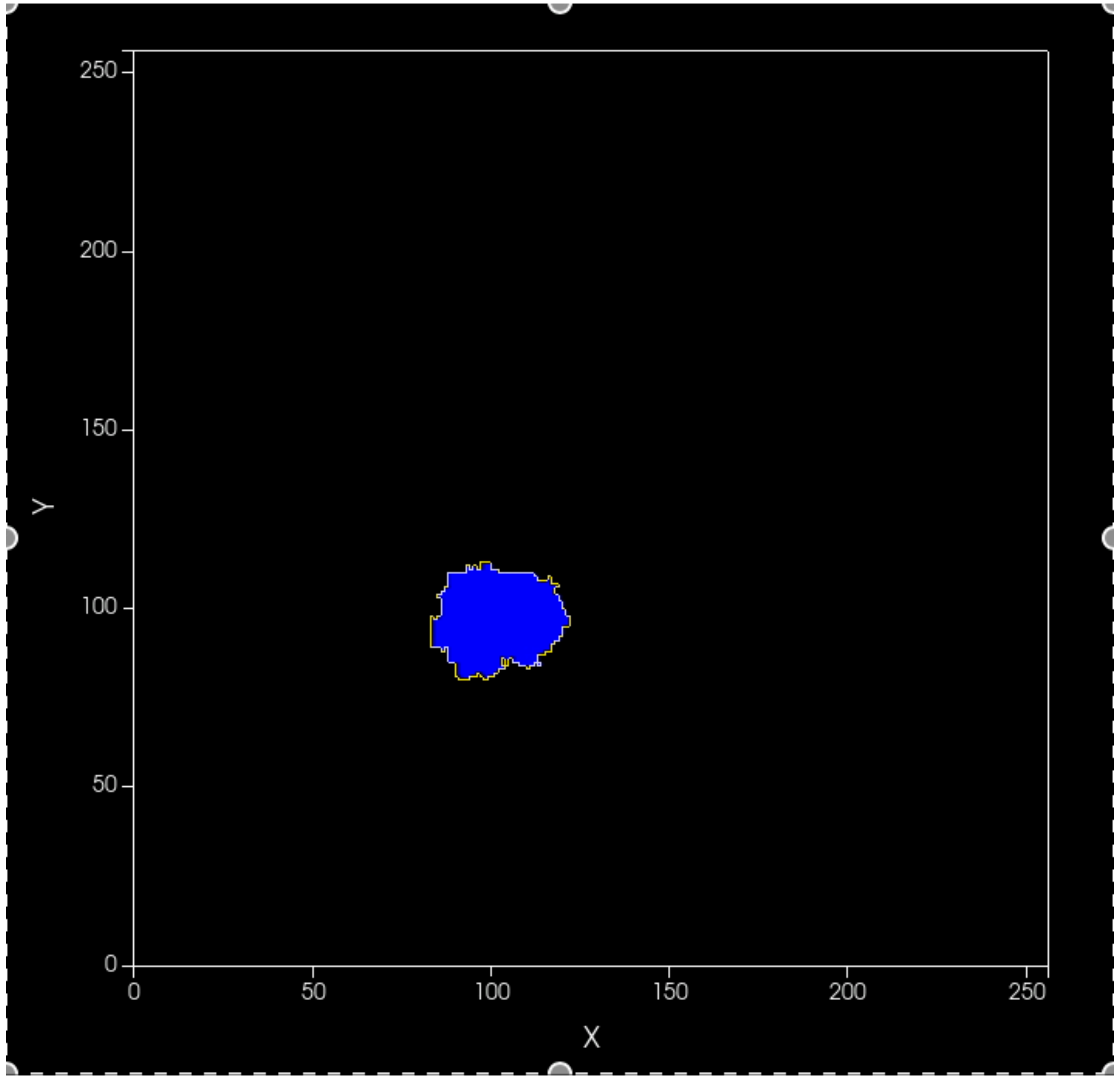
$\lambda_V = 1.0$

Temperature

$$p_{flip} < \exp(-\Delta E_{total}/T)$$



T= 10



T = 100

Other constraints - more terms in equation for $\boldsymbol{E}$

- Surface area constraint (S)
- Length constraint (l)
- Length along x-axis (l_x)
- Anything you like as long as it makes sense !

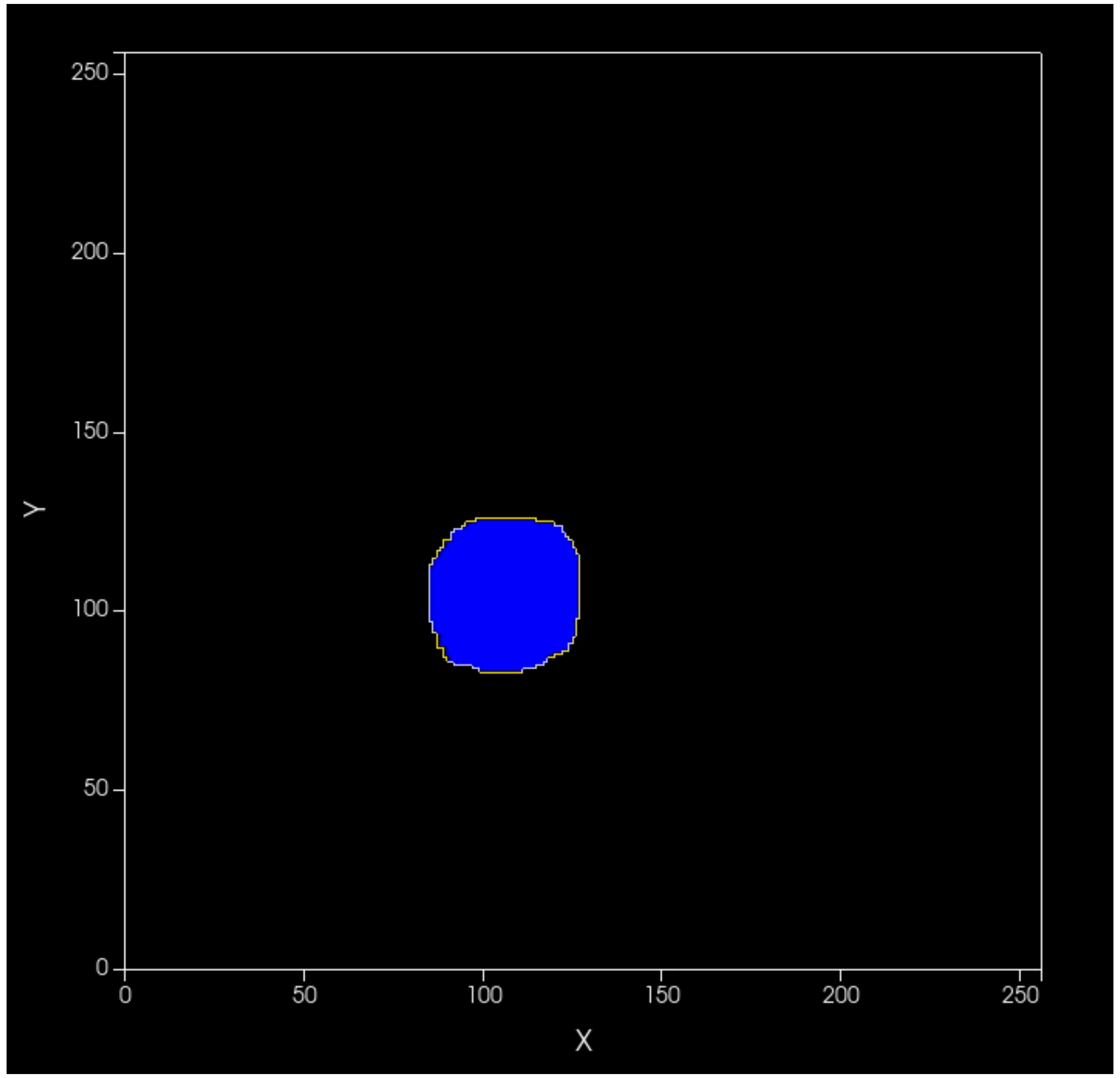
$$\boxed{\lambda_S \sum_{\sigma_i} (S(\sigma_i - S_0(\sigma_i))^2}$$

$$\boxed{\lambda_l \sum_{\sigma_i} (l(\sigma_i - l_0(\sigma_i))^2}$$

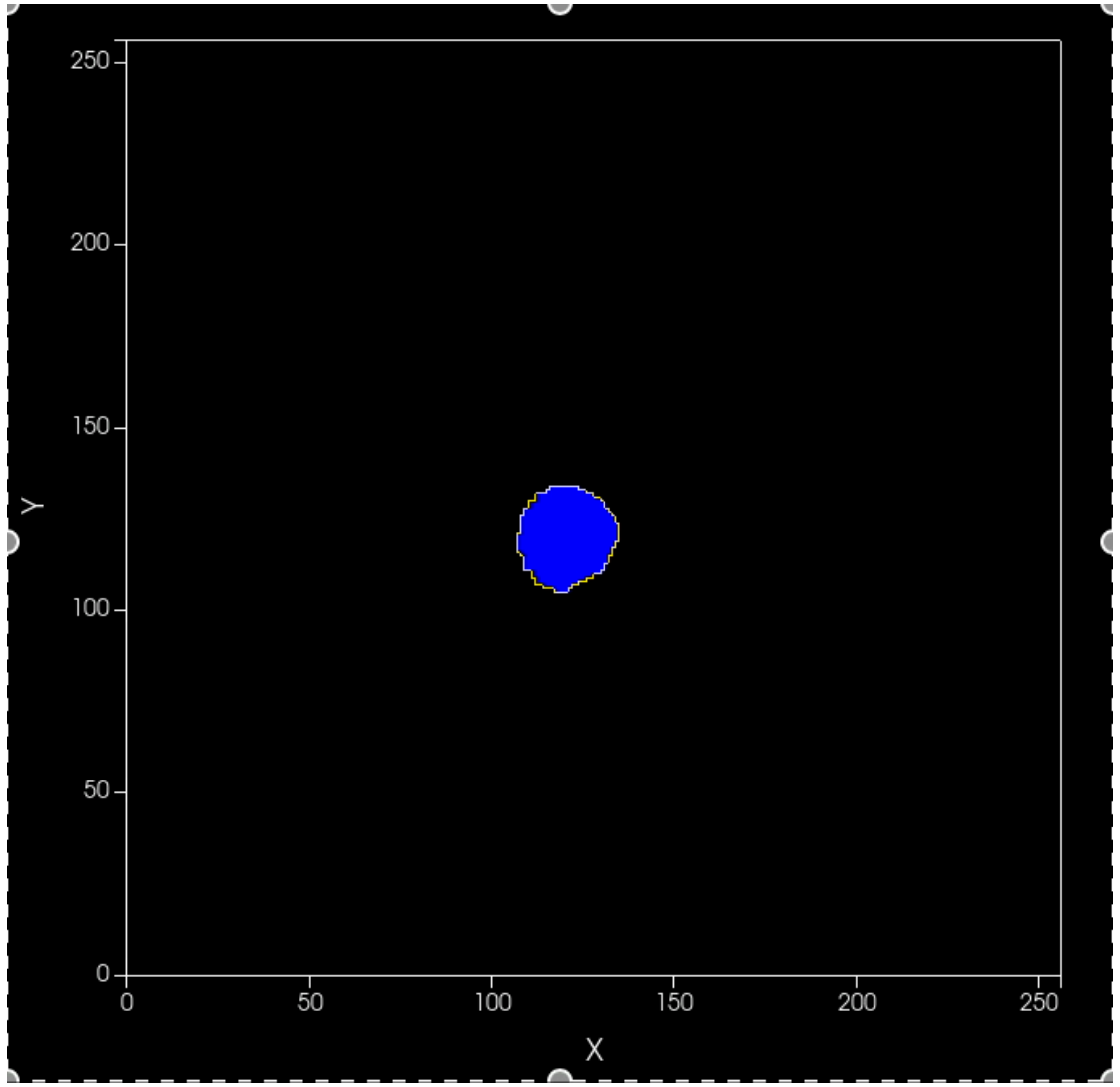
$$\boxed{\lambda_{l_x} \sum_{\sigma_i} (l_x(\sigma_i - l_x^0(\sigma_i))^2}$$

Cell growth and Cell death

- $V_0 \rightarrow V_0(t)$
- $V_0(t+1) = V_0(t) + \Delta V$
- $\Delta V > 0 \rightarrow$ cell growth
- $\Delta V < 0 \rightarrow$ cell death



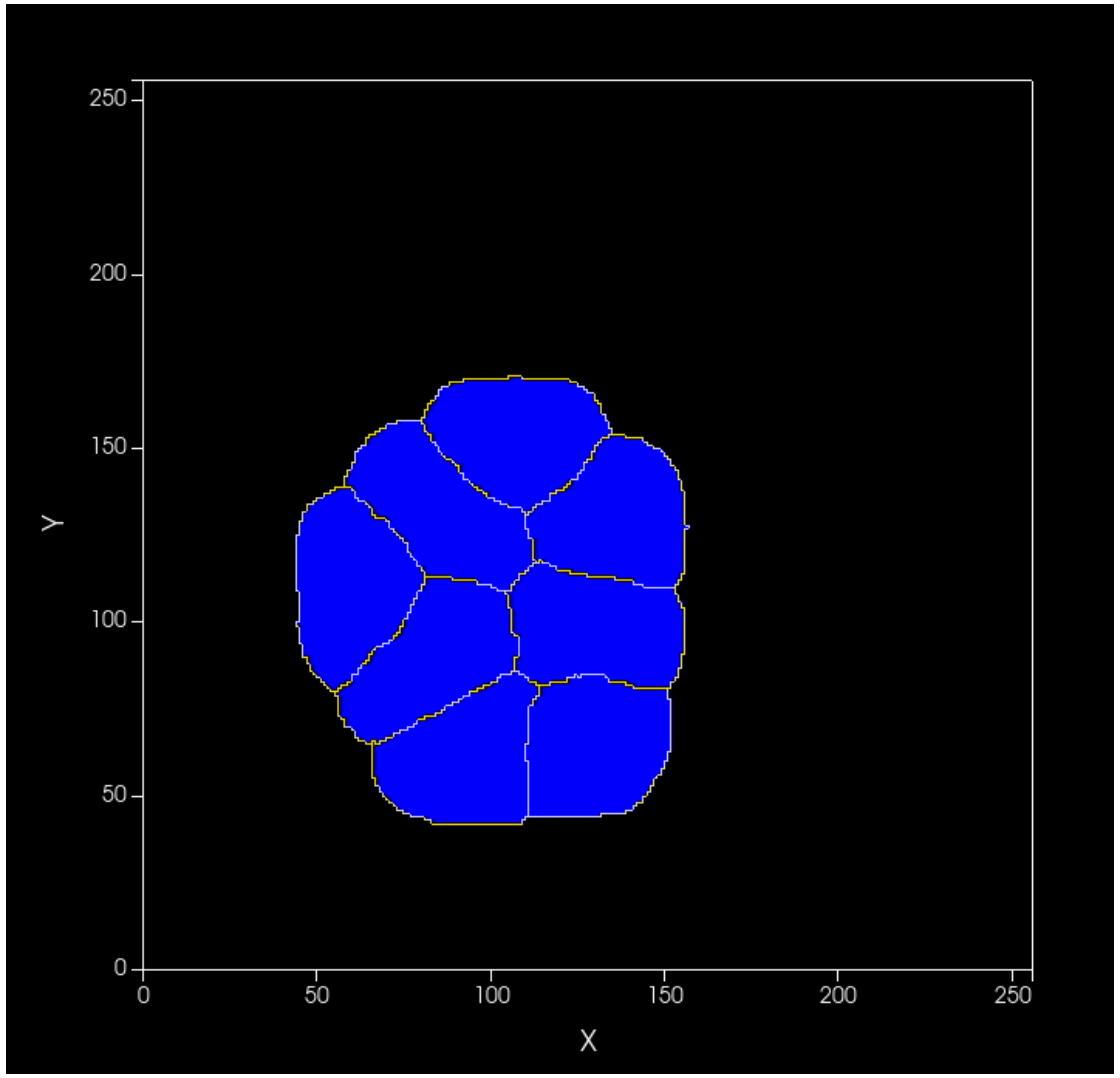
dV = 1



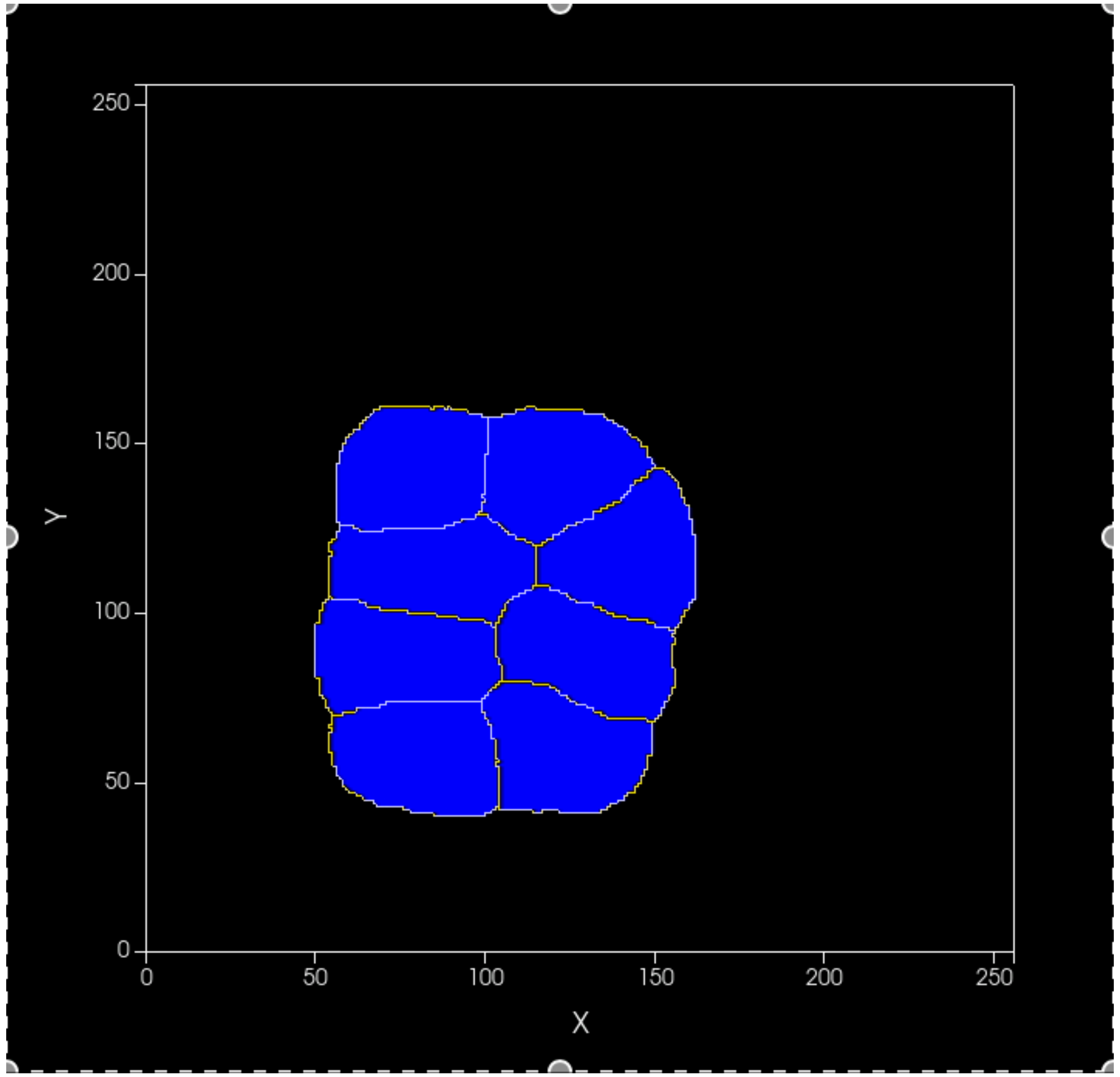
dV = -10

Cell division

- When a cell volume crosses a threshold volume divide into two daughter cells along the axis of division
- The daughter cells need not share the volume equally between them i.e. asymmetric cell division



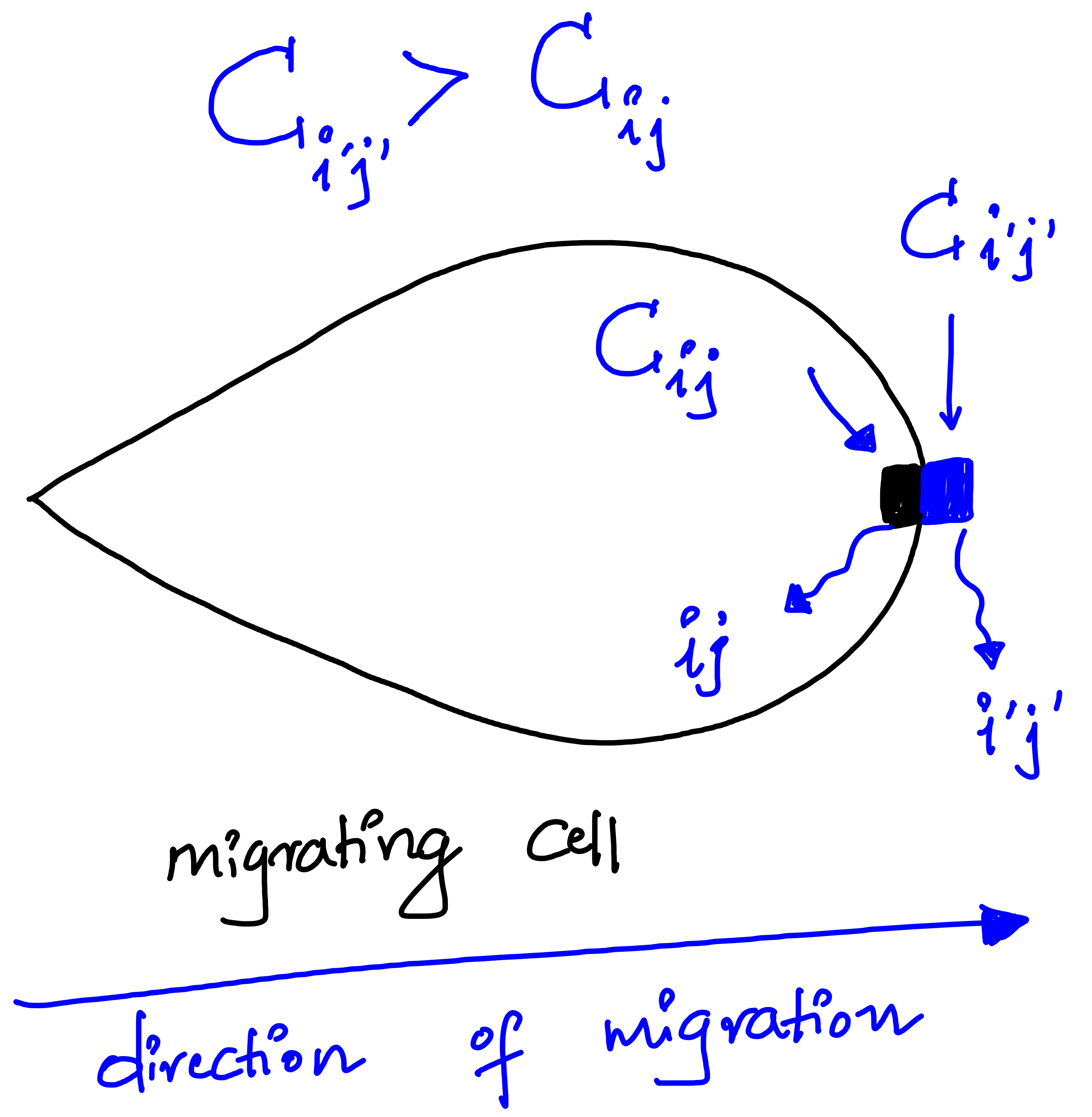
Division along random axis



Division along minor axis

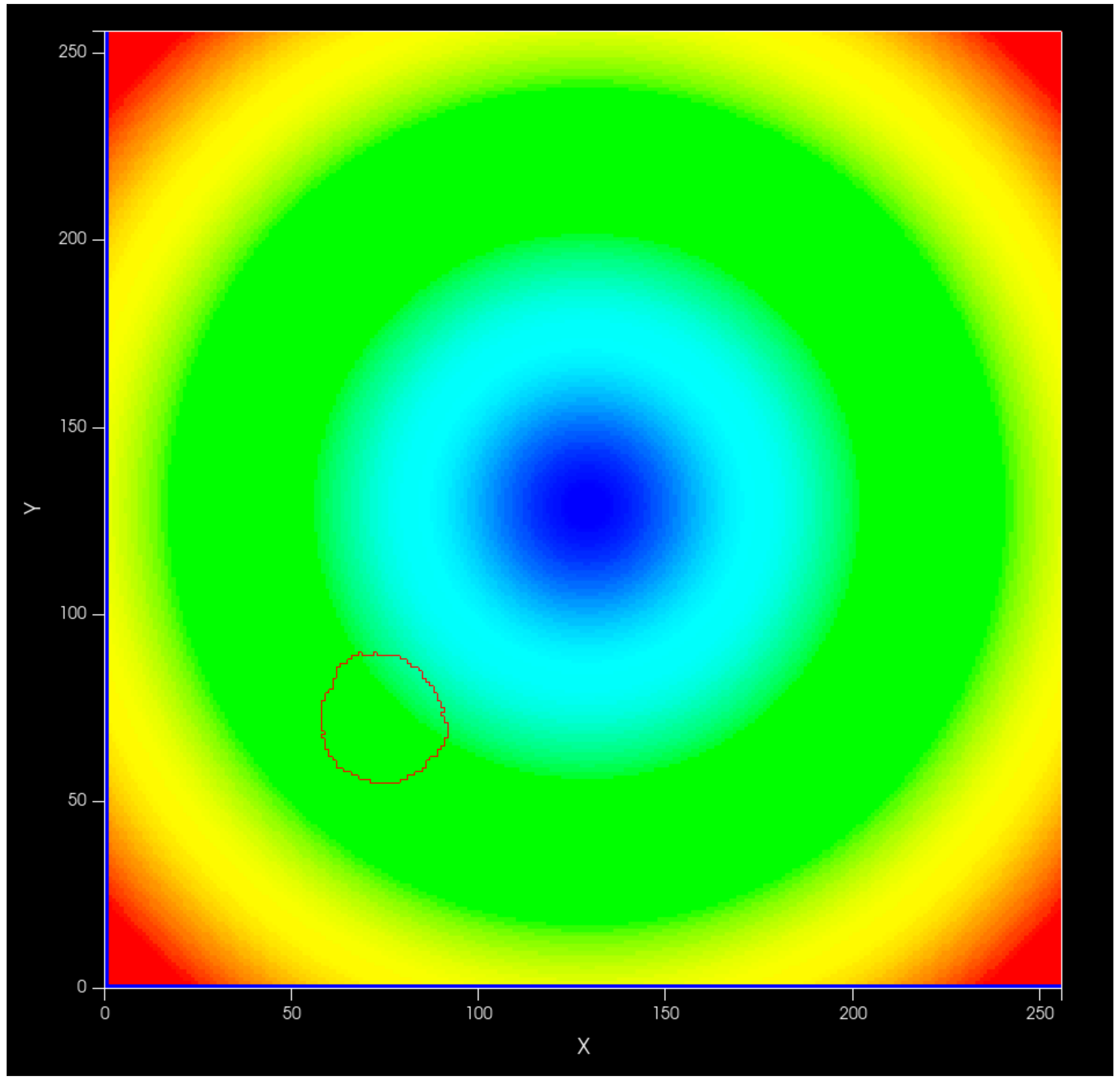
Cell migration - chemotaxis

$$\boxed{\Delta E^{\dagger} = \mu(C_{ij} - C_{i'j'})}$$

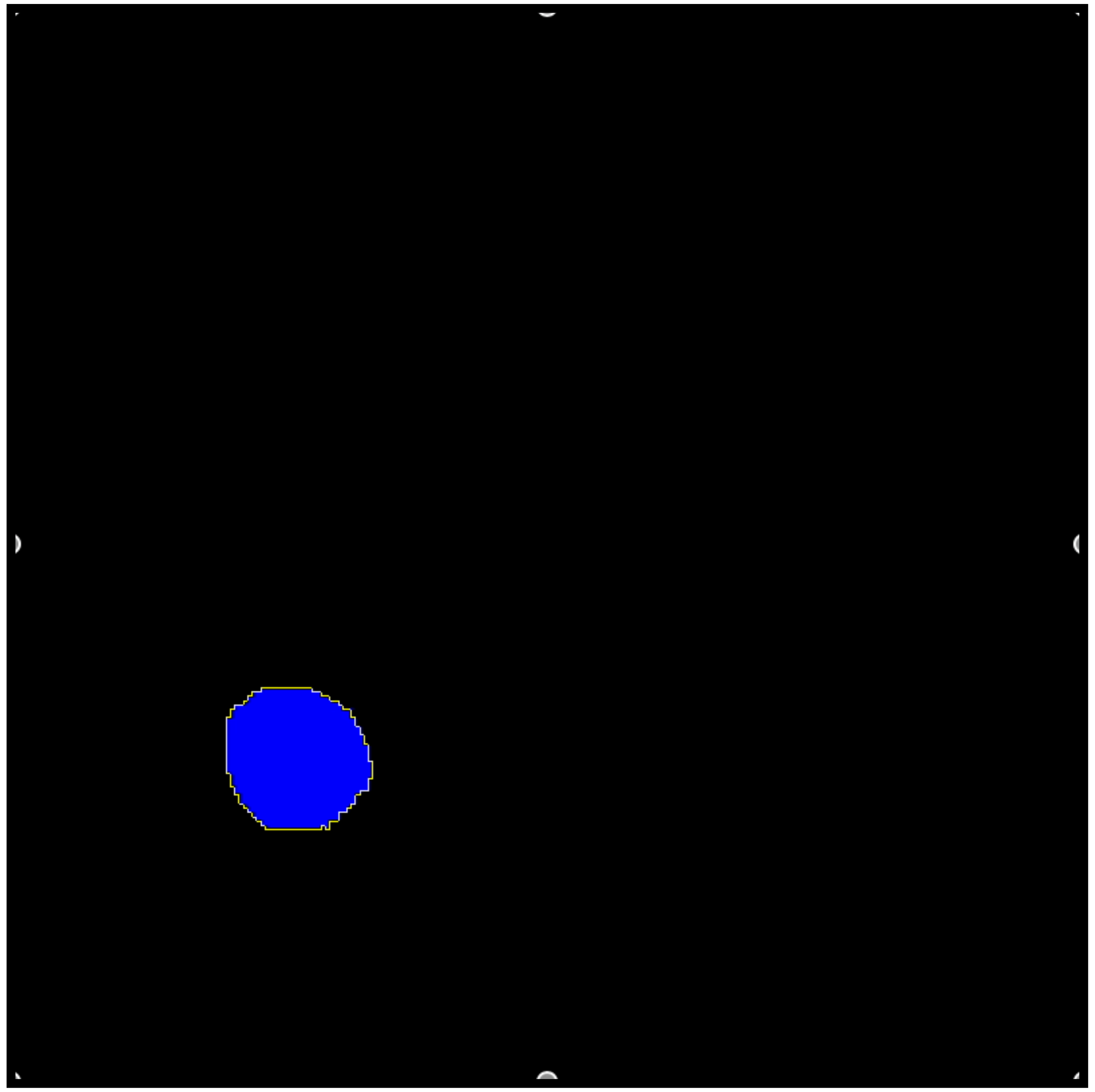


Biased pixel flips during chemotaxis

Radial chemical field



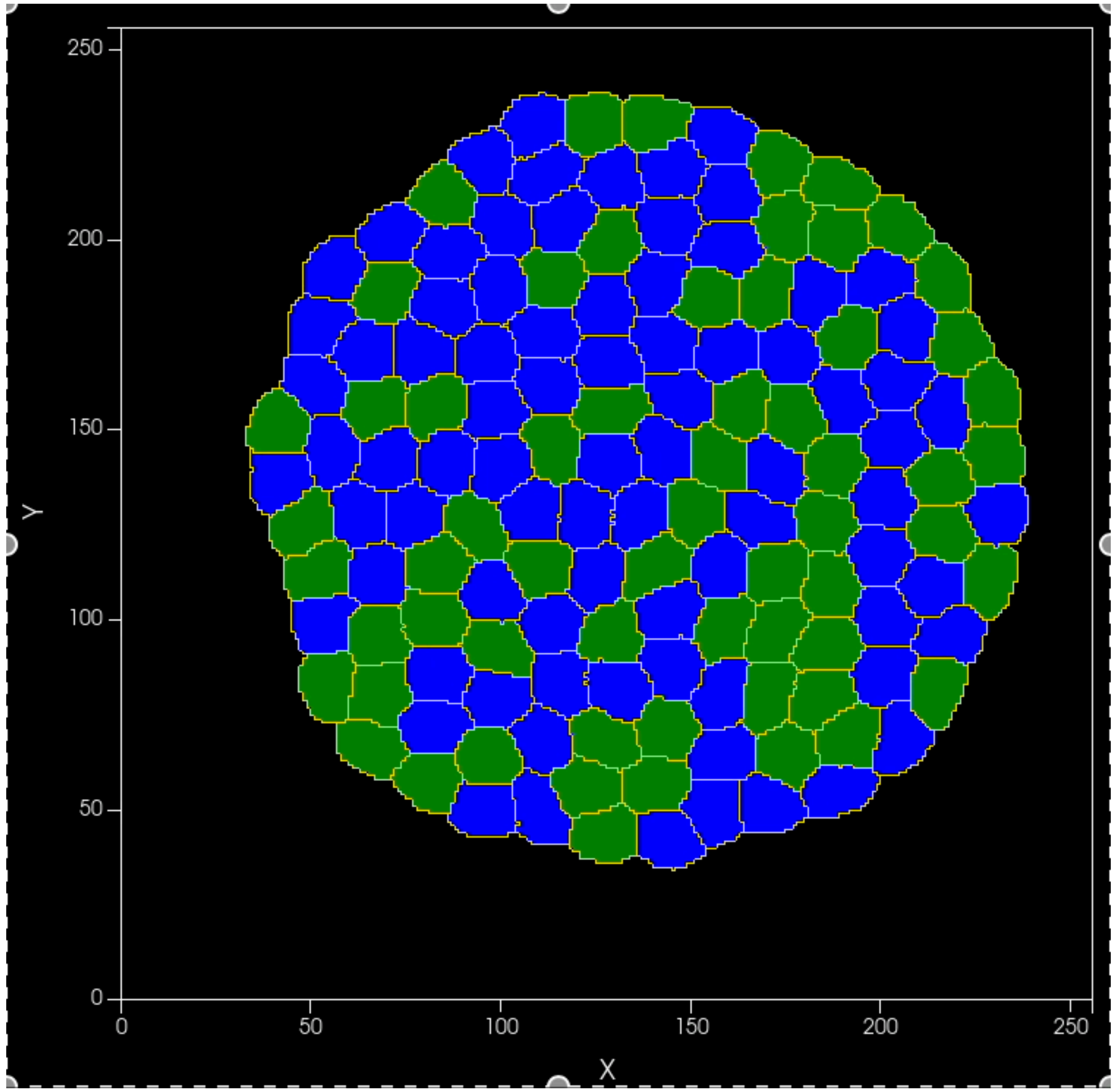
Migrating cell



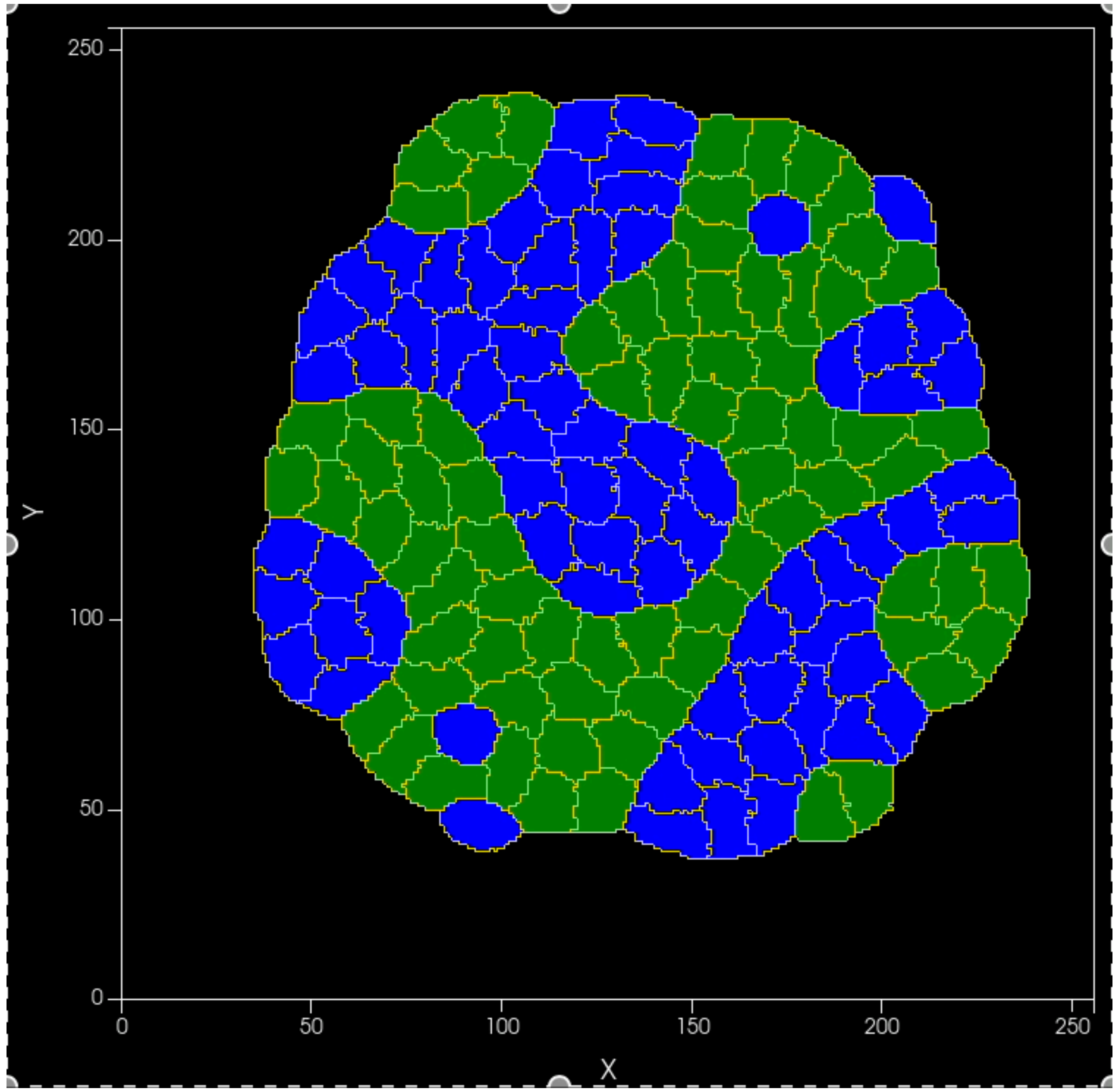
Savill and Hogeweg, JTB 1997

Cell sorting - differential adhesive affinity

- Cell type A (green)
- Cell type B (blue)



$J_{AA} = J_{BB} = J_{BA} = 10$



$J_{AB} = 10\,;\; J_{AA} = J_{BB} = 2$

Thank you for listening

Thanks to Prof. Cassandra Extavour and to all the members of the Extavour lab

Thanks to James Glazier and his team of people who created and maintain **Compucell3D**

https://compucell3d.org/

Questions please