1 Cellular Potts Model - after Merks et al. Cell-oriented modeling of in vitro capillary development. Cellular Automata (2004) p425–434

Another example of this modeling technique applied to morphogenesis see How amoeboids self-organize.

The state space is a finite square lattice where each lattice site i has an identifier $\sigma(i) \in \mathbb{N}$. The set $\sigma^{-1}(n)$ represent the cell n (it better stay connected!). We write $A(\sigma^{-1}(n))$ for the lattice area covered by $\sigma^{-1}(n)$.

In addition we have a type map $\tau : \mathbb{N} \to T$ mapping a cell to its type; minimally we need two types, one for medium M, and one for the cell type of interest say c. Medium is conventionally mapped to $n = 0$.

Neighbours with different σs correspond to boundaries separating cells (perhaps of the same type). We write ∂x for the set of unordered pairs of lattice neighbours (i, i') with different σ's in state x.

§Energy -

We have as parameters:
- a bond energy $J_{\tau\tau'}$ for a contact between type τ, τ'
- a target area A_τ and length l_τ for $\tau \neq M$

The energy of a state (or configuration) is defined as a sum of various contributions (some defined later):

$$\begin{array}{lcll} E_1(x) & = & \sum_{i,i' \in \partial x} J_{\tau(\sigma(i))\tau(\sigma(i'))} & \textit{adhesion term} \\ E_2(x) & = & \lambda \sum_{0<n} (A(\sigma^{-1}(n)) - A_{\tau(n)})^2 & \textit{volume term} \end{array}$$

where λ represent the resistance to compression (note that empty space is ont included in the constraint).

Typical values: $J_{cc} = 5$, $J_{cM} = 20$, $J_{cB} = 100$ to prevent adhesion to the boundary B (a third type).

Observe that the first term will tend to minimize the total boundary length.

§Dynamics -

Pick some site i uniformly at random in ∂x, pick some neighbour i', copy the state of i to that of i' with a certain probability dependent on the energy difference ΔE:

$$\begin{array}{lcll} p(i \mapsto i') & = & e^{-\beta(\Delta E + E_0)} & \textit{if } \Delta E > -E_0 \\ & = & 1 & \textit{if } \Delta E \leq -E_0 \end{array}$$

where β is an inverse temperature, $E_0 > 0$ an energy threshold.

Set $\beta = 1$, $E_0 = 0$ and we get a normal (discrete-time) Metropolis-Hastings.

Set $\beta = 0$ and all moves are equally likely (infinite temperature), $\beta = \infty$ and all are forbidden (zero temperature, frozen world).

Typically $E_0 = 0.1$.

Time is per MCS (Monte-Carlo step) each of which attempting one update step per site on average; meaning δt of a microscopic update (whether succesful or not) is $1/|\partial x|$.

Surface tension: $\gamma_{cM} := J_{cM} - J_{cc}/2$. Here we have $\gamma_{cM} > 0$ which means cells wants to glue together. (Hint: compute the ΔE_1 for glueing:).

§PDE - chemoattractant

The PDE part is discretized on the same lattice (a discrete PDE is a cellular automaton!):

$$\partial_t c(i,t) \quad = \quad D\Delta^2 c(i) + \alpha\delta_{\tau(\sigma(i))c} - \epsilon c \cdot \delta_{\sigma(i)0}$$

The production term is only for sites of type c, while degradation only happens in the medium.

Time calibration: one does 20 steps per MCS (concretely after each MCS round, one iterates the PDE 20 times); each step corresponding to a δt of 0.2 - for these parameters the chemoattractant diffuses much more rapidly than the cells, so we ignore *advection* (due to the cells moving, usually modelled as $\partial_t c = -v\partial_x c$). Boundary values are set to zero (boundaries absorb the chemoattractant).

§chemotaxis -

$$E_3(x) \quad = \quad -\chi \textstyle\sum_i c(i,t)\delta_{\tau(\sigma(i))c} \quad \textit{chemotactic term}$$

The ΔE_3 of a swap is thus $-\chi(c(i',t) - c(i,t))$ so there will be force moving towards higher concentration; χ measures the strength of this.

In fact they use a slightly different term:

$$E_3(x) \quad = \quad -\chi \textstyle\sum_i \dfrac{c(i,t)}{s \cdot c(i,t) + 1}\delta_{\tau(\sigma(i))c} \quad \textit{chemotactic term with saturation}$$

Typically $s = 0.01$. For $s = 0$, this is amounts to the first case, there is no saturation.

§cell elongation -

$$E_4(x) \quad = \quad \lambda_L \textstyle\sum_{0<n} (l(\sigma^{-1}(n)) - l_{\tau(n)})^2 \quad \textit{elongation term}$$

where $l(X)$, X a connected subset of the lattice is its length along the main axis.

Think about how E_2, E_4 can be recomputed after a move. The more incremental the better. There are problems with cells disconnecting.

§Experiments -

A 500×500 lattice, where each lattice site represents an area of about $4\mu m^2$. Cells have actual areas of around 45 lattice sites, equivalent to a typical endothelial cell. Initially dispersed randomly.

Remains to test the appearance of network like structures for various parameters. One can also observe the mean size of a medium connected component to capture the network like character in a number.