

Cell Motility: A Systems Approach

We have discussed many of the principles of individual cell systems and now we want to put them together to understand how a cell will accomplish an integrated function. This requires us to look at the details of a given process to determine what are the important elements and how they might be controlled. We will take the example of the neural crest cell migration and then try to map out the details of what is involved.

Description of Process

The peripheral nervous system is created by a spatiotemporally co-ordinated migratory process during which the precursor cells, the neural crest (NC) cells, traverse the embryo to reach distantly located sites. Original transplantation experiments implicated the extracellular matrix (ECM) as a pivotal factor in the regulation of this process, and subsequent *in vitro* and *in vivo* studies have uncovered a number of ECM molecules potentially responsible for the NC cell–ECM interaction. Recent genetic manipulations in mice sustain the importance of certain matrix constituents, while precluding a significant role for others and, surprisingly, for all primary integrin receptors expressed by NC cells. The gradually crystallizing paradigm envisions that guidance of the disseminating NC cells, as well as the arrest at their final tissue locations, is governed by specific ‘inhibitory’ ECM-associated signals. This implies that homing of peripheral neurons and their supportive cells might be dictated by a delicate equilibrium between the multiple actions of stimulatory and inhibitory molecules, which is modulated further by defined responses of the dispersing cells to these ECM components during their successive phases of phenotypic diversification. (taken from a review in *Trends Neurosci.* (1997) 20, 23–31) (Remember that you can download this review over the internet by going to the e-journals at the Biology library site)

Definition of Steps in the Process of Neural Crest Migration

Initiation of migration (epithelial-mesenchyme transition)

- Transition from tissue ball to migratory cell

- Loss of cadherins

- Acquisition of Integrins

- Acquisition of motile machinery

- Stimulus to migrate

Migration

- Actin-dependent extension

- Adhesion of integrins to matrix

- Contraction

- Release

- Recycling

Homing

Stop signal-inhibitors of motility
Differentiation
Specific signals to differentiate as a neuron or pigment cell

Important Aspects of Migration

1. Isovolumic
2. Constant Membrane Area
3. Actin filament assembly and disassembly
4. Actin filament contraction
5. Matrix binding
6. Response to Matrix Rigidity
7. Release of matrix binding
8. Biochemical stop signals

Osmotic Pressure

Osmotic pressure is defined as the pressure that develops across a semipermeable membrane that separates two compartments. Typically the membrane is permeable to the solvent but not permeable to the solute. We will consider water-based solutions separated by a membrane such as the plasma membrane. Because water has a lower activity in a concentrated salt solution than in a dilute solution, there will be movement of water from a dilute solution to the concentrated solution. If a physical pressure is developed across the membrane, then the water can be forced to move from the concentrated to the dilute solution at the same rate as the water diffuses from the weak salt solution to the concentrated.

$$\text{Osmotic Pressure } P = cRT$$

Where c is concentration in moles per liter and R is the molar gas constant and T is the temperature.

Problems:

1. Cells are about 30 microns across and are on average about 2 microns thick. Assuming that the cell is rectangular, what is the resistance that the cell encounters from fluid drag when moving at the highest velocity observed for mammalian cells of 40 microns per minute. (assume that the medium has the viscosity of water at 25° C).
2. In the model of cell migration that we discussed in class, there were a number of critical parameters that could be controlled to effect the directed movement of neural crest cells to the proper location in the periphery. If we consider the important aspects of cell migration listed above, we can generate several different models for the process of cell migration. The one that I described in class involved the orientation of matrix fibers such that they mechanically directed the cells to the right location. In the description of the process (above) that was lifted from the review

article, another model is outlined. Please describe the important differences between the two models and give one critical difference that you think could be tested experimentally.