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Forces and pattern in limb morphogenesis

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Prior to cartilage and bone formation in the limb bud chondroblasts condense into foci which provide the pattern for subsequent bone development. Formation of these condensations is, finally, a mechanical event, and so it is natural to ask what are the forces responsible for creating them.

We have constructed a model for the process of cell aggregation during chondrogenesis which involves the following forces: (1) the passive elasticity of the extracellular matrix (ECM), (2) the osmotic swelling pressure of the ECM, which is generated principally by the hyaluronate (HA) component, (3) the active cell tractions developed by the chondroblasts. By examining the balance of forces between the cells and matrix, we find that patterns of cell aggregation can spontaneously arise by an instability mechanism analogous to that which occurs in chemical pattern formation models.

According to our model, the following scenario creates the chondrogenic pattern. (a) Cells emerge from the progress zone and commence to manufacture the HA component of the ECM. (b) Because of its high fixed density, the HA component generates a powerful swelling pressure which inflates the limb bud. (c) At the time of condensation the cells commence to produce hyaluronidase (HAase). This initiates a partial osmotic collapse of limb bud core which draws the cells closer together. (d) With the collapse of the HA barrier, which keeps cells apart, cells are brought into close apposition and intercellular contacts increase in number and strength. (e) At this point cell traction forces commence to become effective, and the final condensation pattern emerges.

Following aggregation the cells begin to resecrete HA and the core of the condensations rehydrates and swells. This creates a stress pattern which generates the perichondrium.

Pattern regulation in one- and two-dimensional morphogenetic fields

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In the framework of reaction-diffusion theory a gradient S can be formed which is approximately a homogeneous function of the positional value x and the total linear length L of the morphogenetic field. The profile of S is the following (Papageorgiou, 1980):

$$S(x,L)=L^p f(x/L) \qquad (1)$$

The scaling function f depends only on the relative distance x/L while the scaling factor L^p is position-independent. A paradigm of reaction-diffusion systems in one-dimensional fields has been worked out (Papageorgiou and Venieratos, 1983) leading to gradients of the form (1) where $p=-1$. It is then straightforward to form a new gradient (Papageorgiou, 1980) which depends only on f(x/L) thus achieving pattern regulation on a one-dimensional field. The model can account for the regulation as observed quantitatively by Cooke (1981) on early amphibian embryos.

From dimensional considerations we expect that $[S]=[\text{length}]^{-d}$ where d is the space-dimensionality. For a linear gradient the above value of p is consistent with the canonical dimension of S(d=1). Going over to two dimensions (d=2) and with the same reaction-diffusion equations, it turns out that $p=-1$. Therefore S develops 'anomalous' dimensions as in the critical phenomena of phase transitions (Wilson, 1983).

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