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Building a Morphogen Gradient without Diffusion in a Growing Tissue

In many developmental systems, spatial pattern arises from morphogen gradients, which provide positional information for cells to determine their fate. Typically, diffusion is thought to be the mechanism responsible for building a morphogen gradient. An alternative mechanism is presented here. Using mathematical modeling, we demonstrate how a non-diffusive morphogen concentration gradient can develop in axially growing tissue systems, where growth is due to cell proliferation only. Two distinct cases are considered: in the first, all cell proliferation occurs in a localized zone where active transcription of a morphogen-producing gene occurs, and in the second, cell proliferation is uniformly distributed throughout the tissue, occurring in both the active transcription zone and beyond. A cell containing morphogen mRNA produces the morphogen protein, hence any gradient in mRNA transcripts translates into a corresponding morphogen protein gradient. Proliferation-driven growth gives rise to both advection (the transport term) and dilution (a reaction term). These two key mechanisms determine the resultant mRNA transcript distribution. Using the full range of uniform initial conditions, we show that advection and dilution due to cell proliferation are, in general, sufficient for morphogen gradient formation for both types of axially growing systems. In particular, mRNA transcript degradation is not necessary for gradient formation; it is only necessary with localized proliferation for one special value of the initial concentration. Furthermore, the morphogen concentration decreases with distance away from the transcription zone, except in the case of localized proliferation with the initial concentration sufficiently large, when the concentration can either increase with distance from the transcription zone or sustain a local minimum. In both localized and uniformly distributed proliferation, in order for a concentration gradient to form across the whole domain, transcription must occur in a zone equal to the initial domain size; otherwise, it will only form across part of the tissue.