From Dynamic Expression Patterns to Boundary Formation in the Presomitic Mesoderm

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Somitogenesis is a process in embryonic development fundamental for the segmentation of the vertebrate body. In mice, repeatedly every two hours, small groups of cells separate themselves from the rest of the presomitic mesoderm (PSM) and develop into distinct epitheliased structures called somites, which later in development give rise to two half-vertebrae, muscles, dorsal epidermis etc. . Until the end of the growth phase of the embryo the PSM is replenished at its posterior end, so its length remains roughly constant.
Repeated, periodic gene expression precedes the formation of morphologically visible boundaries between the forming somites and the rest of the PSM. The gene Mesp2, controlled by Delta/Notch signalling, plays a decisive role in this.
Based on experimental results we formulated a gene regulatory network (GRN) for Mesp2 and the genes controlling it in somitogenesis. We examine the consequences of this network with our simulation program (H. Tiedemann et al. , JTB 2007), which models the growing PSM with many ‘virtual cells’ by solving numerically the differential equations describing the GRN in each ‘cell’ and displaying the concentration of gene products as intensity of coloration of each cell.
The negative feedback of the transcription factor Hes7 (or Hes1) on itself forms the core of the so-called somitogenesis clock, controlled by inter-cellular Delta-Notch-signalling. Along the PSM posterior-to-anterior gradients of the Wnt3a and Fgf8 signal transduction pathways

influence the oscillations of the somitogenesis clock in each cell, slowing it ever more as the growth zone of the tail bud recedes, until it comes to a standstill near the anterior end of the PSM. A negative feedback of Hes1/7 on Dll1 leads to oscillating Dll1 expression and consequently to a dynamic ‘wave’ of Notch intracellular domain which together with the transcription factor Tbx6 (and suppression by Fgf8 in the caudal PSM) leads to periodic Mesp2 expression along the growing PSM.