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From Gene Networks to Tissue Engineering: Computational Models of Pattern Formation

Limb bud development has long served as a paradigm of organogenesis and pattern formation. Decades of genetic and biochemical studies provide us with a wealth of information about the molecular circuits that control cell expansion and position-dependent cell differentiation in the developing limb bud. In spite of much detailed biological knowledge and much theoretical work a detailed mechanistic understanding of how the genes and regulatory circuits interact to control limb organogenesis is still lacking. In collaboration with the Zeller group at the Department of Biomedicine of the University of Basel we are developing detailed computational models for limb development in mice. By combining mathematical modeling with experimentation we seek to understand how key processes at the microscopic level interact to give rise to patterning at the macroscopic level.

The signaling pathways (Fgf, Shh, Bmp, Gremlin) that regulate limb bud development are strikingly similar to those that regulate lung morphogenesis. Based on the model for limb development we have also developed a mechanistic model for the regulatory network that governs lung branching. The branching of the bronchi in the lungs is highly stereotyped and results from a highly regulated process that restricts the types and sequence of branching modes.

In the long run we seek to use our mechanistic insights in the engineering of tissue and bone.