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The *de novo* formation of a vascular network, in warm-blooded embryos, occurs via a self-assembly process that spans multiple length and time scales

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Taking advantage of wide-field, time-lapse microscopy we examined the assembly of vascular polygonal networks in whole bird embryos and in explanted embryonic mouse tissue (allantois). Primary vasculogenesis assembly steps range from cellular (1-10 μm) to tissue (100μm-1mm) level events: Individual vascular endothelial cells extend protrusions and move with respect to the extracellular matrix/surrounding tissue. Consequently, long-range, tissue-level, deformations directly influence the vascular pattern. Experimental perturbation of endothelial-specific cell-cell adhesions (VE-cadherin), during mouse vasculogenesis, permitted dissection of the cellular motion required for sprout formation. In particular, cells are shown to move actively onto vascular cords *that are subject to strain via tissue deformations*. Based on the empirical data we propose a simple model of preferential migration along stretched cells. Numerical simulations reveal that the model evolves into a quasi-stationary pattern containing linear segments, which interconnect above a critical volume fraction. In the quasi-stationary state the generation of new branches offsets the coarsening driven by surface tension. In agreement with empirical data, the characteristic size of the resulting polygonal pattern is density-independent within a wide range of volume fractions. These data underscore the potential of combining physical studies with experimental embryology as a means of studying complex morphogenetic systems.

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