Mathematical modelling of vasculature regression during cartilage condensation

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Embryo growth beyond a size of approximately 2 mm is heavily reliant on a functional vascular system, which must be fully functional and constantly remodeling to support all tissues during early development. However, the mechanisms that underlie the complex 3D architecture of blood vessel networks during organogenesis remain poorly understood. This is particularly true in the case of limb development, where vasculature plays a crucial role not only in nutrient supply but also in limb patterning. Previous studies have shown that blood vessels regress from the region where cartilage condensation begins, while being maintained in other parts, although the underlying mechanisms remain unclear.

Recent *in vitro* experiments and preliminary literature findings suggest that the transcription factor Sox9 may be involved in regulating the expression of VEGF, which is responsible for this phenomenon. Specifically, Sox9 may play a role in controlling the pattern of VEGF expression that leads to blood vessel regression in the region where cartilage condensation begins. However, the specific mechanisms that link Sox9 expression and blood vessel regression have not yet been exhaustively characterized.

To fully understand this process, we developed a hybrid mathematical model that (1) simulates contact interactions between endothelial cells, (2) reproduces mechanical interactions between these cells, (3) models and control the Sox9 pre-pattern, and (4) examines the influence of mechanics on the Sox9 pattern. Combining an approach at the edge between biology and mathematical modelling we provide a first step in understanding how the vasculature network forms inside the limb and how it orchestrates organogenesis.