Computational model

In our tissue modeling approach we utilized a particle-and-beam framework (Czirok and Isai, 2014) in the purely elastic regime – i.e., without plastic deformations. Cells and their mechanical interconnections are represented by particles and elastic beams, respectively. The beams that connect particles (cells) can be compressed, stretched, bent and twisted. Therefore, these links can exert torques and forces that are not parallel to the line connecting the particles. The tissue is assumed to be in mechanical equilibrium, i.e., the tissue environment is expected to quickly accommodate changes due to cellular activity.

We represent cell activities such as contraction and the generation of bending moments by manipulating the particle-specific parameters that characterize mechanical equilibrium. In particular, the interparticle bond is capable of exerting non-central forces and torques. The central component of the force, F, is determined by a rule resembling Hooke's law:

$$F \sim \ell - \ell_0 \tag{1}$$

where ℓ is the actual length of the link, and ℓ_0 – a parameter assigned to each link – is its "natural" length (the length of the link in mechanical equilibrium, in the absence of external forces). Similarly, bending moments are explicit model variables, which are associated with each link's endpoints. In particular, we assume that a torque, $\vec{M}$, is exerted on the link if its direction, $\vec{u}$, is different from its "neutral" direction, $\vec{t}$, and the torque is proportional to the difference:

$$\vec{M} \sim \vec{u} \times \vec{t}. \tag{2}$$

The neutral direction ($\vec{t}$) vectors rotate together with the particle, while the $\vec{u}$ vectors are determined by the spatial positions of the particles. So, we can represent an autonomous tendency of the cells to bend by aligning the $\vec{t}$ vectors onto the surface of a cone.

The purpose of our model is to understand how the autonomous activities of myocardial progenitors can drive tissue movements. Thus, we keep the modeled anatomy simple and schematic-like. As we describe below, we use three coordinates to describe anatomical locations. The left-right coordinate (x) is zero at the embryonic axis, and positive at the embryonic right in ventral view. The anterior-posterior coordinate (y) is increasing in the anterior direction, and it is zero at the anterior-most segment of the anterior intestinal portal (AIP). The dorso-ventral coordinate (z) is positive in the ventral direction, and $z = 0$ marks a frontal plane section that cuts through the foregut, the coelom and the flanking mesoderm.

1 Mesoderm and myocardium structure

The left and right myocardial fields are embedded in bi-lateral lobes of non-myocardial mesoderm (see Supplenetal fig 2) that delineate the medial and ventral portion of the intraembryonic coelom. On both the left and right sides of the model the folded mesoderm is represented as two layers that merge at their medial-most boundary. These medial-most mesodermal positions form a funnel-like structure in a frontal plane which we describe as

$$f(x,y) = y - \frac{0.2}{x^2} + \frac{1}{2}x^2 = 0. \tag{3}$$

This function reflects the widening of the AIP, hence the increasing separation of the left and right coelom boundary, at progressively posterior locations.

Particles representing mesodermal cells are randomly positioned along two surfaces. For the x and y coordinates we require the $f(x,y) > 0$ constraint. The dorso-ventral coordinate is determined as

$$z = \pm\sqrt{d(x,y)}, \tag{4}$$

where $d(x,y)$ is the distance between the point (x,y) and the boundary $f(x,y) = 0$.

Myocardial progenitors are located at the ventral and medial aspects of the mesodermal sheets (Supplemental Fig 2). At progressively anterior locations the heart field (the myocardium) is situated at increasingly medial locations. Thus the particle at (x,y,z) is myocardial if

$$d_{ventral,lateral}(y) - 2 < d(x,y) < d_{ventral,lateral}(y) \text{ for } z > 0 \tag{5}$$

and

$$d(x,y) < d_{dorsal,lateral}(y) \text{ for } z \leq 0, \tag{6}$$

where

$$d_{ventral,lateral}(y) = 1 + 2e^{-\frac{4+y}{3}}. \tag{7}$$

and

$$d_{dorsal,lateral}(y) = 2 - d_{ventral,lateral}(y) \tag{8}$$

Thus, the posterior heart field is entirely on the ventral mesodermal sheet. At more anterior locations myocardial progenitors occupy a progressively more medial location and eventually "spill over" to the dorsal coelom boundary.

2 Endoderm structure

Our simulated structure is covered by the endoderm: on the dorsal side by the ventral foregut epithelium, while at the ventral side by the embryonic epithelium. These endodermal sheets are continuous across the AIP.

The frontal section of the AIP is modeled by the parabola

$$g(x,y) = y - 0.7x^2 - 2 = 0. \tag{9}$$

The coordinates of a model endodermal cell satisfy (1) $g(x, y) > 0$ and (2) z is chosen in a way that its distance to the mesodermal layer is constant (1 unit). This way, both the ventral and dorsal endodermal layers are continuous across the embryonic midline, while the mesodermal sheets are not.

3 Material properties

Model particles also satisfy the conditions described in Czirok and Isai (2014): two adjacent particles cannot be closer than a threshold value, voronoi neighbors are linked in the myocardial and endodermal sheets. Finally, pairs of adjacent myocardial/mesodermal and endodermal cells are also connected by elastic beams.

The model has three microscopic parameters that describe the spring constant, bending and torsional rigidity of the links. According to the calibrating procedure described in detail in Czirok and Isai (2014), these model parameters correspond to macroscopic material properties of the simulated multicellular sheets. We have chosen parameters that correspond to $E \sim 1kPa$, a small Poisson number $\nu \sim 0.1$, and a bending rigidity that would correspond to a three cell layers thick sheet.

4 Cellular activities (growth laws)

We prescribed the following autonomous activities that were driving the elastic response of the model:

Endoderm movement. To represent the regression of the AIP, we prescribed external forces at the ventral endodermal surface. We selected the forces in such a way that the yielded displacements were perpendicular to the AIP $g(x, y) = 0$ and were of uniform magnitude throughout the ventral endoderm.

Myocardial contraction. Myocardial contraction was modeled by a 25% shortening of the equilibrium length of the beams interconnecting myocardial cells.

Myocardial bending moments. Bending moments, intrinsic to the tissue, are modeled by changing the equilibrium link direction vectors (see Eq.(1) in Czirok and Isai, 2014) from a plane to a conical surface with an aperture angle of $\sim 150^o$. Thus, the mechanical equilibrium configuration of these particles is a sphere which consists ~ 12 particles across its circumference, a value matching our experimental observations in Fig. 4.

Reference

A. Czirok and D. G. Isai. Cell resolved, multiparticle model of plastic tissue deformations and morphogenesis (preprint). `http://arxiv.org/abs/1408.3055`