Tension around the clock

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The formation of body segments in vertebrate embryos has been traditionally attributed to spatio-temporal patterning of molecular signals. A study in zebrafish embryos establishes a shape adjustment mechanism driven by tissue mechanics to ensure the precision of body segment length.

Not all clocks are precise. The segmentation clock is the molecular oscillator that regulates the formation timing of somites, the multicellular blocks that periodically bud off on both sides of the neural tube during vertebrate development[1]. As one pair of somites is formed during one oscillation cycle of the segmentation clock, the initial size of the somite is determined by the oscillation frequency and the cell movement speed from the posterior side of the embryo (Fig. 1). On page XX of this issue, Naganathan et al. demonstrate that the initial length of somites is surprisingly imprecise and provide a new mechanism for length adjustment during zebrafish somitogenesis[2]. Rather than being based on the segmentation clock, this mechanism is based on a single mechanical property of the somite – its surface tension.

By using sophisticated 3D imaging, the authors observed that the anteroposterior (AP) length of the somites immediately after their formation was highly heterogeneous. However, over the course of two hours, somites adjusted to a target length of 51 µm. To explain this length adjustment, the authors considered several potential mechanisms. First, they tested whether somite length adjustment could be explained by the segmentation clock. They ruled out this possibility by showing that perturbation of the clock does not change the dynamics of length adjustment. Second, they considered mechanisms based on the crosstalk between left and right somites. They ruled out these mechanisms by showing that perturbation of somitogenesis only on one side of the embryo does not affect length adjustment on the other side. A third possibility was that length adjustment could be explained by differential growth rates within somites. This possibility was rejected by the observation that somite volume is constant during length adjustment. Instead, the authors found that changes in the AP length are balanced by changes in the medio-lateral length of the somite.

The authors then proposed that the somite shape adjustment is driven by a mechanical property of the somite, namely its surface tension. The role of surface tension in somites can be understood in analogy with the intuitive mechanics of a fluid droplet. When the droplet is squeezed between two parallel non-adherent surfaces, it will deform to the imposed separation length, but upon sudden removal of the squeeze, it will adopt its original spherical shape. The rate at which the droplet will regain sphericity will mainly depend on its surface tension, which tends to speed up the process, and on its viscosity, which tends to slow it down.

Much as a fluid droplet, somites also display a tension at their surface and a viscosity in their bulk, but the origin of these physical properties is more complex than in the simple fluid droplet. Tension at the somite surface arises from actomyosin contractility, cell-cell adhesion, cell-extracellular matrix

(ECM) adhesion, and their mutual crosstalk[3]. Conversely, viscosity arises mainly from cells and the ECM in the somite bulk. The authors established that somites indeed behave like a fluid with a surface tension by showing that they rounded up when explanted from the embryo and that the cells in the somite bulk display diffusive dynamics. The time scale of rounding was of the same order of magnitude than the process of length adjustment. Moreover, perturbations of the actomyosin cytoskeleton, cell-cell adhesion, and cell-ECM adhesion slowed down the rounding of somite explants and impaired AP length adjustment in the embryos. This evidence, together with a mechanical model that incorporates stresses applied on somite boundaries, indicates that somite surface tension buffers AP length in newly formed somites.

These findings imply the contribution of tissue mechanics to left-right (LR) symmetry of somites. As somites become bilateral organs in later stages, such as ribs and skeletal muscles, their LR symmetry is crucial. Symmetry was historically attributed either to the symmetric somite formation (ensured by the precision of the clock) or to the LR crosstalk[4]. Both mechanisms are inconsistent with this study, which proposes that symmetry arises unilaterally; the robustness of somite surface tension combined with the boundary stresses in the system ensures that somites from both sides will adjust to the same target length and therefore ensure LR symmetry.

The proposed mechanism prompts several questions and expectations. For instance, even after the somite surface tension reduces the variability in somite length, this variability will eventually increase again as somites develop into bilateral skeletons and muscles. Is there an additional mechanism, mechanical or nonmechanical, that reduces the variability in later stages or a crosstalk mechanism between the left and right somite derivatives?

The paper also raises intriguing questions about the material properties of the PSM and their role in somitogenesis. Previous work had established that the PSM is in a solid-like state at the timescales of somite formation, which would seem inconsistent with the fluid behavior reported here[5]. One possibility to reconcile both observations is that mechanical stress is generated to transiently fluidize the tissue during somite formation. One potential source of stress is the contractile ring that separates adjacent somites or the active fluctuations within the somite bulk[6].

While this paper focuses on somitogenesis in zebrafish, studying somite surface tension and LR symmetry in other species will be interesting, considering that the zebrafish segmentation clock is significantly faster than mammalian clocks[1] and that fish somites adopt a specific chevron shape[7]. Even though live imaging and mechanical manipulation of mammalian somitogenesis is challenging, recent advances in *in vitro* models of somitogenesis from pluripotent stem cells may open a possibility to compare somite mechanics across species[8,9].

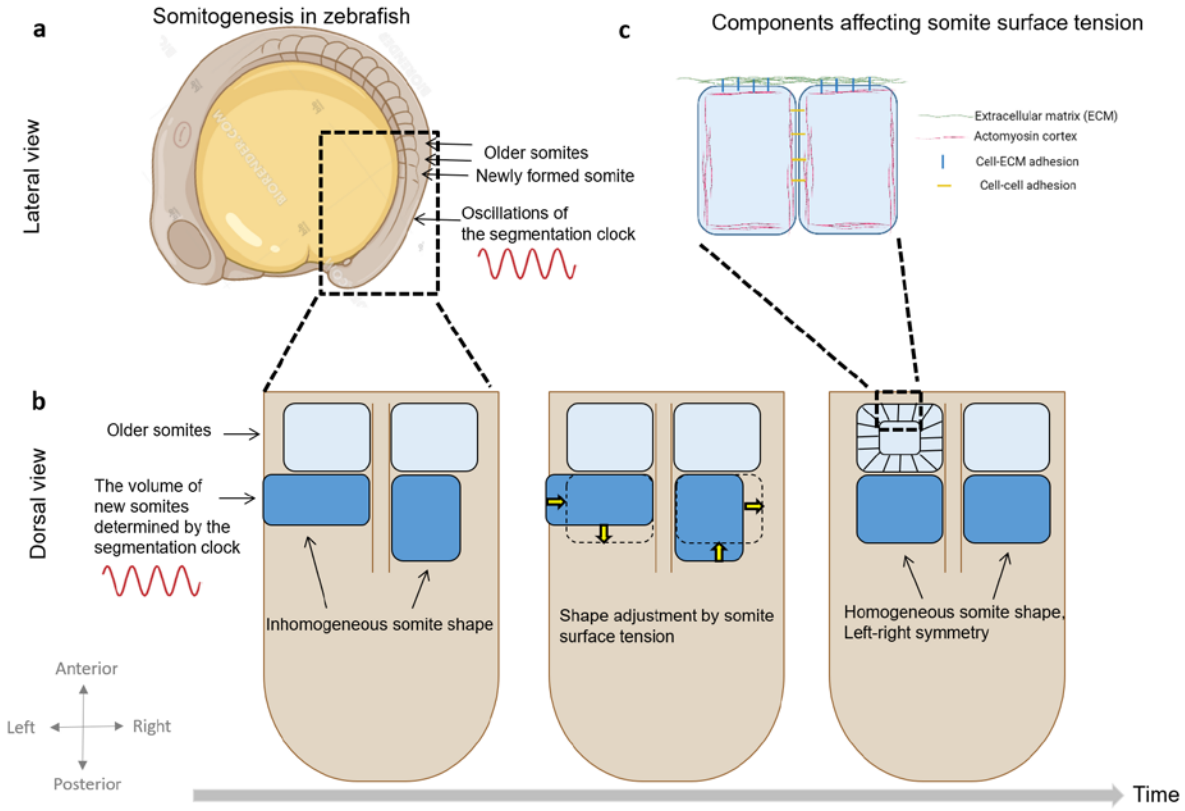

Figure 1: Adjustment of somite length by surface tension. a) During vertebrate segmentation, somites are formed periodically from anterior to posterior following the oscillations of the segmentation clock. **b)** The initially heterogeneous length of newly formed somites is adjusted to a target length by surface tension. **c)** Somite surface tension arises from the actomyosin cortex, cell-cell adhesion and cell-ECM adhesion.

References

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