BIOCHEMOMECHANICAL FRACTURE MECHANICS MODEL FOR DORSAL CLOSURE IN *DROSOPHILA* EMBRYOGENESIS

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Abstract
Dorsal closure is an essential developmental process of *Drosophila* embryogenesis, during which the ectoderm fuses the two sides of a gap into a complete ectodermal epithelium. A multiscale fracture mechanics model that involves active contractions of filopodial and lamellipodial protrusions is established to elucidate the biochemomechanically coupled mechanisms in the dorsal closure. The results agree well with relevant experiments.

1. Introduction

Morphogenesis of tissues and organs involves sophisticated biochemomechanicalprocesses of embryonic development, in which individual cells are orchestrated to attain specific forms. Mechanical forces play an essential role in the shaping of organs and embryos. Specifically, the dorsal closure in *Drosophila* embryogenesis is a representative example. During the late embryogenesis of a *Drosophila* embryo, an eye-shaped epidermal gap is left on its dorsal side, covered by an extra-embryonic amnioserosa, as shown in Fig. 1(a). Subsequently, this transient dorsal gap is closed by a cascade of active events at different spatial scales, including actin retrogradation regulated by the Rho-GTPases and local modulation in Rho activity at the subcellular scale, cell fusion at the cellular scale, and gap closure at the tissue scale [1]. The whole closure process must be precisely controlled; otherwise, any deficiency may cause scars or embryonic lethality. It remains unclear how the active forces generated at different spatial scales are coordinated in this mechanical–chemical coupling process. Therefore, a multiscale theoretical model is desired to reveal the mechanical mechanisms behind the dorsal closure.

2. Theoretical model

From the perspective of morphology evolution and stress state, dorsal closure resembles an inverse process of crack propagation in fiber-reinforced composites, as shown in Fig. 1(b). We build a multiscale crack-bridging model by treating the dorsal closure as a crack healing process, as shown in Fig. 2(a). The contribution of mechanical forces at different scales to dorsal closure is evaluated in terms of stress intensity factors. The total stress intensity factor K_{I} due to these forces can be obtained by

$$K_{\mathrm{I}} = K_{\mathrm{I}}^{\infty} + K_{\mathrm{I}}^{\mathrm{AS}} + K_{\mathrm{I}}^{\mathrm{ad}}, \tag{1}$$

where K_{I}^{∞}, $K_{\mathrm{I}}^{\mathrm{AS}}$, and $K_{\mathrm{I}}^{\mathrm{ad}}$ are the the stress intensity factors induced by the far-field tensile stress σ_{∞} of epidermal cells, the contractile amnioserosa stress σ_{AS}, and the adhesive tractions in the zipping zone σ_{ad}, respectively. A spatiotemporal cohesive law accounting for the active contraction of the filopodial and lamellipodial protrusions, σ_{ad}, in the zipping zone is established by considering the retrogradation of the F-actin bundles. Then $K_{\mathrm{I}}^{\mathrm{ad}}$ can be calculated as

$$K_{\mathrm{I}}^{\mathrm{ad}} = -2\sqrt{\frac{L}{\pi}}\int_{a}^{L}\frac{\sigma_{\mathrm{ad}}(x)}{\sqrt{L^2-x^2}}\mathrm{d}x. \tag{2}$$

We introduce the intrinsic parameter, K_{I}^{0}, to characterize the resistance of the tissue to closure. The dorsal closure progress occurs when the total contribution of all forces K_{I} overcomes the barrier K_{I}^{0}, that is, $K_{\mathrm{I}} + K_{\mathrm{I}}^{0} \le 0$. This model can be solved numerically to investigate the dynamics of dorsal closure.

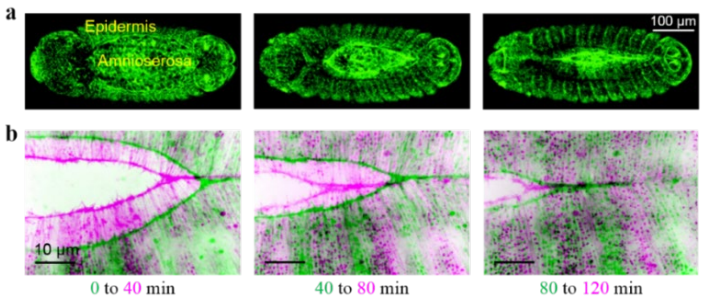

Fig. 1 – Dorsal closure in *Drosophila* embryogenesis. (a) The dorsal epidermal gap is sealed within a few hours [1]. (b) Advancing zipping fronts in discrete time windows during dorsal closure [2].

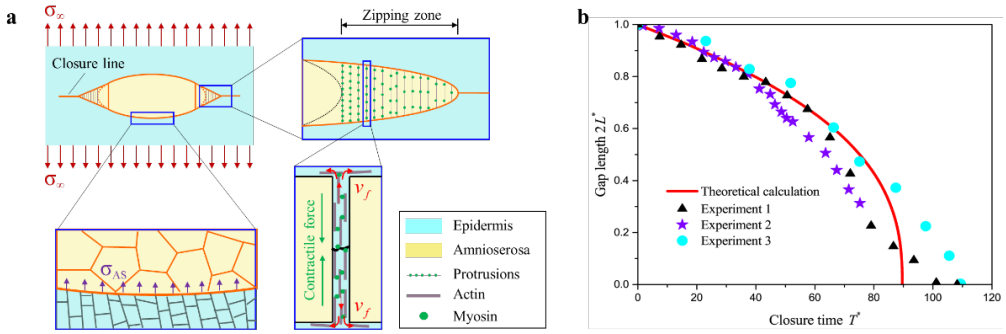

Fig. 2 – Multiscale crack-bridging model for dorsal closure and numerical results.

3. Results

The evolution of the dorsal gap length and the shape evolution of the zipping zone predicted by our model agrees well with relevant experiments [2], demonstrating that our fracture mechanics model can capture the prominent dynamic features of the dorsal closure in *Drosophila* embryogenesis (Fig. 2(b)). We demonstrate that the static tissue elasticity, dynamic protrusion retrogradation, and spatiotemporal geometry of the zipping zone play an integrated role in the accomplishment of dorsal closure. Numerical results show that the magnitude of the stress intensity factor induced by the contraction of protrusions in the zipping zone is close to a constant in the closure process, except in the very late stage.

4. Conclusions

We have establish a biochemomechanical fracture mechanics model to analyze the dorsal closure in *Drosophila* embryogenesis. The theoretical model can be generalized to explore some other biological and pathological processes of tissues and organs, e.g., the wound healing in epithelial monolayers and ventral enclosure in *C. elegans*.

Acknowledgements

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References

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