Oct 26

HKU ME scientists make breakthrough in cell and tissue mechanics

A research team led by Dr. Yuan Lin (including Mr. Fuqiang Sun, Dr. Chao Fang, and Dr. Xueying Shao) from the Department of Mechanical Engineering at the University of Hong Kong has made major breakthrough in elucidating the initiation and propagation of plastic deformation in cells and tissues, a fundamental question not well understood by scientists before. The findings have recently been published in the prestigious international academic journal *Proceedings of the National Academy of Sciences USA* (https://www.pnas.org/doi/10.1073/pnas.2305375120).

Although irreversible deformation in cells and tissues has been found to play crucial roles in collective cell migration, cancer metastasis and morphogenesis, the fundamental question of how plasticity is initiated in individual cells and then propagates within the tissue remains elusive. In collaboration with researcher from Nanyang Technological University of Singapore, Dr. Lin and his team developed a multi-scale theory (first of its kind) to show that, in response to optical or mechanical stimuli, the myosin contraction and thermal fluctuation-assisted formation and pinching of endocytic vesicles could lead to permanent shortening of cell junctions (Fig. 1). Such plastic constriction can stretch neighbouring cells and trigger their active contraction through mechanochemical feedbacks and their irreversible deformations, ultimately resulting in the propagation of plastic deformation waves (Fig. 2) within the tissue, in quantitative agreement with a variety of experiments.

By elucidating the biophysical mechanisms behind the development of cellular and tissue plasticity at different scales, the theory greatly enhances our basic understanding of how importance processes such as tissue formation and embryogenesis take place. Model predictions could also provide critical insights for the design of new strategies in regenerative medicine in the future.

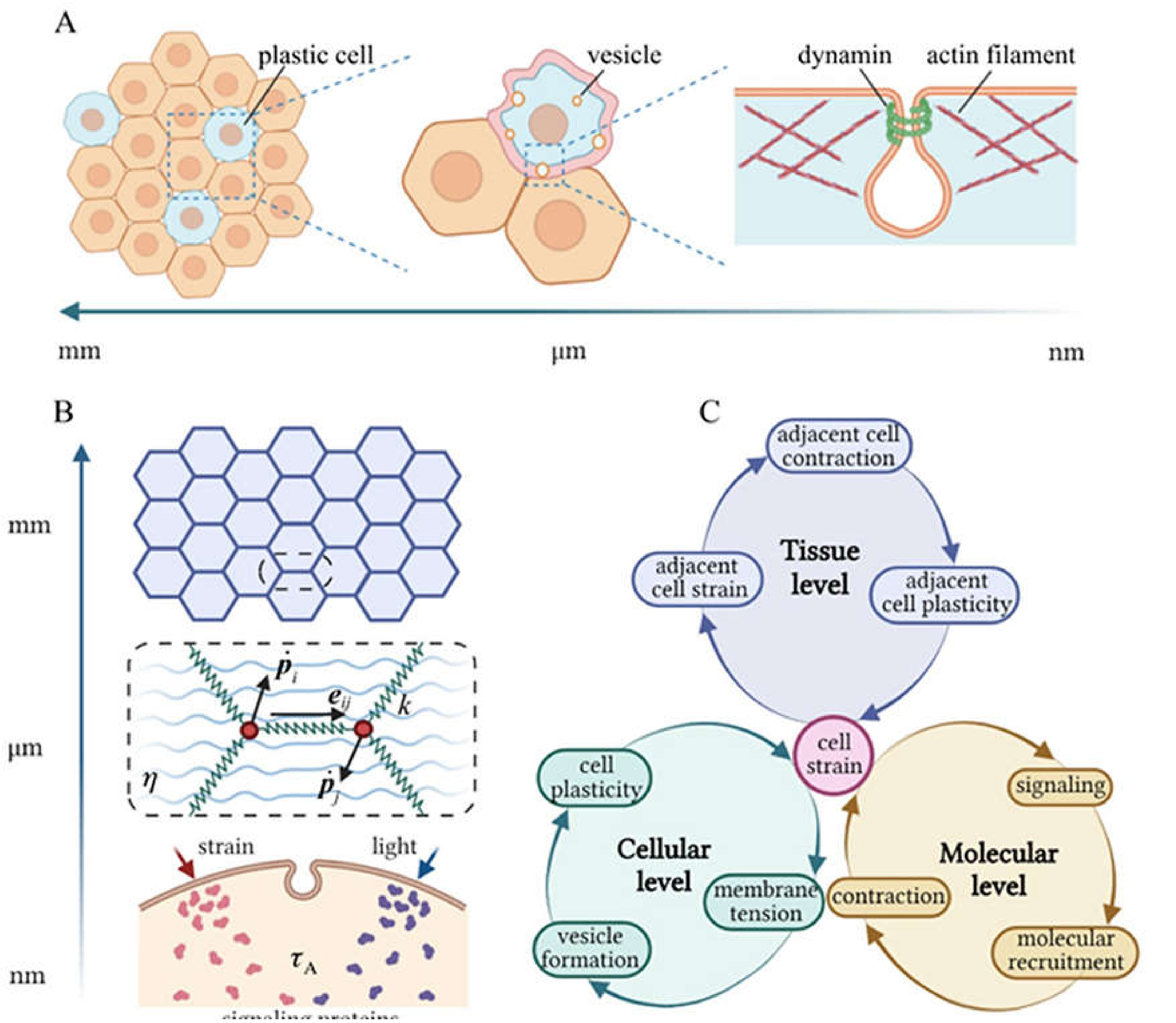

Fig. 1 Cellular plasticity across different scales. (A) Schematics showing that 1) the collective plastic response of cells leads to tissue plasticity at macroscopic scales; 2) formation and scission of membrane vesicles result in irreversible deformation of individual cells; 3) various proteins participate in the initiation and pinching of endocytic vesicles at the subcellular scale. (B) Illustration of the multiscale model where cells are treated as tightly packed hexagons at the tissue level; cell-cell junctions are modeled as springs connecting corresponding vertices at the cellular level; and the activation of signaling molecules (triggered by optical/mechanical stimuli), as well as recruitment of myosin motors to the cell junction, are considered at the subcellular scale. (C) Summary of key processes involved in the development of cellular and tissue plasticity.

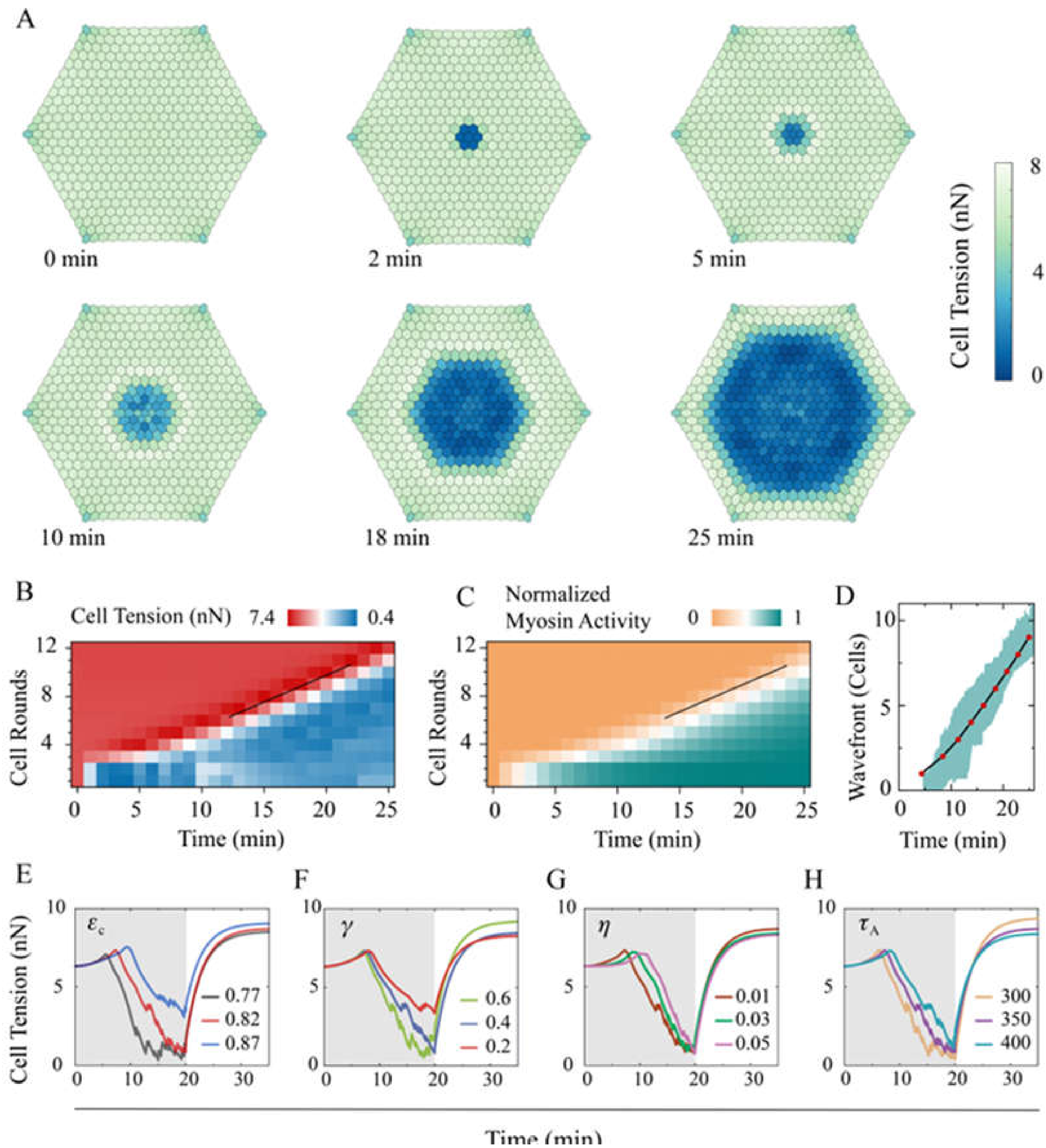

Figure 2. Propagation of a plastic contraction wave within the tissue. (A) Evolution of the average junction tension in each cell. During simulations, the central two-round of cells (i.e., 7 cells at the center) are illuminated and thus activated at . (B, C) Quantitative heatmaps of junction tension (B) and myosin activity (C) during the propagation of the plastic contraction wave shown in (A). The solid black line indicates that such a wave propagates at a speed of ~1 round of cells per 2 minutes. (D) Simulated (red points) and experimentally observed (green belts) locations of the plastic wavefront, where the normalized myosin activity starts to be higher than . (E-H) Propagation of the plastic contraction wave is affected by different physical parameters, including the critical activation strain (E), contraction amplitude (F), viscoelasticity ((G), unit:), and reaction time ((H), unit:).