

How hard can a cell push?

Growth is a fundamental phenomenon in biological systems. It happens daily around us, such as growth of grasses and babies. Microscopically, the growth occurs at the single cell level. The volume of cells is approximately doubled from the birth to the next division. In biological tissues, the growth happens in the forms of volume expansion and proliferation of cells. The growth of cells and tissues will have to push surrounding materials (Fig. 1), similar to the growth of a baby in the womb that causes the belly to bulge in pregnant women. The driving force for pushing, or the growth force, is generated by the cell and can be influenced by extracellular environment.

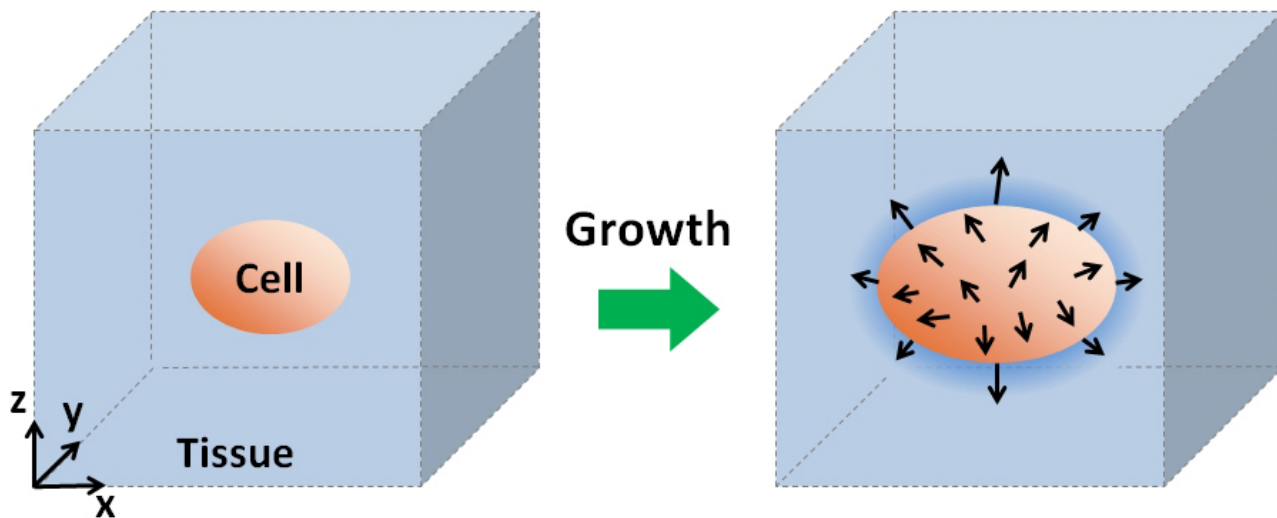


Fig. 1. Schematic of the growth force. When a cell grows in tissue, it has to push surrounding materials. The driving force for pushing is called the growth force as indicated by the black arrows.

The growth force plays important roles in embryogenesis, aging and disease progressions. It can also influence outcomes of tissue engineering, because it causes tissue deformation, changes tissue stiffness, and alter behaviors of cells (e.g., proliferation, apoptosis, differentiation, and migration) and patterns of gene expression. In tumors, the growth force may promote tumor cell invasion and metastasis, and affect tumor pathophysiology. For example, the growth force from tumor cells may compress blood vessels due to cell proliferation in adjacent regions. The compression increases vascular resistance to blood circulation, or even shuts down the circulation. The decrease in blood supply is one of the main mechanisms for hypoxia and insufficient drug and gene delivery in tumor tissues. Therefore, a reduction in the growth force can decompress blood vessels and improve various approaches to cancer treatment, including chemotherapy, immunotherapy, and radiation therapy.

To study dynamics of the growth force and understand how hard a cell can push, we developed a

microscopy technique to quantify three-dimensional distribution of the growth force, and have used it to investigate the growth force per unit surface area, i.e., the growth stress, generated by single tumor cells. Data from the study revealed that cells could exert both normal and shear stresses on surrounding materials. The normal stress increased with time, and its distribution on the cell surface was inversely correlated with surface curvature or distance to the geometric center of the cell. The range of normal stress on the same surface could vary by two orders of magnitude. Another finding in the study was that cells could sense the stiffness of surrounding materials, and alter the growth stress accordingly.

In conclusion, we developed a growth force microscopy technique that can be used to investigate spatial and temporal variations of the growth stress generated by single cells. It can also be used to investigate how the growth stress is controlled by intracellular pressure and cytoskeletal forces, or influenced by factors in cell microenvironment.

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Publication

[Elastic hydrogel as a sensor for detection of mechanical stress generated by single cells grown in three-dimensional environment.](#)

Huang J, Wang L, Xiong C, Yuan F
Biomaterials. 2016 Aug