Full governing equations for linear deformations, and the reduced forms for bending or tension dominance

Bending stiffness

Membrane tension

$$K_b'\left(\frac{\partial^4 u_3}{\partial x_1^4}\right) - N\left(\frac{\partial^2 u_3}{\partial x_1^2}\right) - p = 0$$

$$\frac{Bending}{Tension} \propto \frac{K_b'\bar{u}/\lambda^4}{N\bar{u}/\lambda^2} \propto \frac{K_b}{N\lambda^2} >> 1 \qquad \frac{K_b'}{N\lambda^2} << 1$$

$$K_b'\left(\frac{\partial^4 u_3}{\partial x_1^4}\right) = p$$

$$p = -N\left(\frac{\partial^2 u_3}{\partial x_1^2}\right) \cong N\left(\frac{1}{R}\right)$$

u = displacement p = pressure difference N = membrane tension

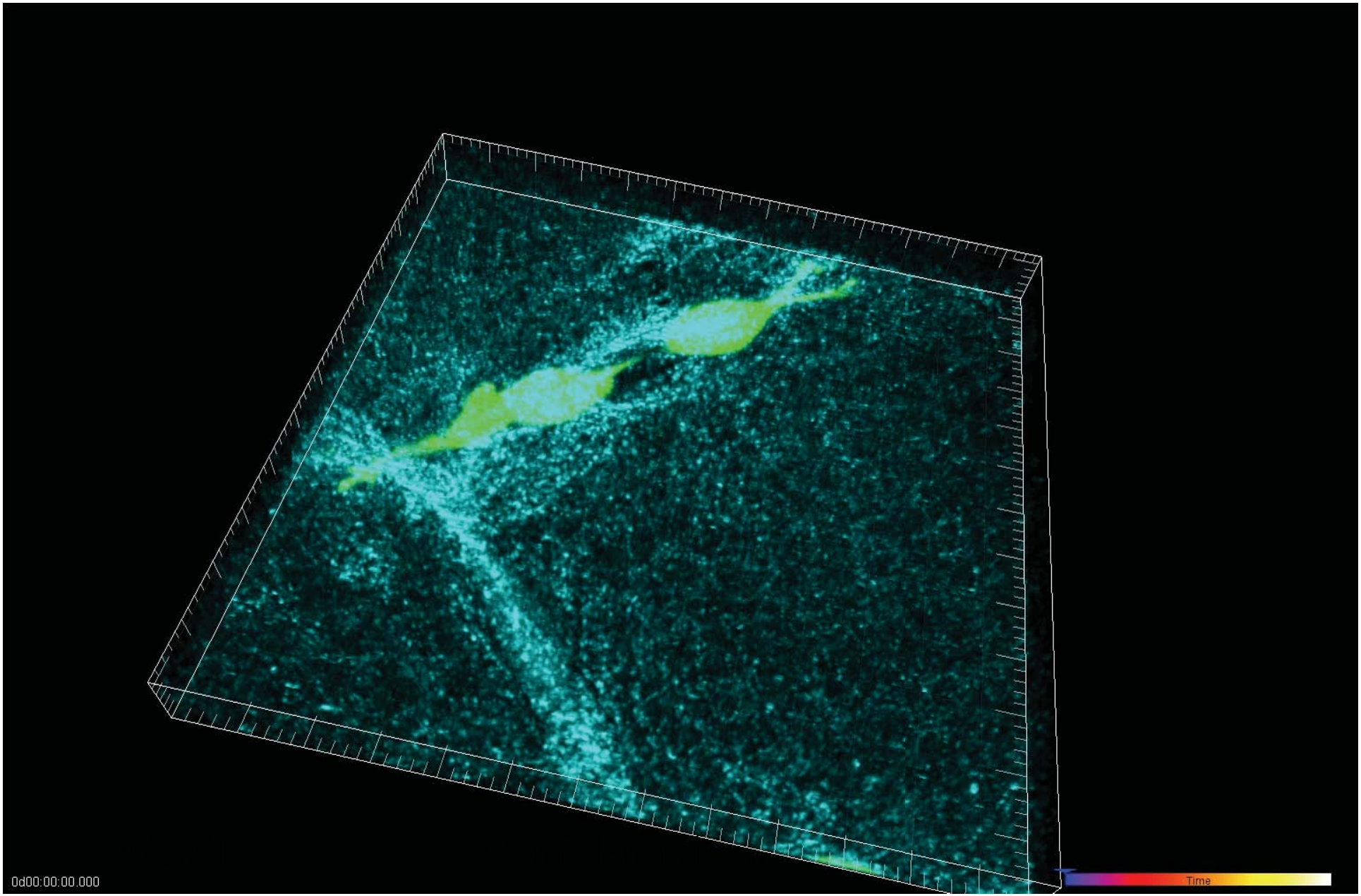
R = radius of curvature x = spatial coordinate λ = characteristic length

Cell Motility: Actin Ruffles, lamellipodia and Blebs in Motile Cells

Charras, et al., Nature, 2005.

Figures removed due to copyright restrictions.

Cell migration in 3D (Polacheck, 2012)



Vascular network formation

Figure of vascular network formation removed due to copyright restrictions.

Real-time imaging of 3D migration

Bill Polacheck

Figures removed due to copyright restrictions.

Tumor cells dispersing from a spheroid

Figures removed due to copyright restrictions.

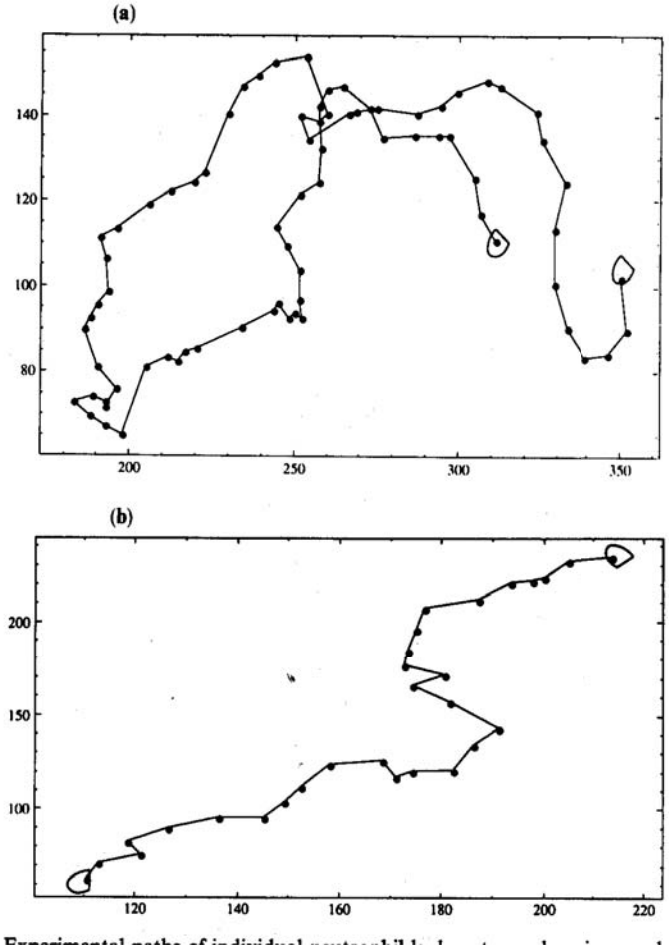
T-cell targeting of liver cancer cells

~23mins / frame

Figures removed due to copyright restrictions.

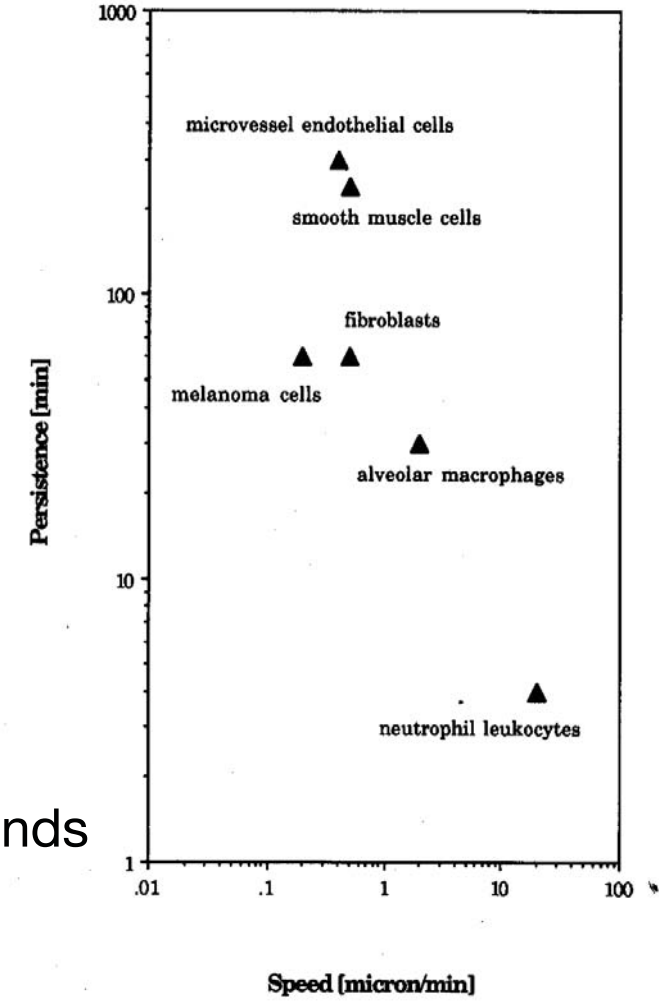
Cell Migration on 2D Substrates

Cell migration patterns. In the absence of an external signal (e.g., chemoattractant gradient), the migration pattern resembles a random walk.



a) Random, non-directed migration.

b) Migration in the presence of a chemotactic gradient



Migration speed (S) tends to vary inversely with persistence time (P). Mean-free-path ~ SP ~ const.

$$\langle d^2 \rangle \sim S^2 Pt$$

Macrophages enhance cancer cell migration

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Different types of cell migration

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Stages of metastatic cancer

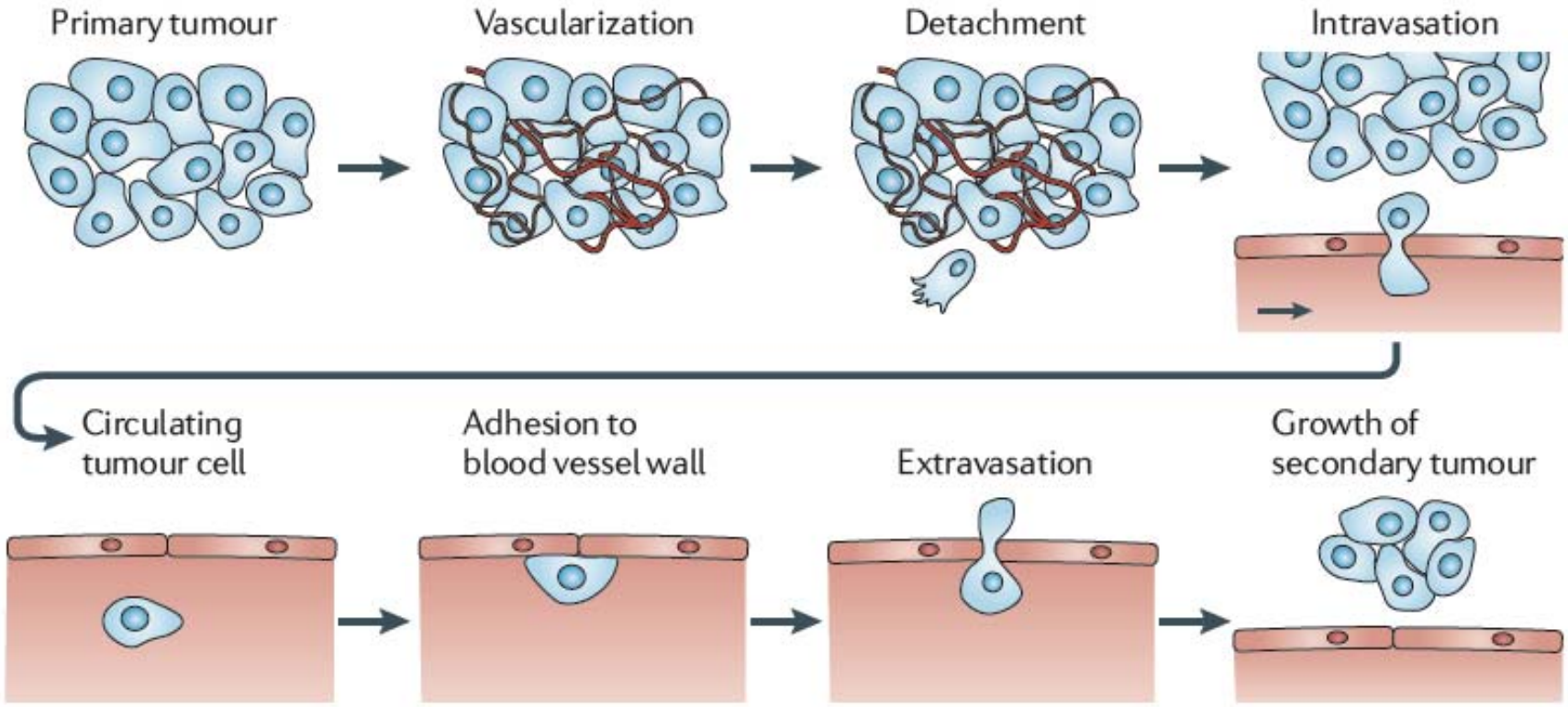


Figure 1 | **The metastatic process.** In this complex process, cells detach from a primary, vascularized tumour, penetrate the surrounding tissue, enter nearby blood vessels (intravasation) and circulate in the vascular system. Some of these cells eventually adhere to blood vessel walls and are able to extravasate and migrate into the local tissue, where they can form a secondary tumour.

Source: Wirtz, Denis, et al. "The Physics of Cancer: The Role of Physical Interactions and Mechanical Forces in Metastasis." *Nature Reviews Cancer* 11, no. 7 (2011): 512-22.

Wirtz et al., Nature Cancer Reviews, 2011

Let's get physical: mechanical forces drive a new field of study

ITHACA, NEW YORK — The cells in Cynthia Reinhart-King's lab are getting a workout. Placed in a variety of man-made environments, these human cancer cells must fight their way through obstacle courses of tangled collagen fibers. Others pull their healthy companions behind them as they slog their way through a viscous terrain.

The Reinhart-King lab here at Cornell University's Center on the Microenvironment and Metastasis hosts this grueling cellular boot camp to study how cells physically respond to environmental forces. In the past, science viewed cancer mostly from a genetics and chemistry view—genes turned off or on stimulating chemical signals and protein cascades—but the role of physics was largely ignored. Now, however, researchers are learning that mechanical forces hold the power to turn healthy tissue diseased or push cancerous cells to leave their home tissue and metastasize. This knowledge, researchers hope, should spur on a new generation of therapeutics to keep cancer cells glued in their tracks.

"Our goal is to cure cancer. I make no bones about it," says Paolo Provenzano, a biomedical

May the force be with you: Cynthia Reinhart-King and her Cornell lab.

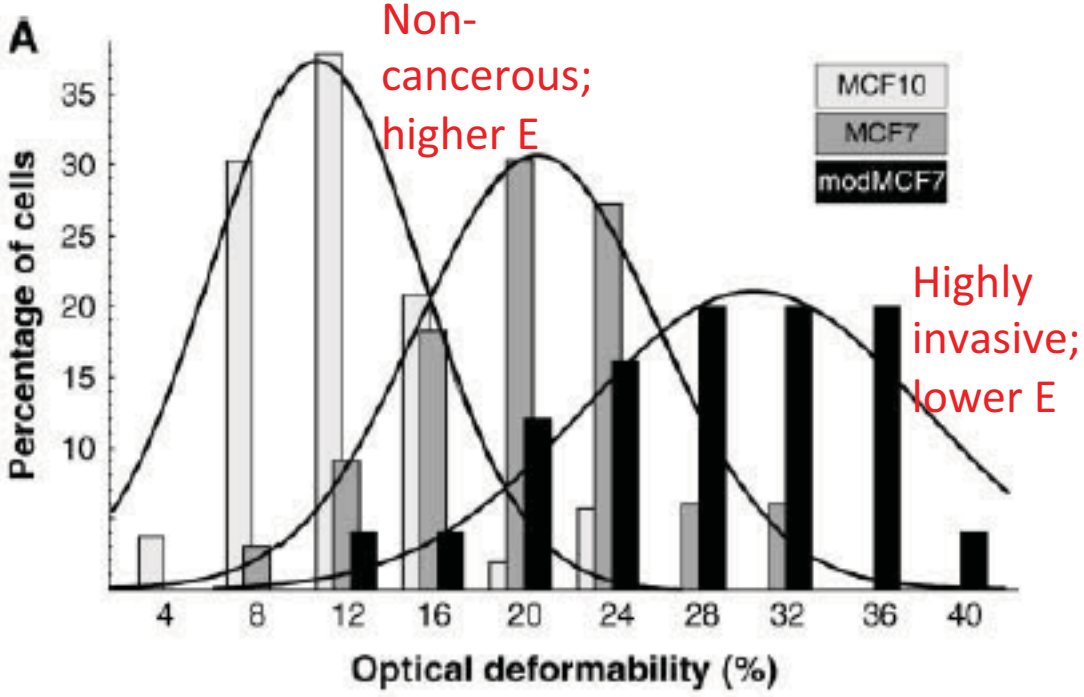
Source: Cahoon, Lauren. "Let's Get Physical: Mechanical Forces Drive a New Field of Study." *Nature Medicine* 17, no. 3 (2011): 271.

Nature Medicine, 2011

Using cell stiffness to detect malignant cells

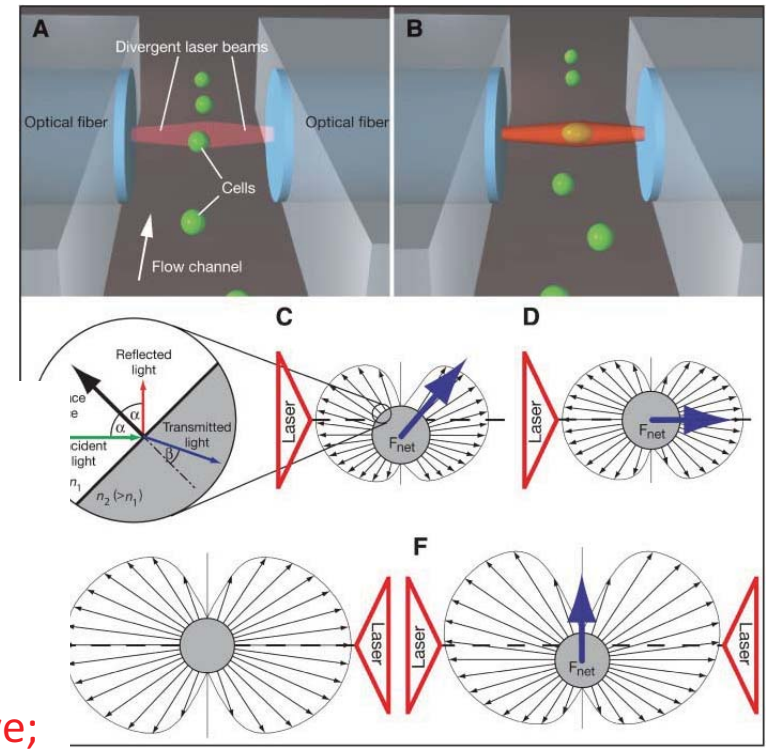
http://www.cell.com/biophysj/supplemental/S0006-3495(05)73417-2

The best-known example is the malignant transformation of cells where morphological changes caused by the cytoskeleton are in fact diagnostic for cancer. During the cell's progression from a fully mature, postmitotic state to a replicating, motile, and immortal cancerous cell, the cytoskeleton devolves from a rather ordered and rigid structure to a more irregular and compliant state. The changes include a reduction in the amount of constituent polymers and ac-



Non-cancerous; higher E

Highly invasive; lower E



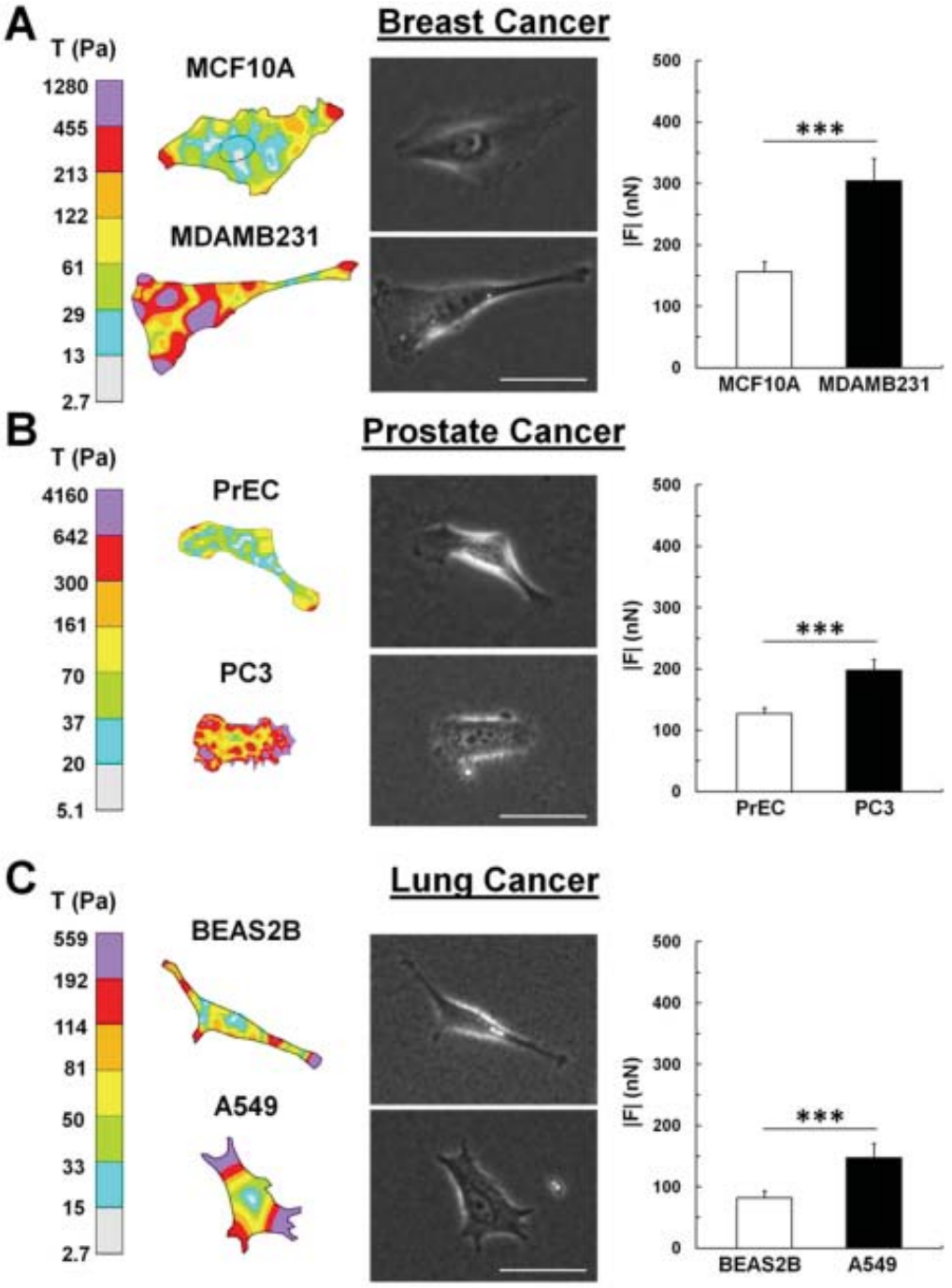
MCF10: nontumorigenic
MCF7: adenocarcinoma (breast)
modMCF7: TPA-treated; more invasive tumor cells

Source: Guck, Jochen, et al. "Optical Deformability as an Inherent Cell Marker for Testing Malignant Transformation and Metastatic Competence." *Biophysical Journal* 88, no. 5 (2005): 3689-98.

Cancerous cells exert stronger forces on a substrate than their non-cancerous counterparts

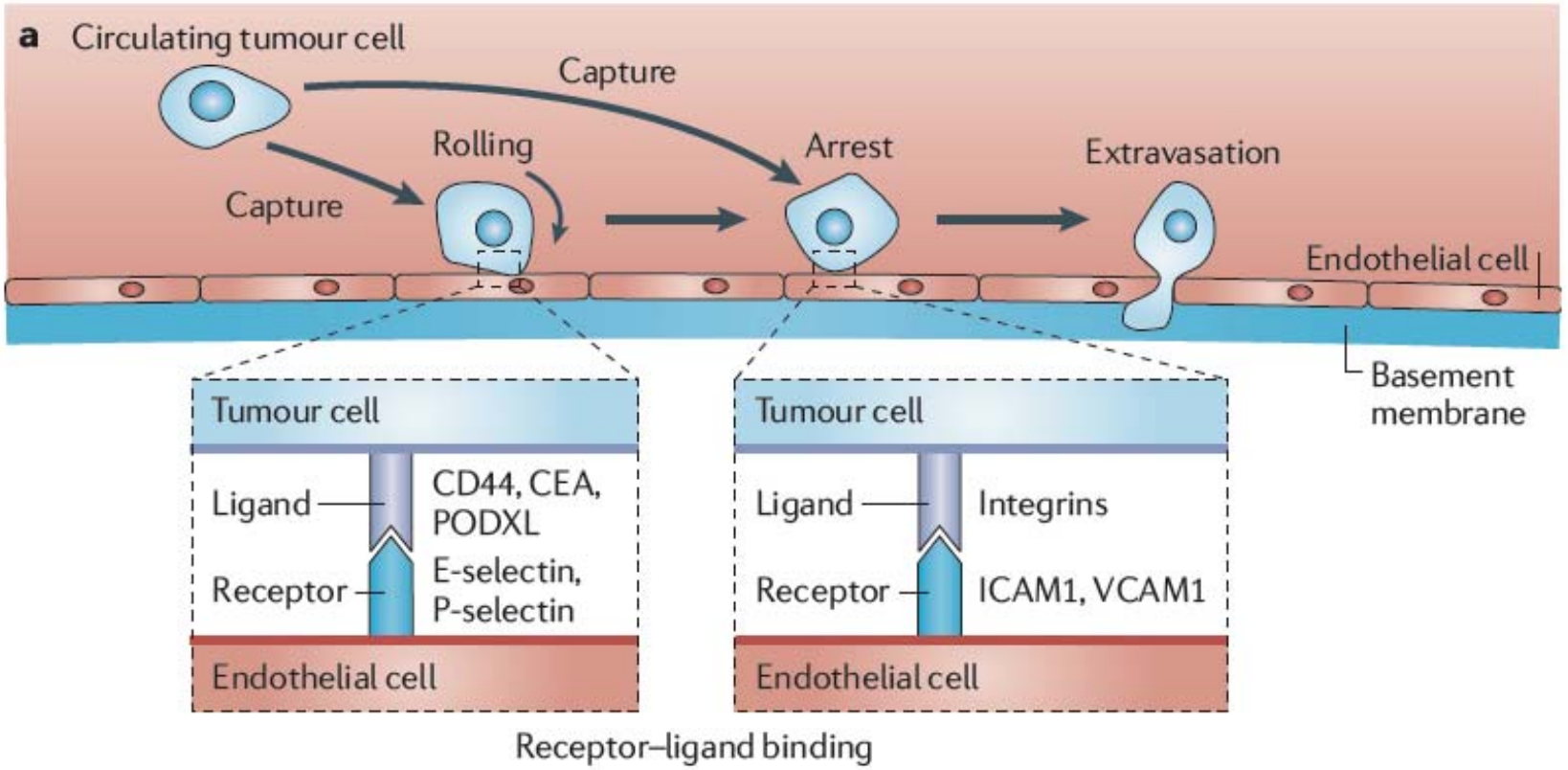
$$|F| = \iint \left(T_x^2(x,y) + T_y^2(x,y) \right)^{1/2} dxdy$$

Kraning-Rush, PLoS ONE, 2012



Source: Kraning-Rush, Casey M., et al. "Cellular Traction Stresses Increase with Increasing Metastatic Potential." *PloS ONE* 7, no. 2 (2012): e32572.

Extravasation



Source: Wirtz, Denis, et al. "The Physics of Cancer: The Role of Physical Interactions and Mechanical Forces in Metastasis." *Nature Reviews Cancer* 11, no. 7 (2011): 512-22.

Wirtz et al., Nature Cancer Reviews, 2011

In vitro model of extravasation

Figures removed due to copyright restrictions.

Tumor cells extravasating

Figures removed due to copyright restrictions.

Tumor cell extravasation

Figure removed due to copyright restrictions.
Source: Chen, Michelle B., et al. "Mechanisms of Tumor Cell Extravasation in an In Vitro Microvascular Network Platform." *Integrative Biology* 5, no. 10 (2013): 1262-71.

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Source: Chen, Michelle B., et al. "Mechanisms of Tumor Cell Extravasation in an In Vitro Microvascular Network Platform." *Integrative Biology* 5, no. 10 (2013): 1262-71.

20.310J / 3.053J / 6.024J / 2.797J Molecular, Cellular, and Tissue Biomechanics
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