Macroscopic forces generated by cell-matrix interactions

I. Cells generate forces after becoming attached to a matrix.

II. How do cells attach to a matrix?

III. Cell-matrix interactions control the spontaneous closure of wounds in organs.

IV. What happens when wound closure occurs by induced regeneration?

I. Cells generate forces after becoming attached to a matrix.

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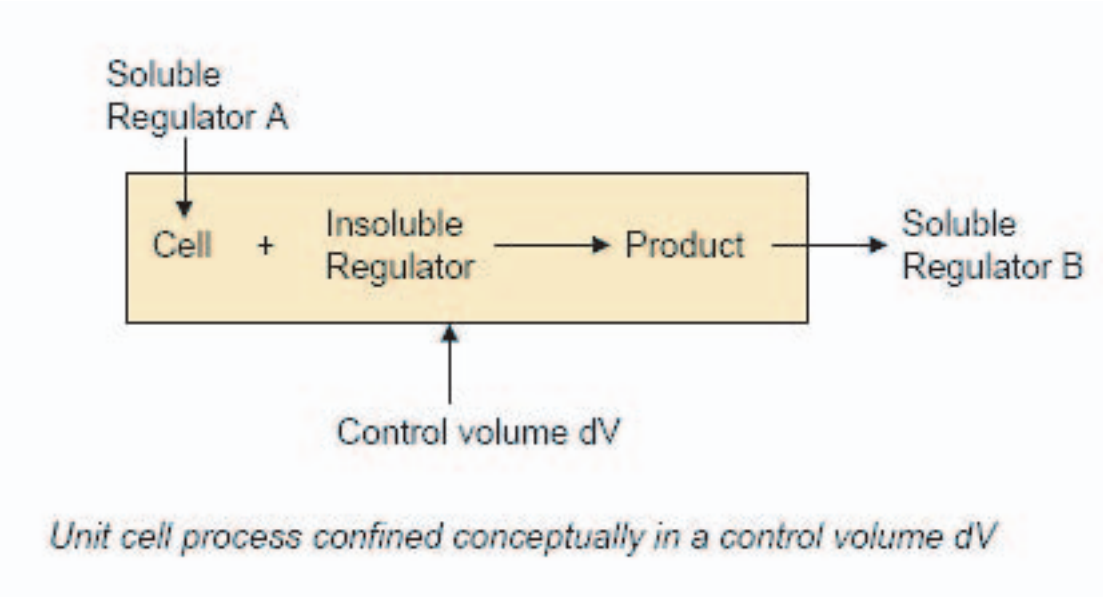
- **Cells develop contractile forces individually, not cooperatively.**
- **Cell elongation, not contraction, occurs first, and eventually leads to matrix deformation.**
- **Contractile forces are force-limited, not displacement-limited.**

A brief review or relevant structures: cell membrane, transmembrane proteins, cell receptors (integrins), cytoplasm, matrix

Definition of unit cell process



Unit cell process confined conceptually in a control volume dV

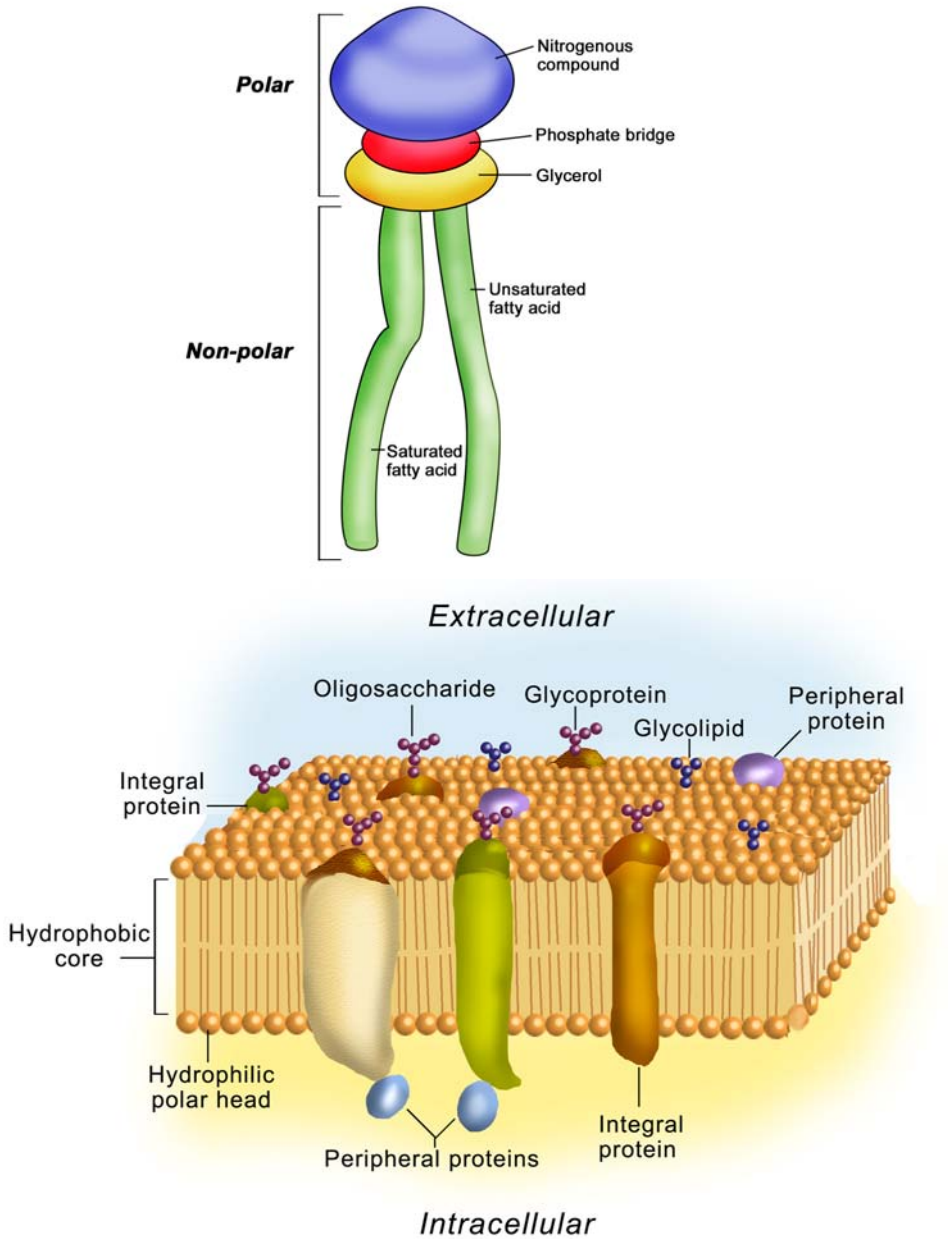
Figure by MIT OCW.

A typified cell diagram showing cell-cell binding

Figure removed for copyright reasons.

From Burkitt et al.

Cell membrane sketch showing transmem-brane proteins



Figures by MIT OCW. After Burkitt et al. (upper) and Darnell (lower).

Specific cell-matrix interaction through integrins

cell membrane

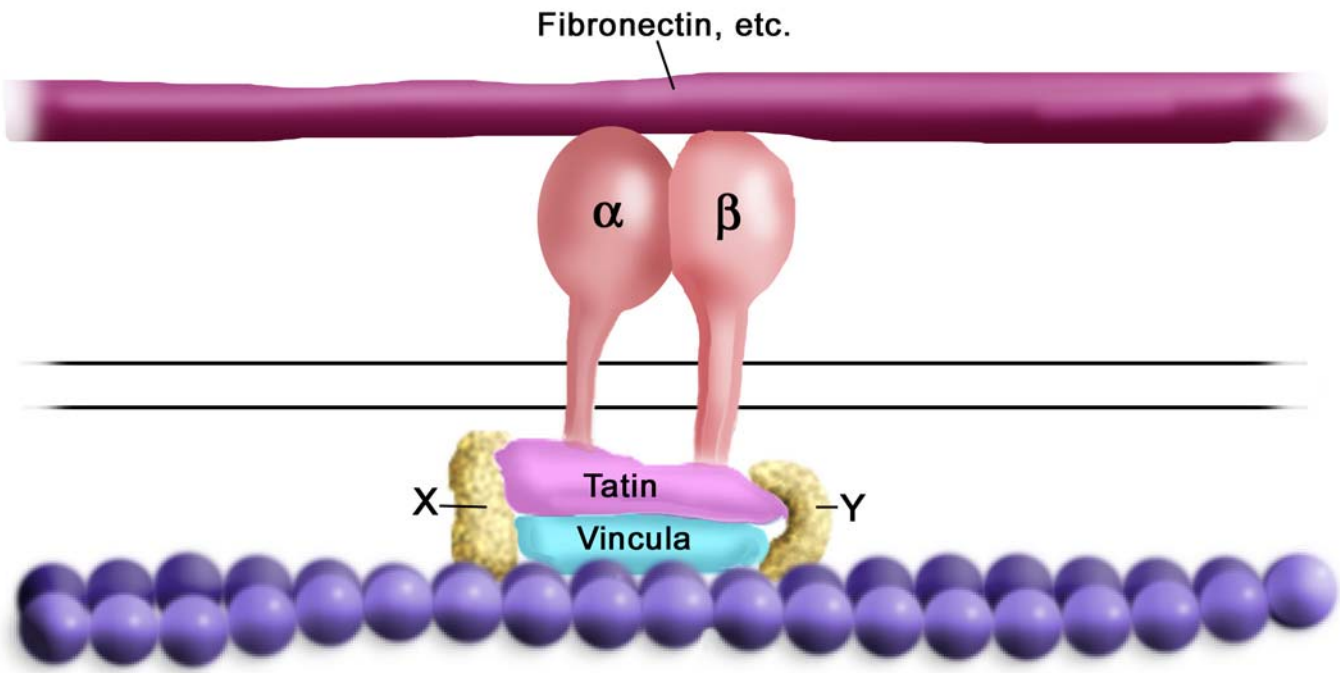


Figure by MIT OCW. After Hynes, 1990

A biologically active ECM analog

Photo removed for copyright reasons.

From Yannas, 2004

FIRST ARTICLE

See Freyman, T.M., I.V. Yannas, R. Yokoo, and L.J. Gibson. "Fibroblast contraction of a collagen-GAG matrix.“ *Biomaterials* 22 (2001) 2883-2891.

- **Represent force-time data by a single residual exponential:**

$$F(t) = F_{\infty}[1-\exp(t/\tau)]$$

- **Asymptotic data (and all isochronous data) represented by linear relation:**

$$F(t) = dk = df_c$$

d = cell density, no./cm^3

f_c = force per cell

Conclusions on Linearity vs. Cooperativity of Fibroblast Contraction of Matrix

- **The contractile force increases linearly with cell density.**
- **The average contractile force is calculated at 1 nN per cell.**
- **The kinetics for development of force are also independent of cell density.**
- **In this model cells must develop contractile forces individually, not cooperatively.**

SECOND ARTICLE

See Freyman, T.M., I.V. Yannas, Y-S. Pek, R. Yokoo, and L.J. Gibson. "Micromechanics of Fibroblast Contraction of a Collagen-GAG Matrix.“ *Experimental Cell Research* 269 (2001) 140-153.

Conclusions on Micromechanics of Fibroblast Contraction

- **The aspect ratio of cells increases with time and eventually saturates, just as the force does.**
- **Initiation of cell elongation occurs stochastically.**
- **The force plateau most simply results from buckling or bending of individual struts in the matrix by cells.**
- **Matrix deformation (contraction) occurs following cell elongation, not following cell contraction.**

THIRD ARTICLE

See Freyman, T.M., I.V. Yannas, R. Yokoo, and L.J. Gibson.
"Fibroblast Contractile Force Is Independent of the Stiffness Which Resists the Contraction.“
Experimental Cell Research 272 (2002) 153-162.

Conclusions on the Effect of Matrix Stiffness on Cell Contraction

- **The contractile force generated by fibroblasts was independent of matrix stiffness in the range 0.7 – 10.7 N/m.**
- **Contractile forces generated by cells are force-limited, not displacement-limited.**
- **As cells elongate, cell-matrix adhesion sites hypothetically form at the cell periphery, increasing length of matrix strut under compressive load and decreasing load required to buckle the strut.**