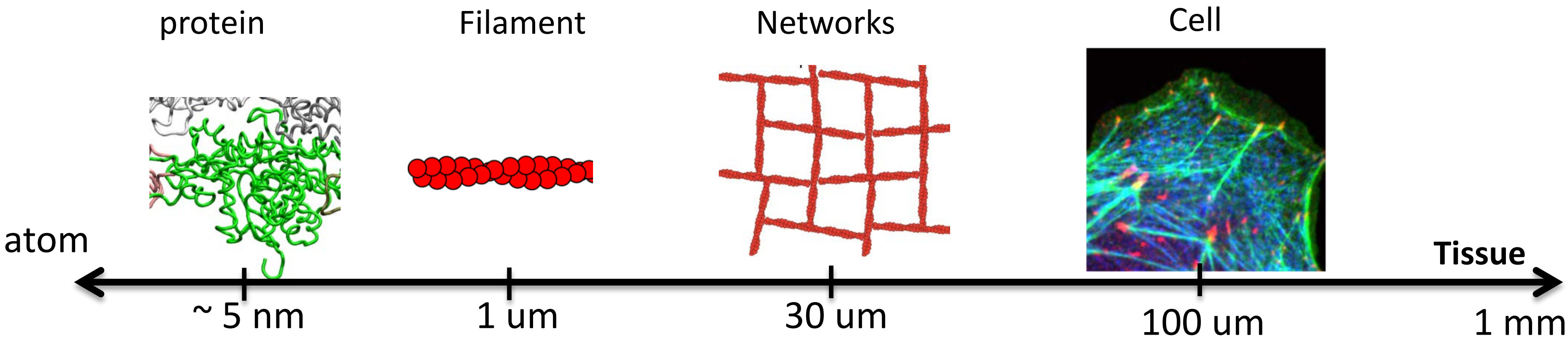
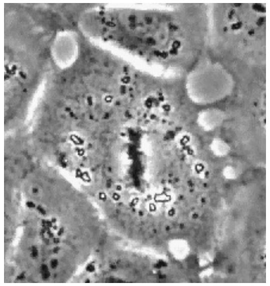
Proteins Self-Organize into Living Materials

Margaret Gardel (Univ. of Chicago)

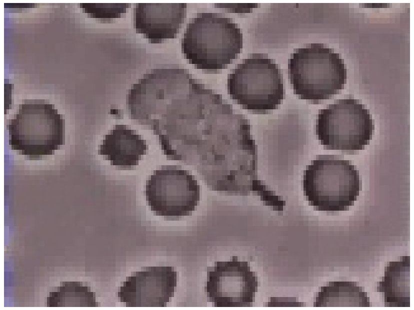


Division



Y.L. Wang

Migration

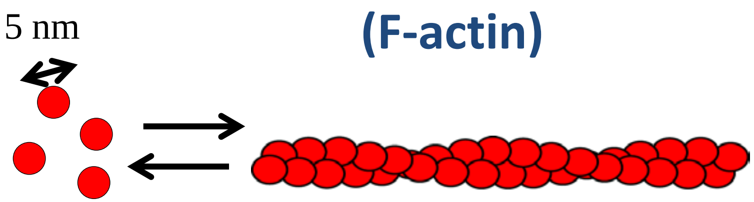


Rogers

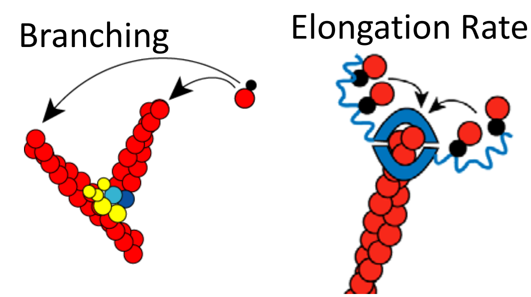
The Cytoskeletal Tool Box

A soft material….. ***…driven far from thermal equilibrium***

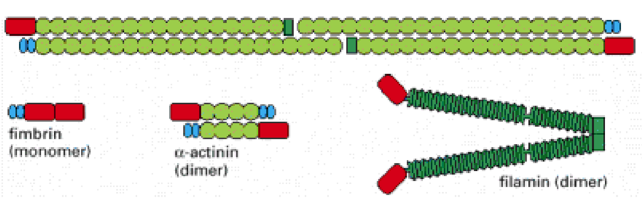
Semi-flexible Polymers (F-actin)



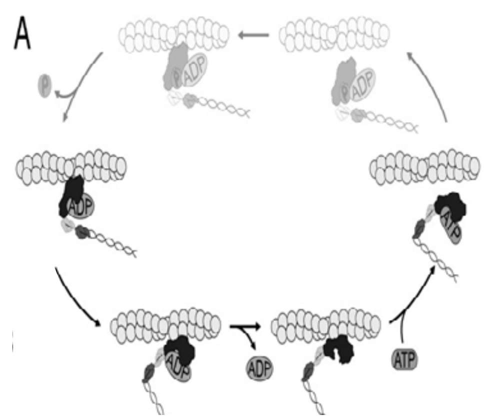
Polymer Assembly

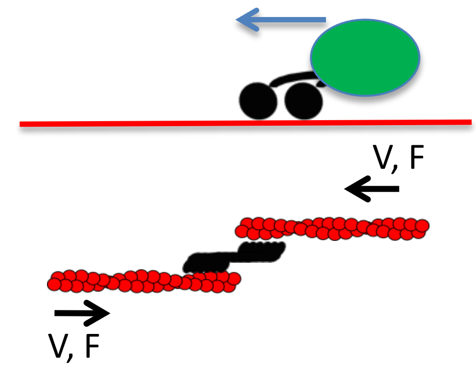


Cross-linkers



Molecular Motors (e.g. myosin)





Mesoscale Priority Research Direction

Self-Organization of Treadmilling Polymer Networks

Opportunity

Living cells utilize treadmilling semi-flexible polymer (e.g. actin and microtubules) arrays as means to generate and response to mechanical stress, drive extreme morphological changes, and drive movement. By learning design principles of such materials, we can design artificial cells as a next generation soft "MEMS" devices.

Approach

Biochemical factors controlling polymer nucleation, elongation and disassembly are well established.

Integration of biochemical and materials science /soft condensed matter approaches is necessary. Light microscopy can be used to measure structures. Tools to measure mechanics at "meso-scales" are necessary (Two-point microrheology?)

Meso Challenge

The challenge is to understand the parameters controlling self-organization of polymers and associated proteins into materials with targeted mechanical behavior and structure. System is far from equilibrium but can be in a dynamic steady state.

Impact

Treadmilling polymer arrays reflect a versatile general class of polymer networks that can utilize chemical energy to do mechanical work. This energy is also utilized to make a material that is robust to external stresses, generates force , is "self-healing" and can drive movement.

References:

D.A. Fletcher and R.D. Mullins, "Cell mechanics and the cytoskeleton", Nature, vol. 463, 485-492, 28 January, 2010.

D.A. Fletcher and P.L. Geissler, "Active biological materials", Annual Review of Physical Chemistry, vol. 60, 469-486, 2009.

Contact: Margaret Gardel (U. Chicago)

Mesoscale Priority Research Direction

Self-Organization of Contractile Matter

Opportunity

Muscles and other contractile tissue in our bodies are formed by the emergent properties of networks of semi-flexible polymers in which stress-generating molecular motors are contained. Understanding design principles of contractile matter will inspire next generation of soft MEMS

Approach

Reconstitution of phenomena using purified protein constituents and study of their biophysical properties is possible. Methods to control self-assembly of protein-based materials still need further refinement.
Challenges are to build artificial motor proteins and semi-flexible polymers that are more stable and resilient to temperature changes.

Meso Challenge

The challenge is to understand what controls the emergent physical behaviors of polymer networks containing stress-generating elements.

Impact

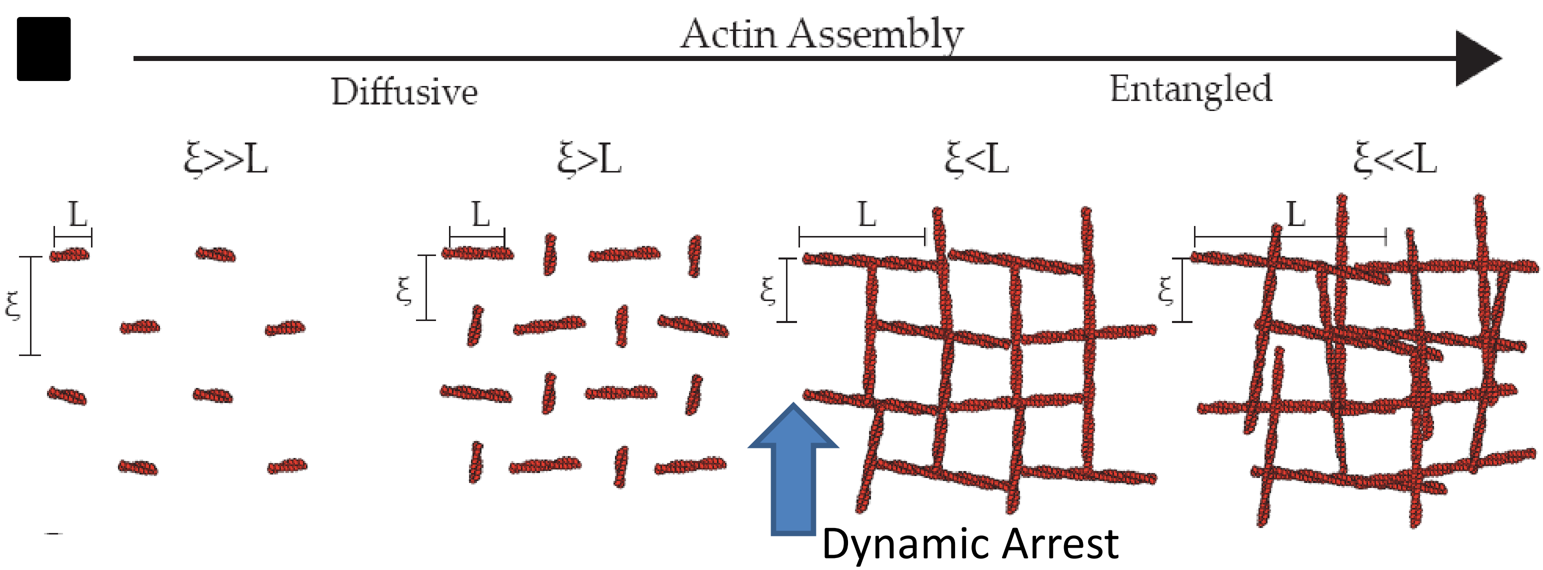
Contractile matter is widely used by living cells to generate stresses and change shape. Understanding the design principles of such living matter will enable new material design.

References:
"Contractile Units in disordered actomyosin bundles arise from F-actin buckling", Martin Lenz, Todd Thoresen, Margaret Gardel, Aaron Dinner, *Physical Review Letters,* to appear
Reconstitution of Contractile Actomyosin Bundles. Thoresen T, Lenz M, Gardel ML, *Biophysical Journal,* **(100)11**:2698-705 (2011)
G.H. Koenderink, Z. Dogic, F. Nakamura, P.M. Bendix, F.C. MacKintosh, J.H. Hartwig, T.P. Stossel and D.A. Weitz, An active biopolymer network controlled by molecular motors, PNAS **106**, 15192–15197 (2009).

Contact: Margaret Gardel (U. chicago)

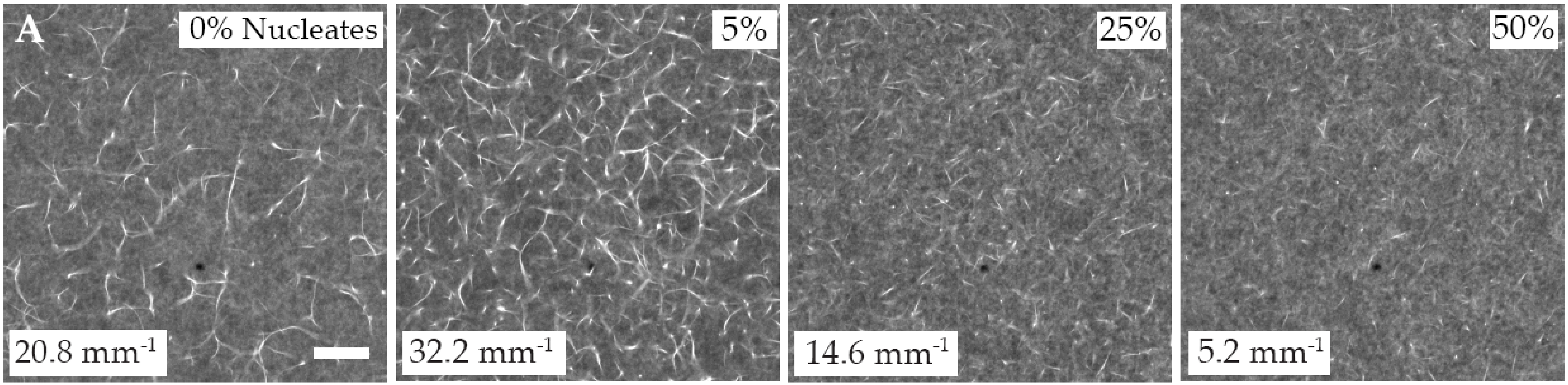
Dynamic Arrest is Controlled by Rates of Nucleation, Elongation and Aggregation

Assembly of Actin network with α-actinin crosslinks
2000 s movie



Morphology of chemically identically samples is modified by changing assembly kinetics

5 μM G-actin
1 μM α-actinin

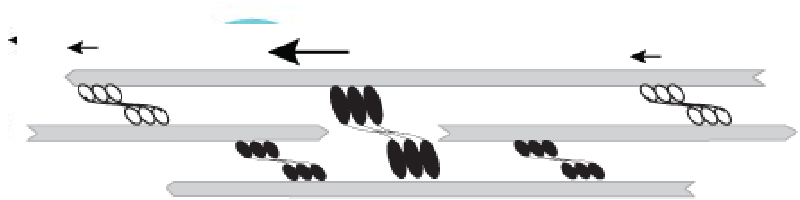


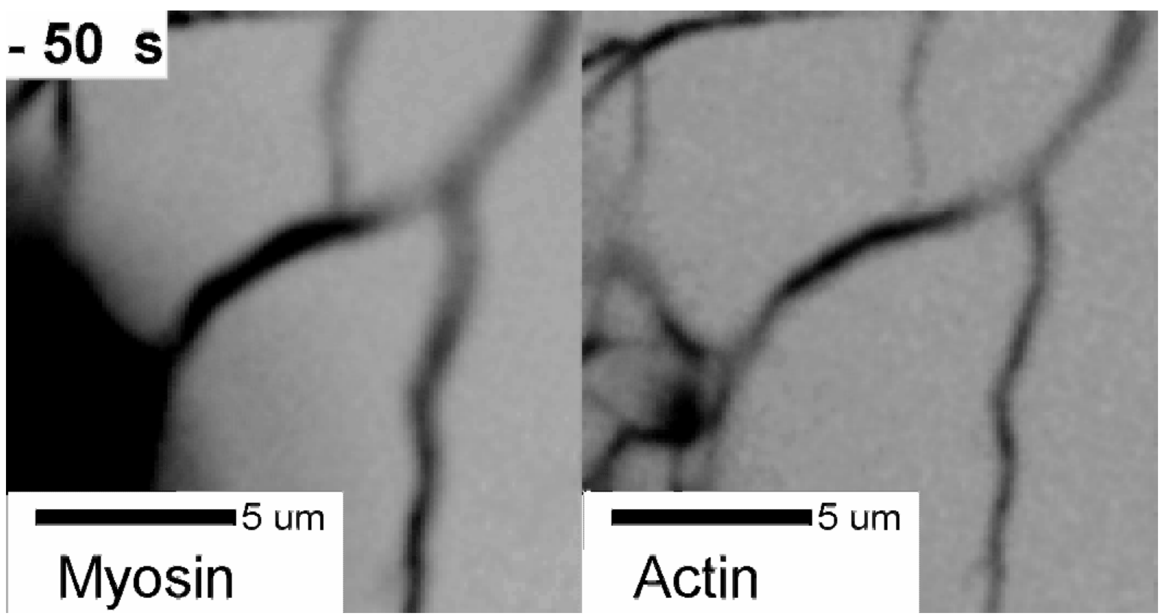
Fraction of G-actin added as F-actin nucleates

T.T. Falzone, M. Lenz, D.R. Kovar and M.L. Gardel, Nature Communications, *to appear*

Contractile Bundles Controlled by Nonlinear Response of F-actin to Stress

1) Distribution of motor speeds to generate stresses
2) Symmetry breaking mechanism to favor tensile stress
→ *Nonlinear Response (*e.g. F-actin buckling)





"Requirements for disordered actomyosin bundle contractility", Martin Lenz, Margaret Gardel, Aaron Dinner, New J. of Physics, 2012
"Contractile Units in disordered actomyosin bundles arise from F-actin buckling", Martin Lenz, Todd Thoresen, Margaret Gardel, Aaron Dinner, *Physical Review Letters,* to appear