Multiscale mechanics of engineered tissues

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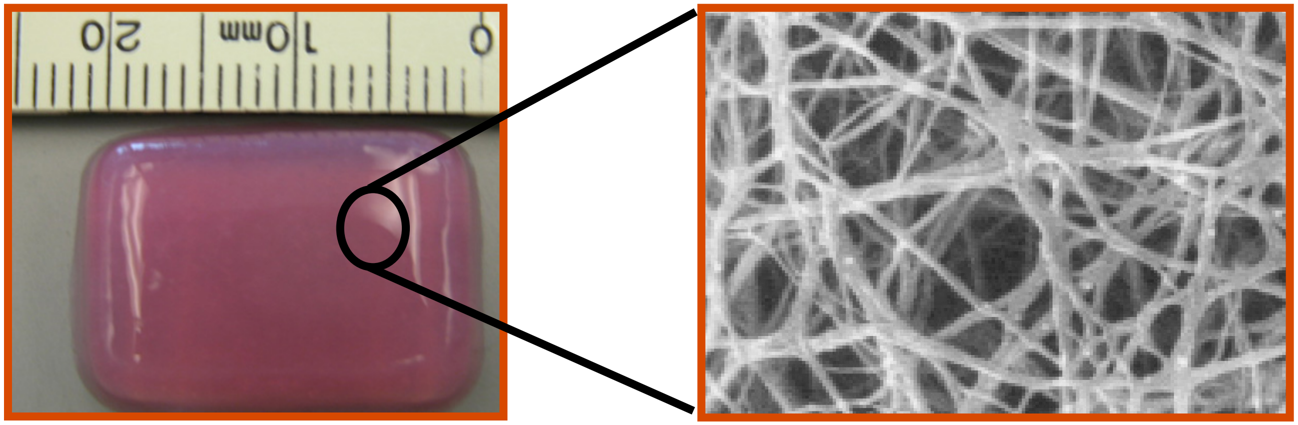
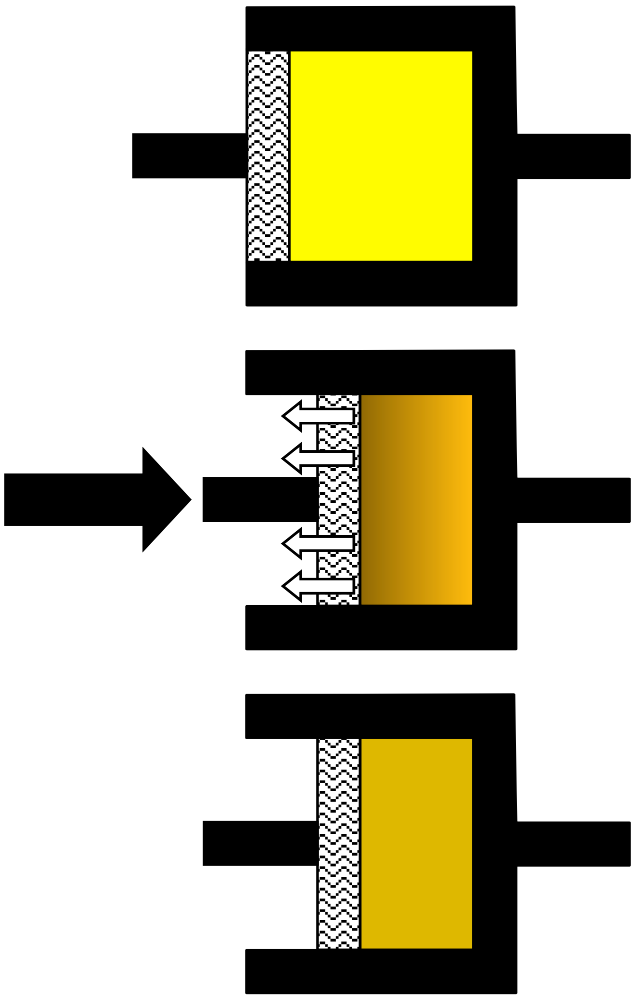
Collagen Gel



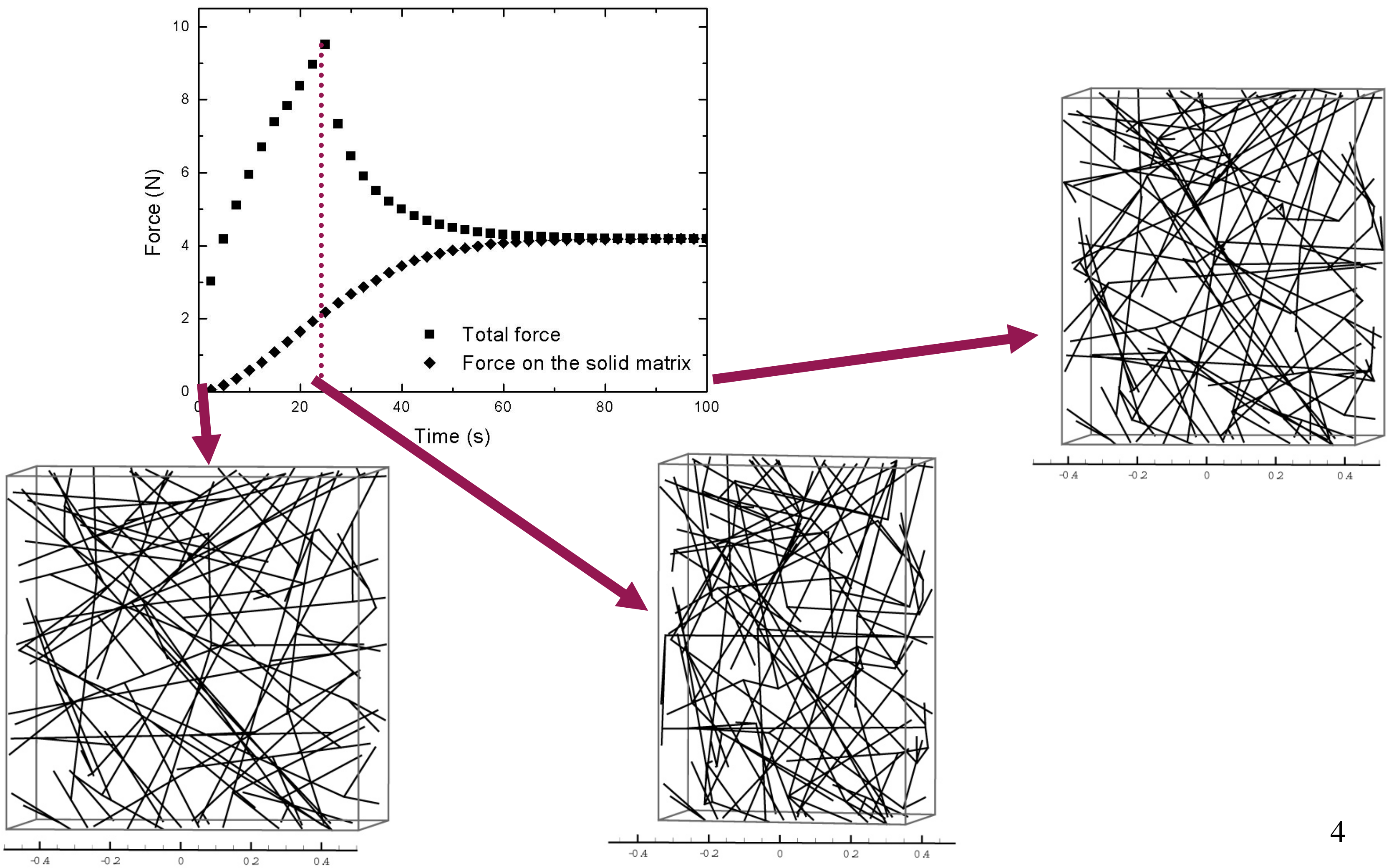
- Reconstituted from type I collagen solution, typically 1-3 mg/ml.
- Continuous on the functional scale, but really a discrete fiber network.
- Interstitial flow can be important.

Interstitial Flow



- Water can flow through the fiber matrix, but there is a resistance to that flow
- In confined compression, the fluid phase can support some of the load.
- The characterizing parameter is the permeability, or the ratio of the superficial velocity to the macro-scale pressure gradient.

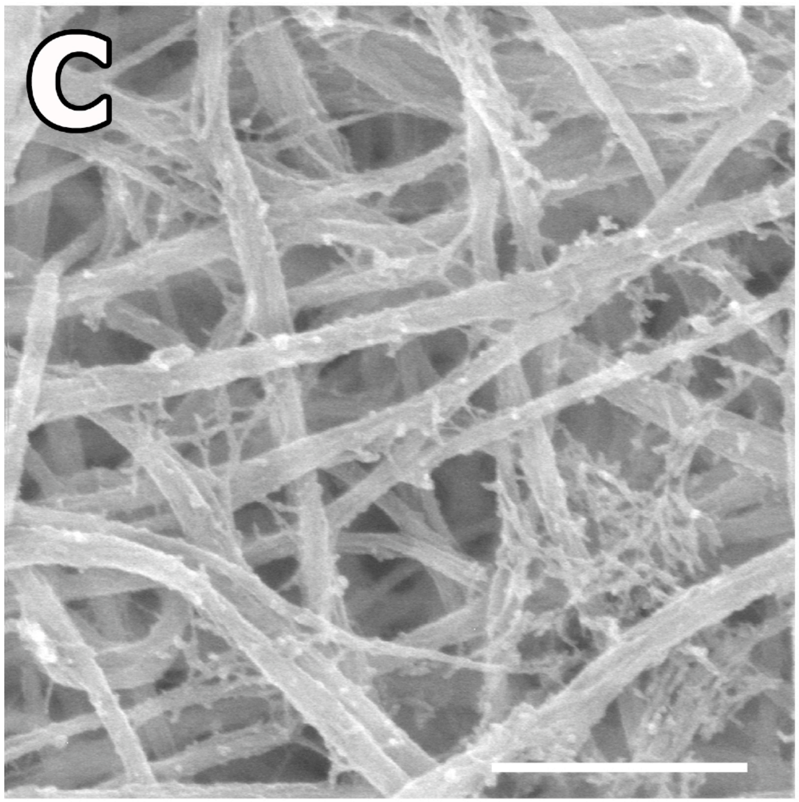
Interstitial Flow

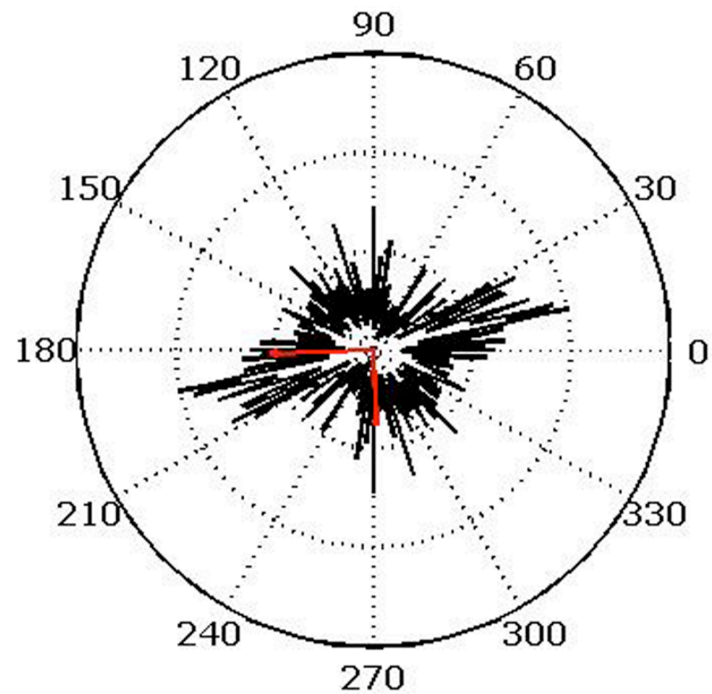


The Challenge

- The network clearly is not regularly structured.
- It is also often anisotropic (but not perfectly aligned).
- We know that the permeability of a network depends on the orientation of the fibers.
- Can we estimate the permeability of a fiber network from experimental or theoretical measures of orientation?

Converting Images to Distributions

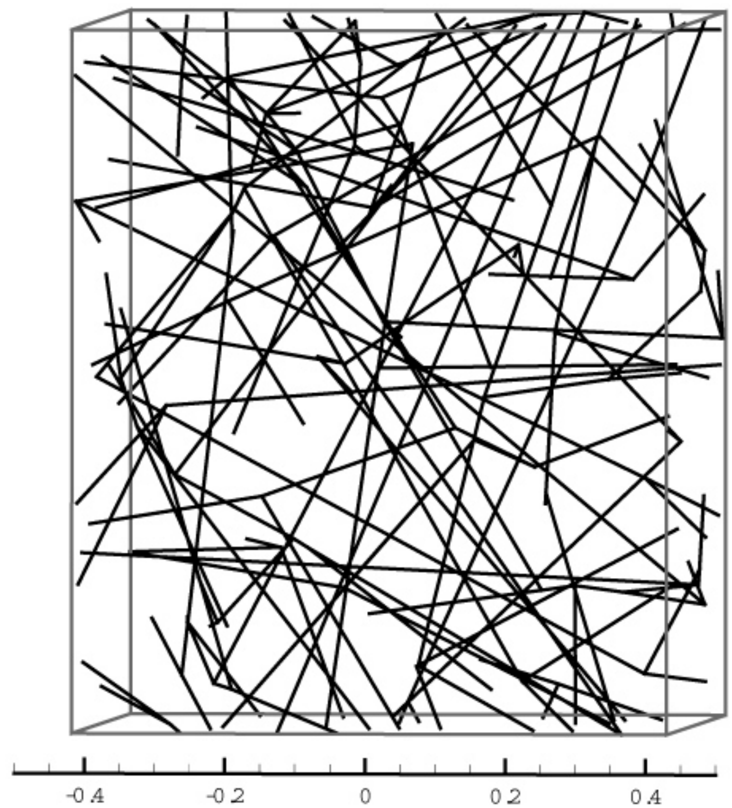




$\alpha = 0.27$

Distributions from Model

- Obviously, if we have a computer model of the network, we know where every fiber is and can get a distribution.



Distribution to Permeability

- The problem, then, is to estimate the permeability from the fiber alignment distribution (and diameters).
- Several studies of structured or isotropic networks.

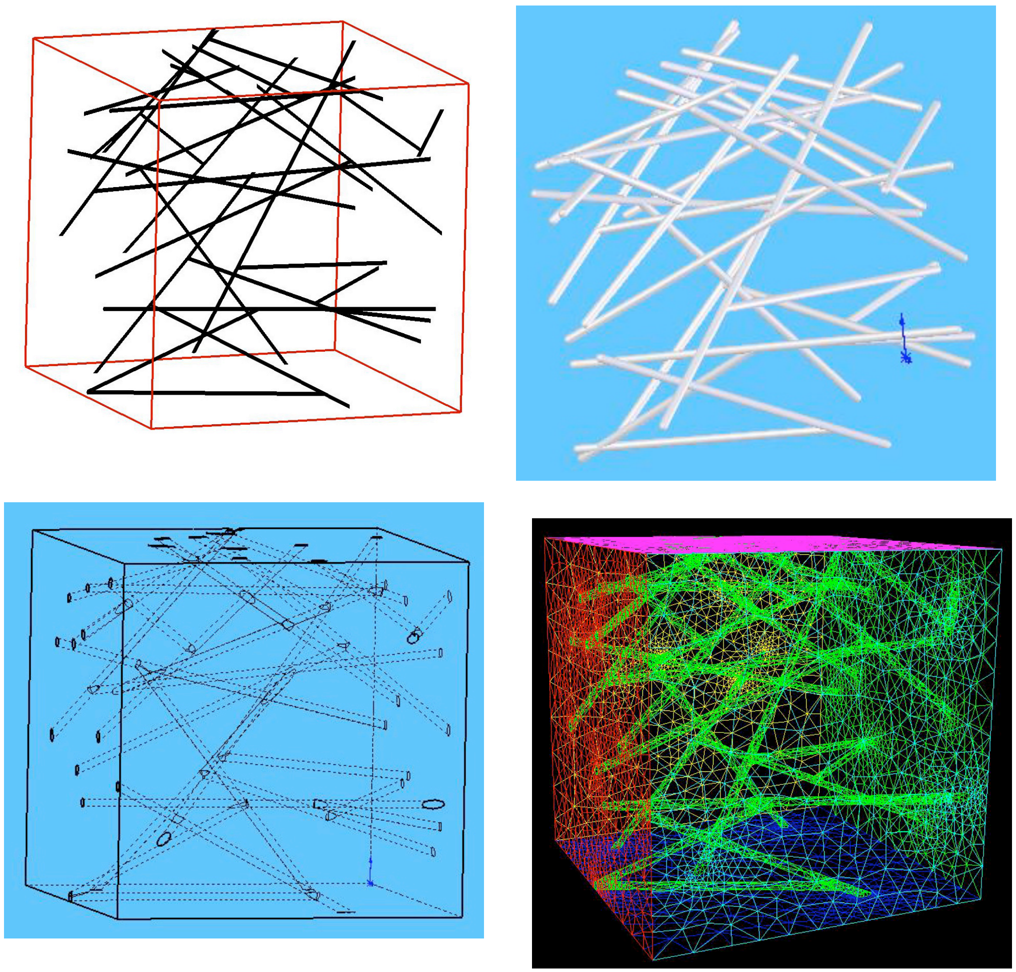
Some Important History

- Cox (1970) - drag on an isolated cylinder
- Sangani and Acrivos (1982) - flow transverse to a periodic array of cylinders
- Drummond and Tahir (1984) - parallel flow

- Higdon and Ford (1996) - cubic arrays
- Palassini and Remuzzi (1998) - tetrahedral array

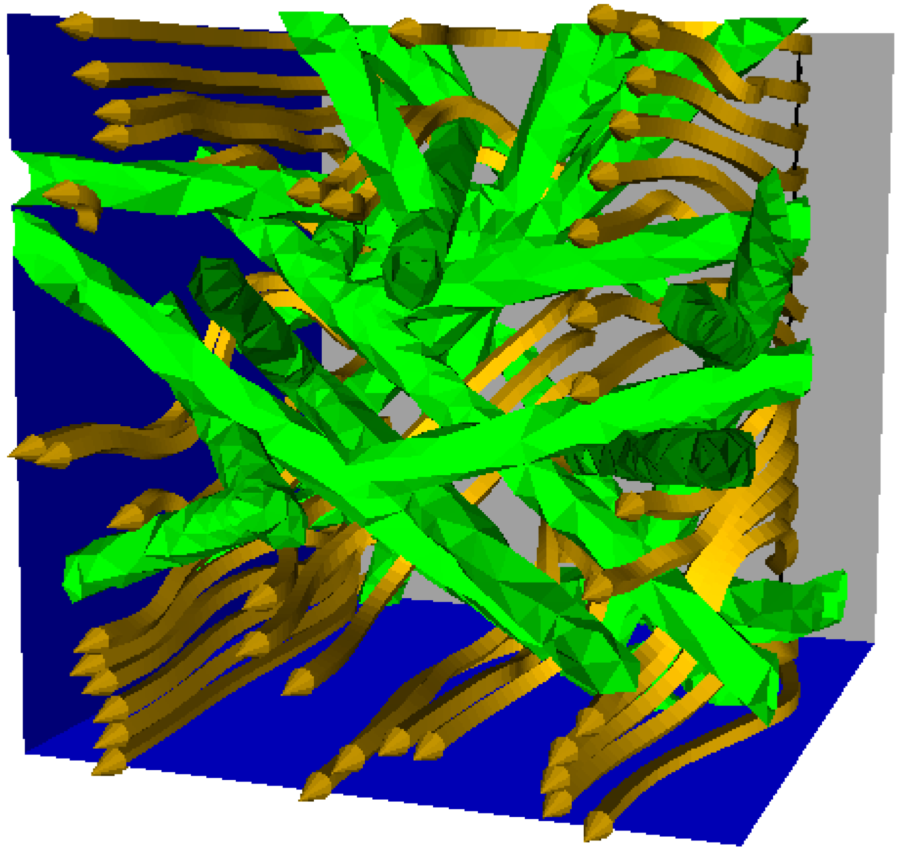
- Numerous studies (e.g., Clague and Phillips, 1997) - Isotropic random arrays

Direct Permeability Calculation



- Although obviously prohibihitive in the multiscale problem, a direct calculation of permeability is possible by
  - Making the network
  - Expanding fibrils to finite size
  - Discretizing the interstitial space
  - Solving the Stokes equations

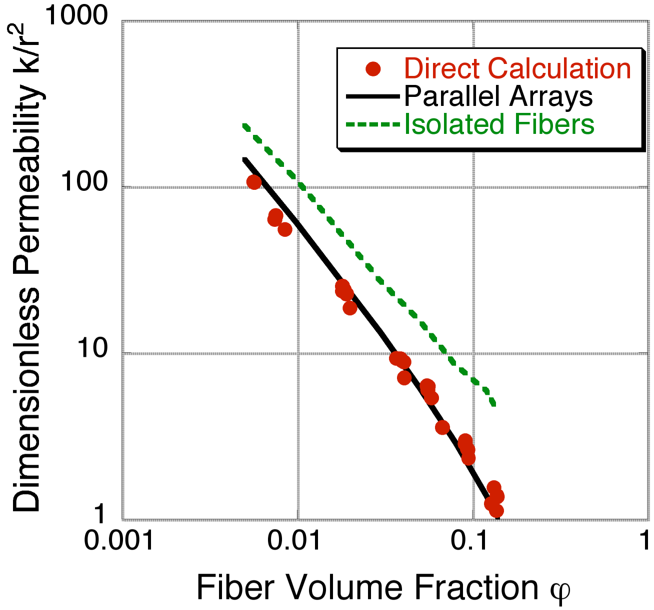
Simulated Permeating Flow



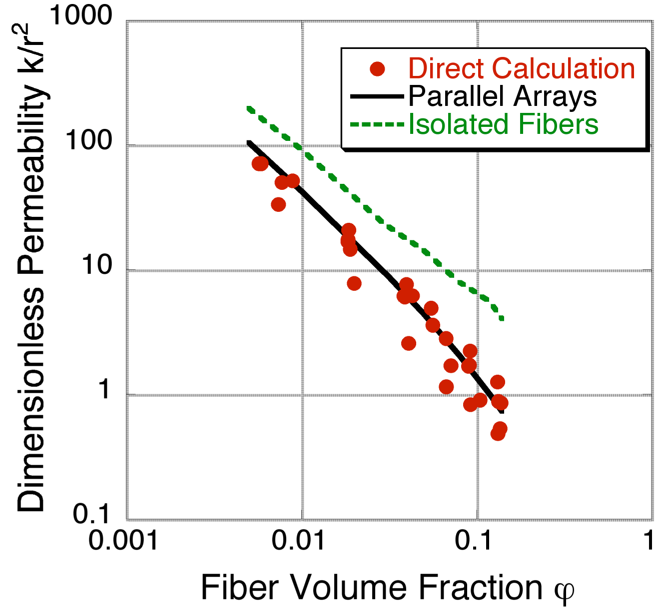
Two Models

- *Isolated Fibers*, in which all fibers are assumed to exert drag as if there were no other fibers. This approach ignores hydrodynamic interactions and thus overestimates permeability.
- *Parallel Arrays,* in which each fiber is assumed to exert drag as if it were part of an infinite array.

Moderately Aligned Networks

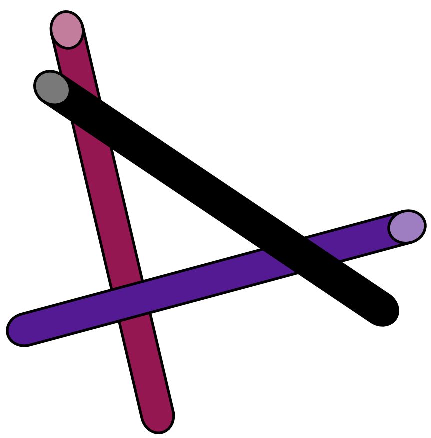


Parallel

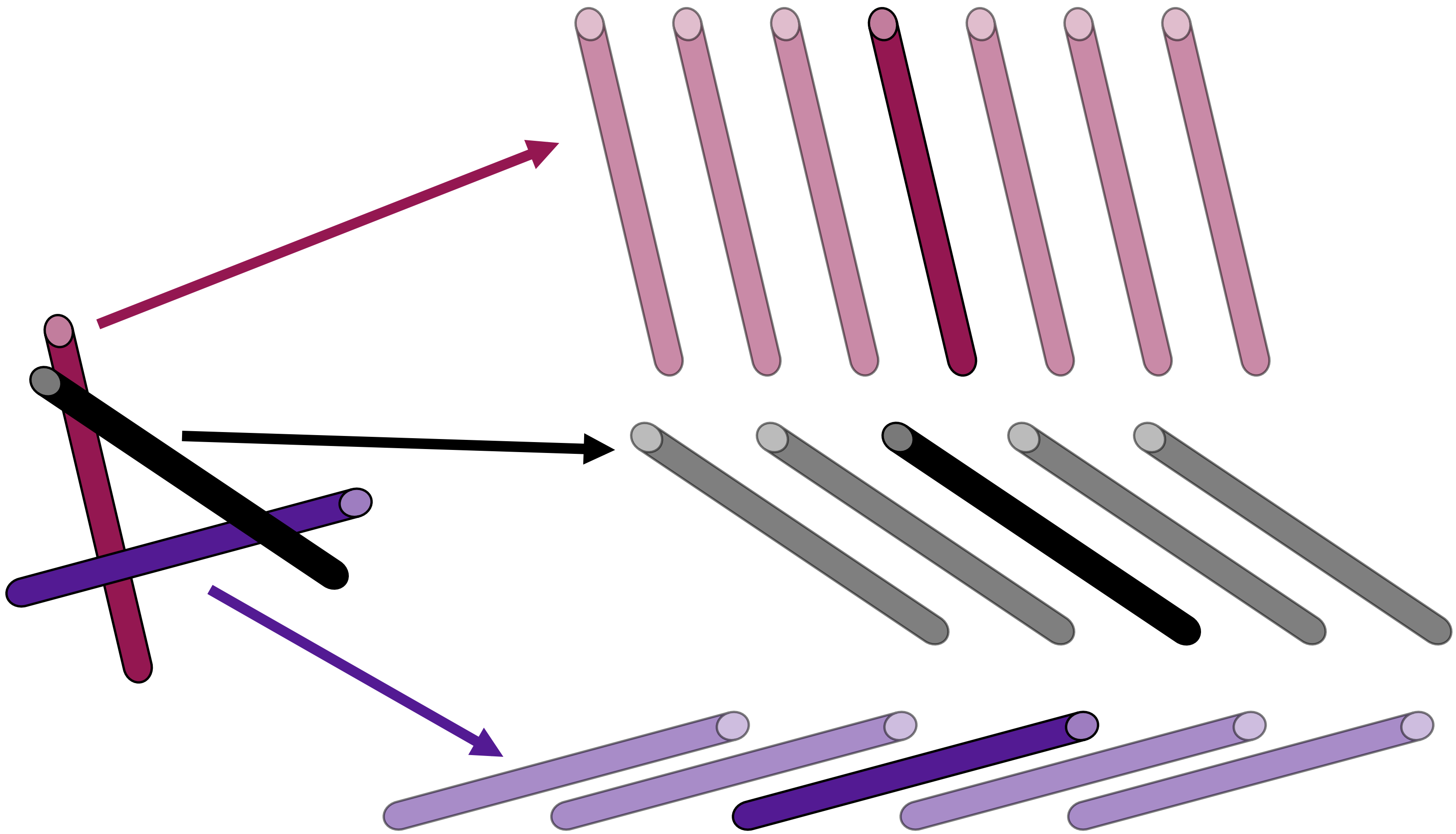


Transverse

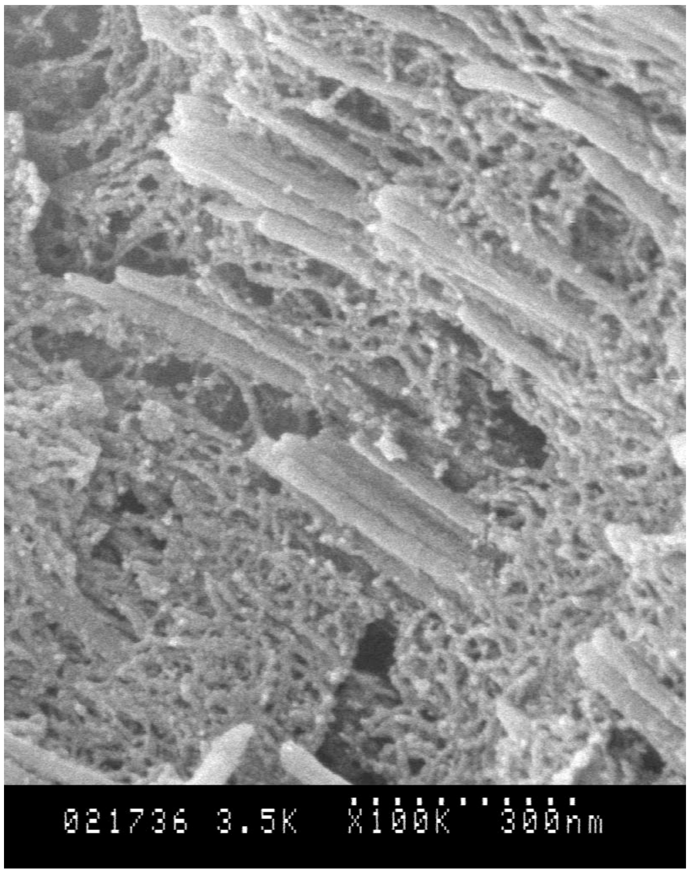
Decomposition



Decomposition



Challenge: Multiple Components



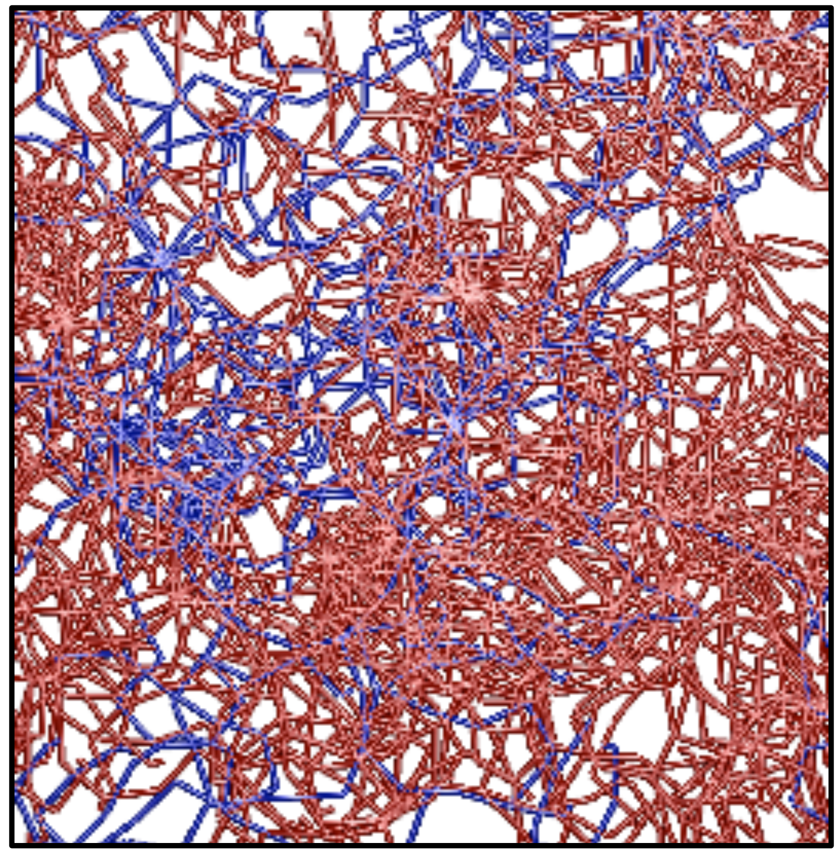
- A real artificial tissue (like a real real tissue!) contains multiple components
- These must be separated in order to construct an appropriate model.
- For sufficient homogeneity, our direct calculation should provide the basis for an estimate.
- Can we use the same summation strategy as before? Even if the populations have different orientations?

Challenge: Heterogeneity

- We have been doing some research on the type IV collagen network in basement membrane.
- One question that we need to address is how network *heterogeneity* affects permeability.
- We have the expectation that more heterogeneity will give more permeability since flow through pores and holes scales by more than area.

An Image

- This is a simulated type IV collagen network.
- The red and blue lines indicate different collagen isoforms.
- Because of slight differences between isoforms, the blue components tend to cluster, creating a structural inhomogeneity.
- How do we account for this in our model?



Some Ideas

- We could do what we did before, but the heterogeneity would mean that we would need a much larger domain, probably prohibitive for our FEM calculations
- Can we do a lattice-Boltzmann calculation?
- We are also considering making a large-scale (2” or so) analog

Acknowledgments

- Triantafyllos Stylianopoulos
- Ed Sander

- Bob Tranquillo (UMN)
- Jan Stegemann (RPI)
- Mark Shephard (RPI)
- Jeff Derby (UMN)
- Andrew Yeckel (UMN)

- Minnesota Supercomputer Institute
- RPI Scientific Computation Research Center (SCOREC)
- NIH (R01 EB005813, R21 GM082823)