Mechanobiology of the musculoskeletal system
Lecture II: Fluid flow in musculoskeletal tissue

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C6: Engineering Science

BME2: Biomedical Engineering

HT 2008

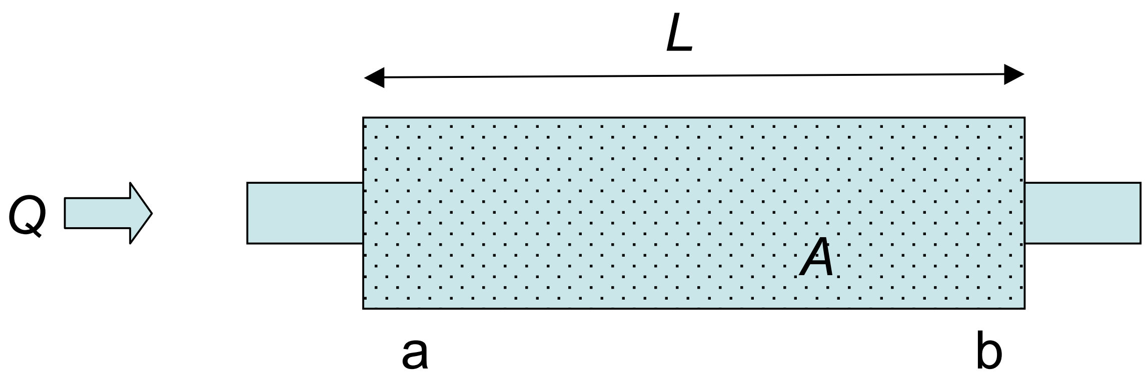
- Lecture 1
  - Cell mechanics and bone mechanosensitivity
    [cells, local structure, bone mechano-regulation]
- Lecture 2
  - Fluid flow in musculoskeletal tissue
    [material models, focus on cartilage]
- Lecture 3
  - Tools for mechanobiology
    [digital image correlation, models]
- Lecture 4
  - Mechanobiology theories and applications
    [bone healing, tissue continuum models]

Fluid flow through porous media

- Henry Darcy (Dijon, 1803 - 1858)
  - Water flow through sand beds (laminar):
    - Darcy's Law:

$$Q = -\frac{\kappa A}{\mu}\frac{(P_b - P_a)}{L}$$

    - Where Q is volume flow rate [m^3s^{-1}], κ is permeability [m^2], μ is viscosity [Pa s], P is pressure [Pa], A is cross section area



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    - Where Q is volume flow rate [m^3s^{-1}], κ is permeability [m^2], μ is viscosity [Pa s], P is pressure [Pa], A is cross section area
    - Generalising:

1D:

$$\frac{Q}{A} = q = -\frac{\kappa}{\mu}\frac{\partial P}{\partial x}$$

3D:

$$q = -\frac{\kappa}{\mu}\nabla P(x,t)$$

WARNING!

- Permeability has at least 3 different definitions:
  - Intrinsic permeability, κ [m^2]
    - Basic material property
  - Dynamic permeability, $\kappa_{dynamic}$ [m^{4}N^{-1}s^{-1}]

$$\kappa_{dynamic} = \kappa \frac{1}{\mu}$$

e.g. Mow et al 1980 J Biomech Eng 102, 73-84

  - Soils permeability, κ_{soils} [ms^{-1}]

$$\kappa_{soils} = \kappa_{dynamic} \rho g = \kappa \frac{\rho g}{\mu}$$

e.g. ABAQUS

ρ is fluid density, g is gravity

- In this course permeability $\equiv \kappa$ [m^2]

Biological materials

- Permeability
  - Cancellous bone: 1×10^{-10} m^2
    - Bone cement - 3 mm penetration required
    - Cementation pressures of c. 1 MPa
  - Cortical bone
    - Haversian canal: 1×10^{-13} - 1×10^{-15} m^2
    - Canaliculi: 1×10^{-19} - 1×10^{-22} m^2
    - Load induced fluid flow, osteocyte stimulation

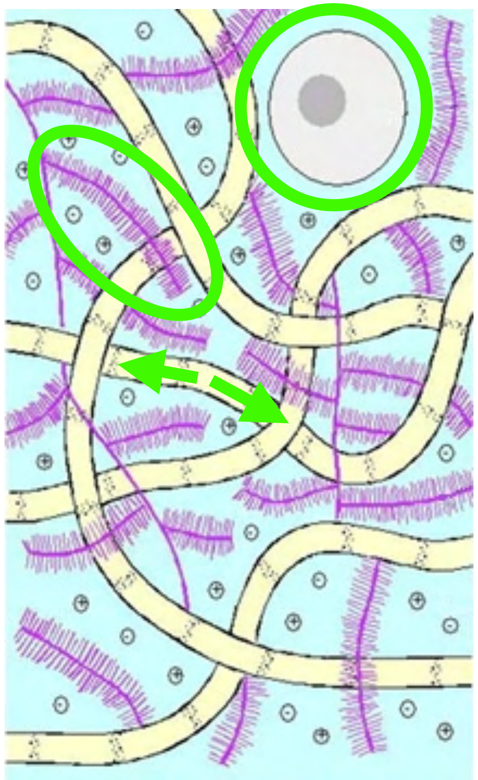
Beno et al 2006 J Biomech 39, 2378-87

Biological materials

- Cartilage
  - Chondrocyte
  - Proteoglycan:
    - Water affinity: swelling pressure
  - Collagen   in tension
- Loading: fluid support
  - Biphasic theory

    Mow et al 1980 J Biomech Eng 102, 73-84
  - Measurement

    Soltz & Ateshian 1998 J Biomech 31, 927-34



- Cartilage
  - Chondrocyte
  - Proteoglycan:
    - Water affinity: swelling pressure
  - Collagen II in tension
- Loading: fluid support
  - Biphasic theory

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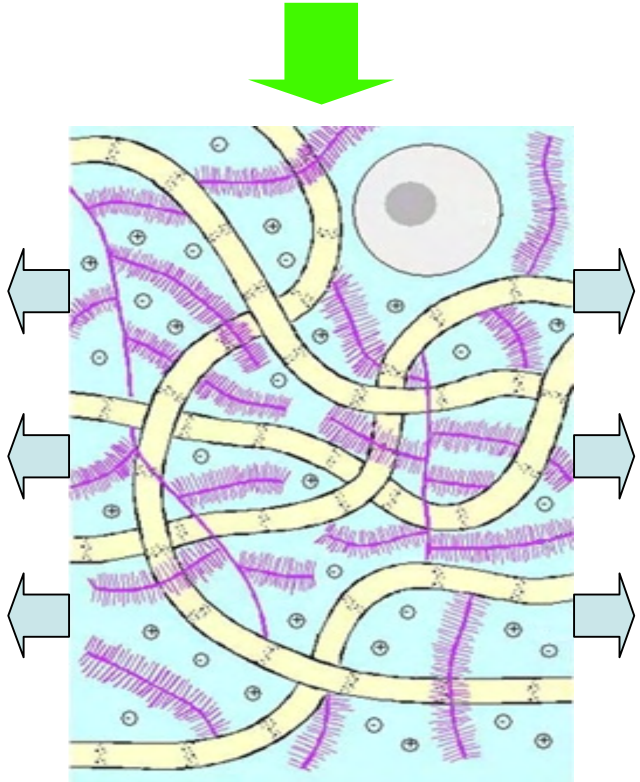


Biphasic / poroelasticity theory (1D)

- Cartilage: confined compression

$$\sigma(z,t) = -p(z,t) + H_A \frac{\partial u}{\partial z}$$

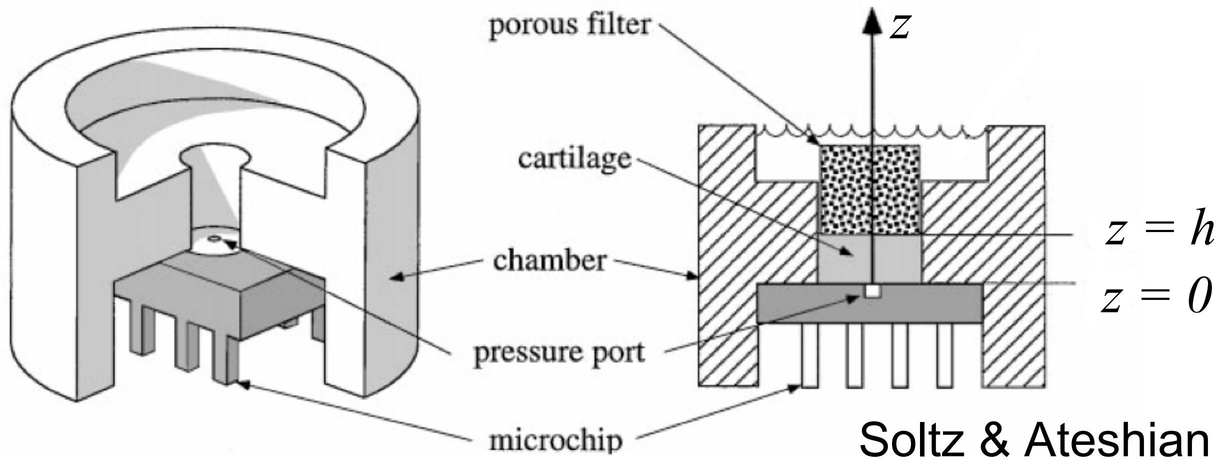
σ is stress, p is fluid pressure, $u(z,t)$ is displacement

$$H_A = E\frac{(1-\nu)}{(1-2\nu)(1+\nu)}$$

H_A is "aggregate" modulus

$$\frac{\partial^2 u}{\partial z^2} - \frac{\mu}{H_A \kappa}\frac{\partial u}{\partial t} = 0$$

continuity, solid & fluid: in equilibrium, incompressible



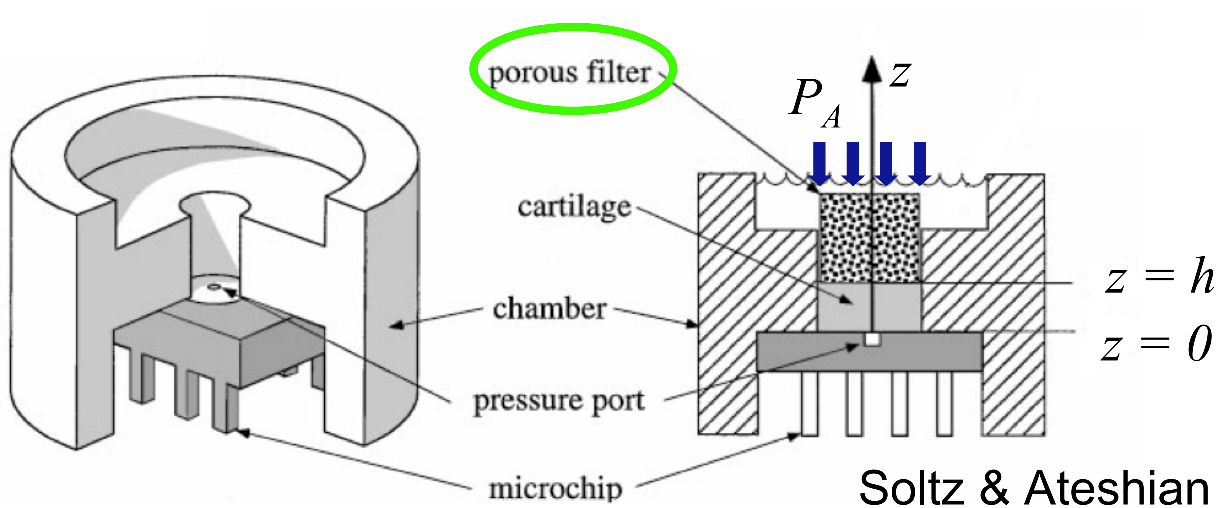
Soltz & Ateshian 1998 J Biomech 31, 927-34

Biphasic / poroelasticity theory (1D)

- Cartilage: confined compression
  - Creep under constant pressure load, -P_A

$$p(h,t)=0 \quad \text{so} \quad \sigma(h,t)=-P_A=H_A\left.\frac{\partial u}{\partial z}\right|_{z=h}$$

also $u(z,0)=0$ and $u(0,t)=0$



Soltz & Ateshian 1998 J Biomech 31, 927-34

Fluid flow through porous media

- Cartilage
  - Biphasic / poroelasticity theory (1D)
    - Solution by power series method (e.g. Kreyszig)

$$u(z,t) = -\frac{P_A}{H_A}\left[z - \frac{2h}{\pi^2}\sum_{n=0}^{\infty}\frac{(-1)^n}{\left(n+\frac{1}{2}\right)^2}\sin\left[\left(n+\tfrac{1}{2}\right)\frac{\pi z}{h}\right]\exp\left(\frac{-H_A\kappa}{h^2\mu}\left(n+\tfrac{1}{2}\right)^2\pi^2 t\right)\right]$$

    - Surface displacement, first term of the sum

$z = h$ and $n = 0$

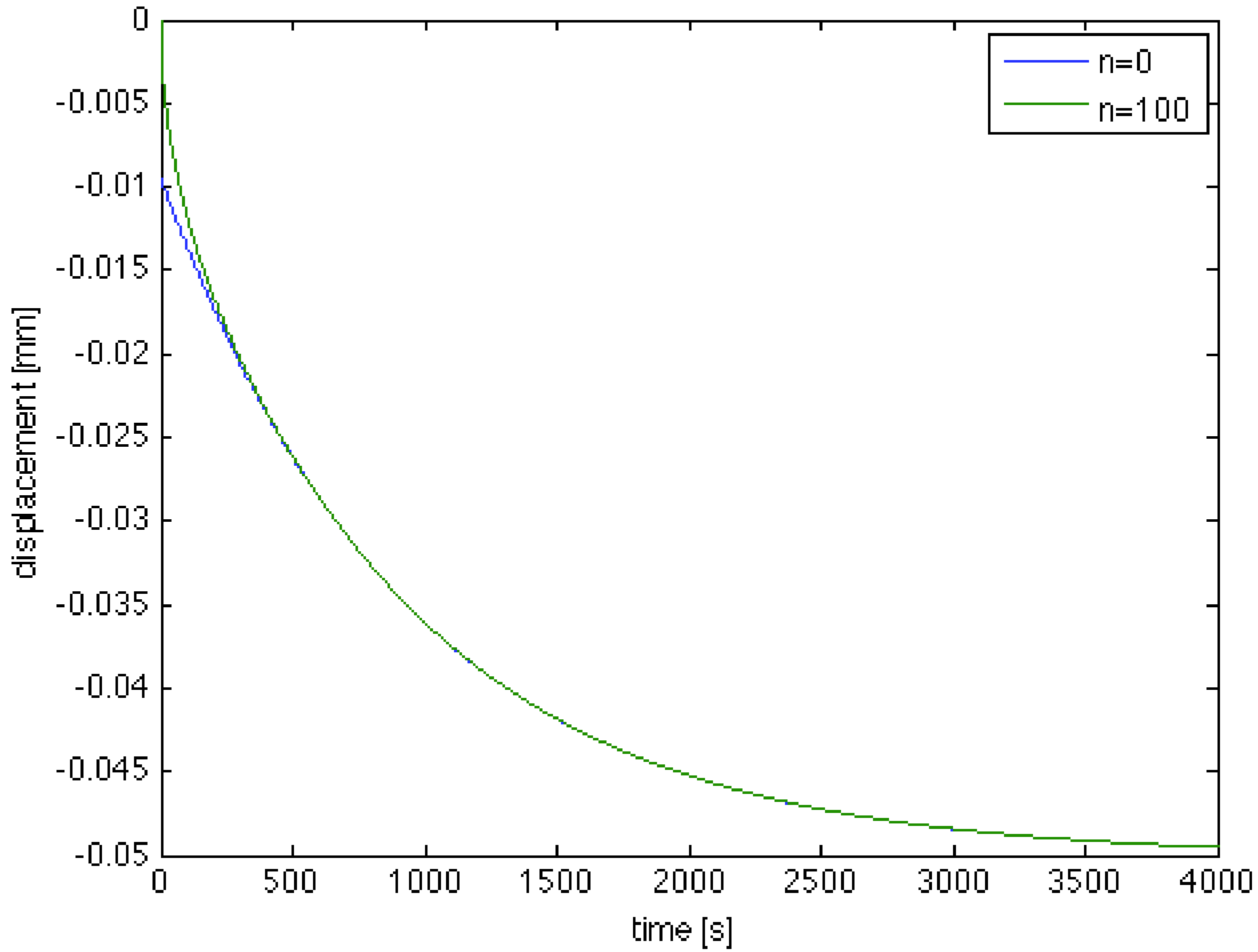
$$u(h,t) = -\frac{P_A}{H_A}\left[h - \frac{8h}{\pi^2}\exp\left(\frac{-H_A\kappa}{4h^2\mu}\pi^2 t\right)\right]$$

Kreyszig 2005 Advanced Engineering Mathematics

Soltz & Ateshian 1998 J Biomech 31, 927-34

Fluid flow through porous media

http://www.eng.ox.ac.uk/obme



Fluid flow through porous media

- Analytical solution for creep response
  - Extract biphasic parameters from test data
  - Optimization: minimize error
  - Typical cartilage values:

    H_A = 0.55 ± 0.12 MPa

    κ = 6.21 x 10^{-19} ± 2.5 x 10^{-19} m^2
- More general loading conditions
  - Finite element analysis
  - Iterative optimization (inverse problem)

Soltz & Ateshian 1998 J Biomech 31, 927-34

Fluid flow through porous media

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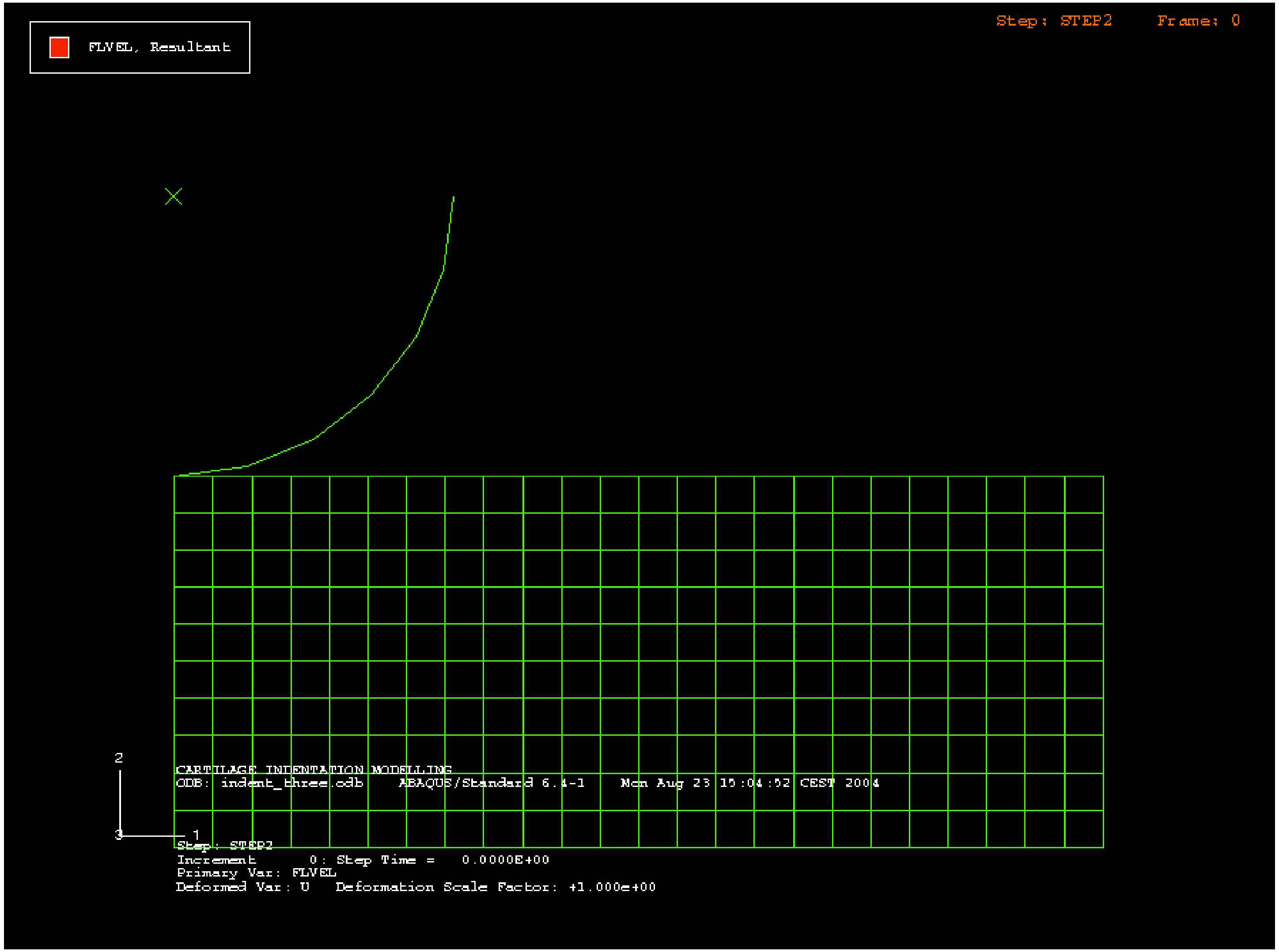


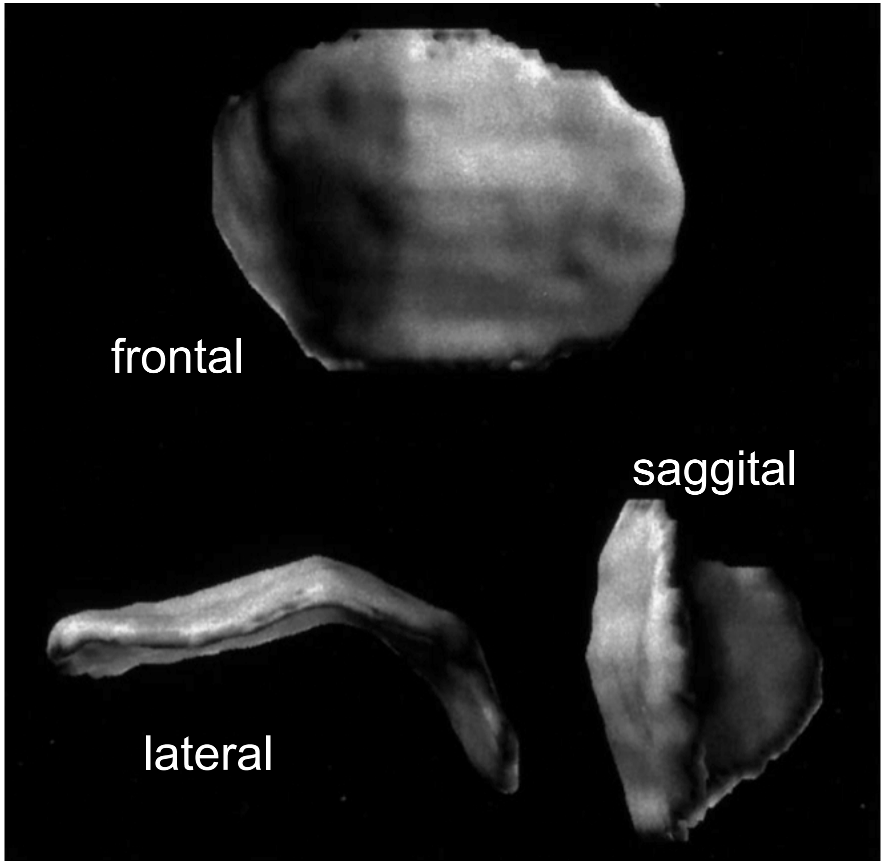
Axi-symmetric model

Indentation test

Common clinical test - arthroscopic

Fluid flow through porous media

- MRI confirmation (1.5 T)
  - Patella cartilage
    - 5 MPa physiological
  - 50 knee bends
    - 6% volume reduction
  - 50 further knee bends
    - No further volume reduction
  - Recovery ~ 90 mins
  - Flow rate
    - 0.16 $mm^3 min^{-1}$



Eckstein et al 1999 Anat Embryol 200, 419-24

Chondrocytes

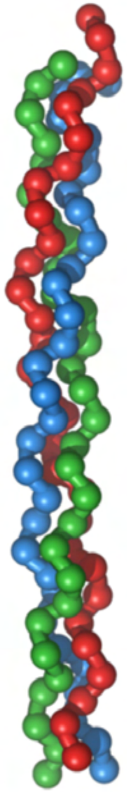
- Catabolic and anabolic activities in balance
  - Synthesis and degradation of collagen, proteoglycan, other proteins
- Sparse in matrix
  - 7×10^6 g^{-1} (40 years) - 1×10^6 g^{-1} (90 years)
  - Also decreases with osteoarthritis
- Metabolism / nutrition
  - No blood vessels in cartilage -> nutrient diffusion
    - Mechanically assisted
  - Low [O_2] -> anaerobic metabolism

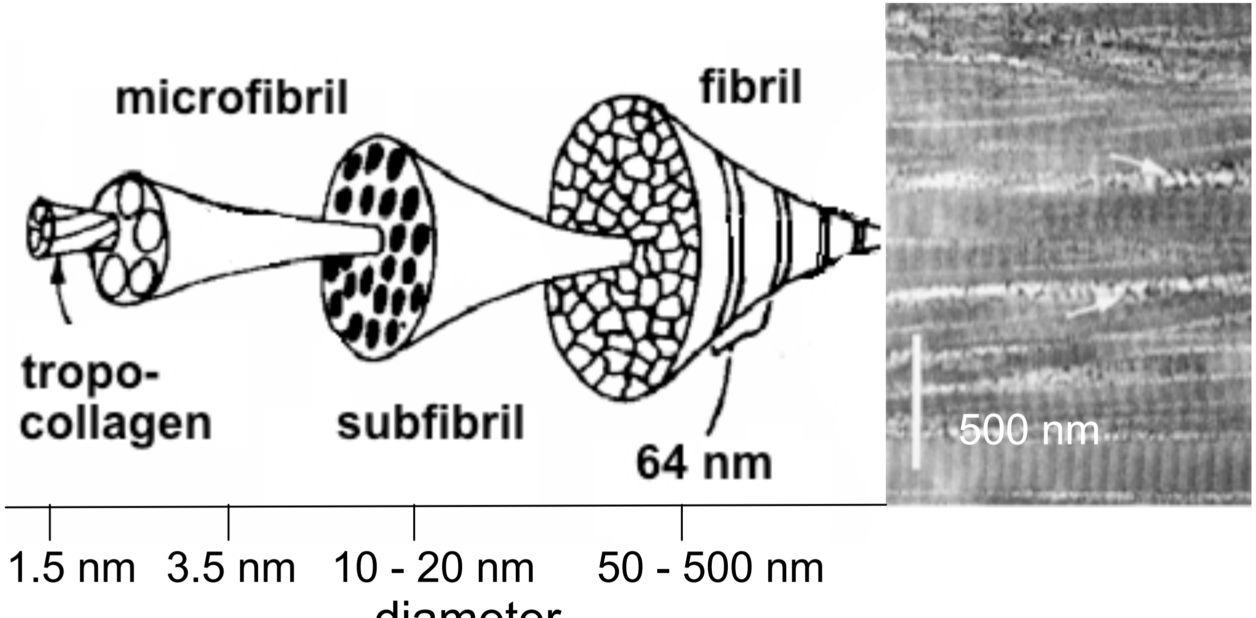
Bobacz et al 2004 Ann Rheum Dis 63, 1618-22

Collagen

- Collagen type II - main tensile element (12%)
  - (also IX and XI)
- Triple helix tropocollagen (1961) XRD
  - Spontaneously self-associates

Altgelt et al 1961
PNAS 47, 1914-24





Proteoglycan

http://www.eng.ox.ac.uk/obme

- Proteoglycan (8%)

Hyaluronan backbone

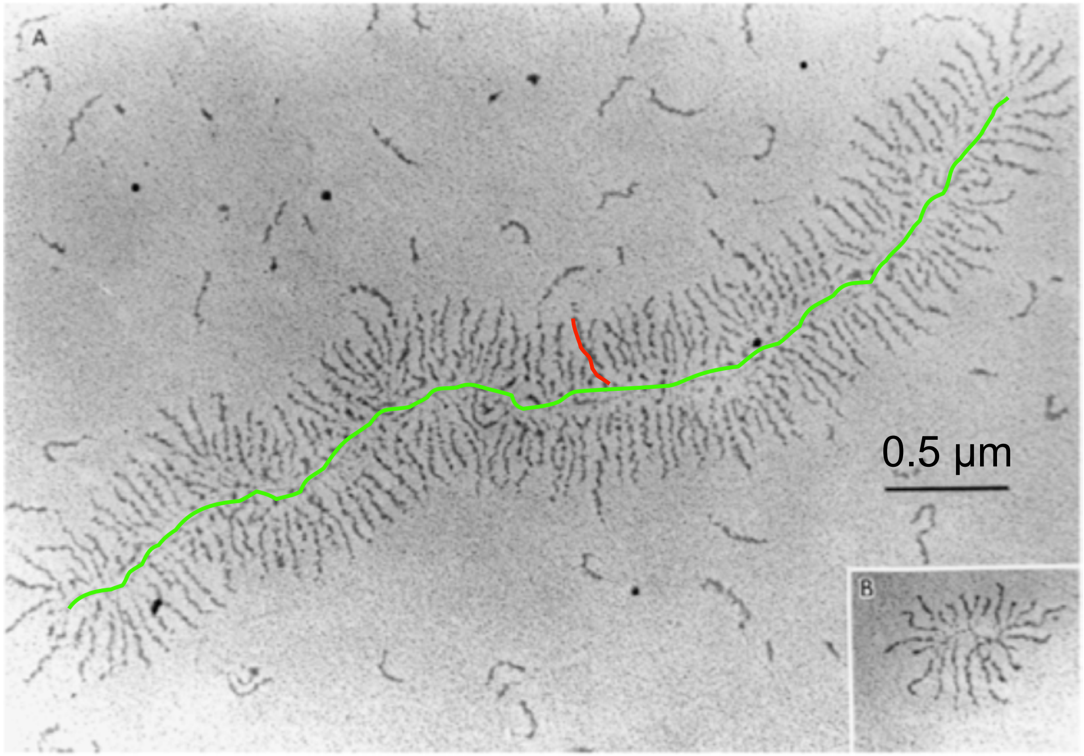
Aggrecan side chains

form large aggregates

both are

Glycosaminoglycans:

Protein core filament
&
polysaccharide chains
-ve charge



[Cation$^+$] increases -> osmotic pressure

- Water! (80%)

Buckwalter & Mankin 1997 JBJS 79-A, 612-32

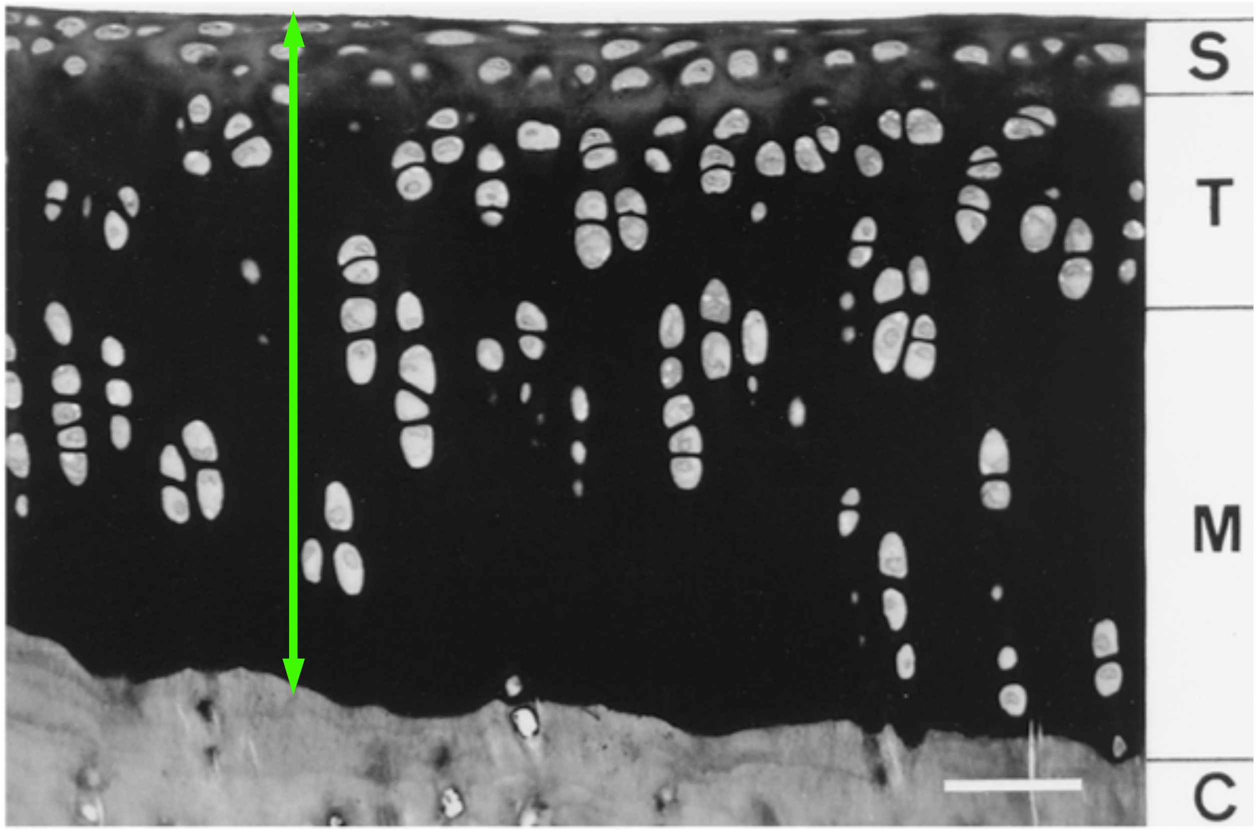
Cartilage structure

- 4 distinct zones:

  superficial (S),
  transitional (T),
  deep (M) and
  calcified (C)

- Thickness

  human 3.6 mm
  bovine 4.4 mm
  porcine 2.0 mm
  canine 1.8 mm
  ovine 1.5 mm
  rabbit 1.4 mm
  rat 0.4 mm



Buckwalter & Mankin 1997 JBJS 79-A, 612-32

Cartilage structure

http://www.eng.ox.ac.uk/obme

- 4 distinct zones:

  superficial (S):
  Dense parallel
  collagen II fibres

  Low [proteoglycan]

  High [water]

  transitional (T):

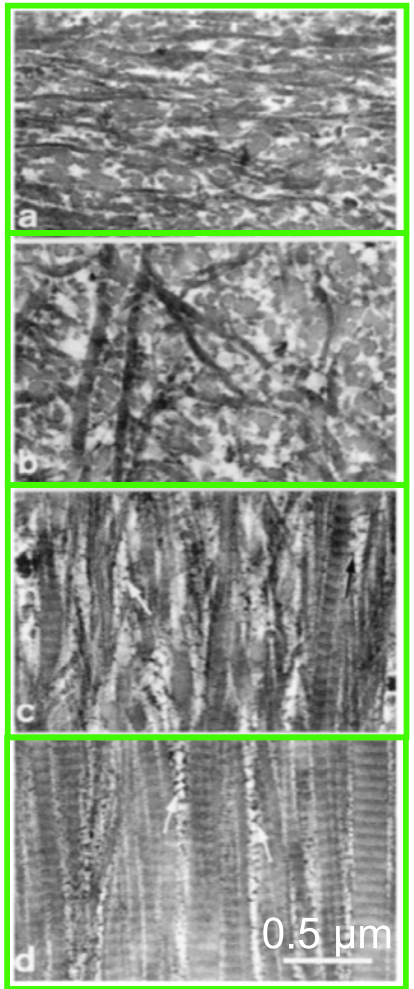
  deep (M):

  Largest ∅ fibrils

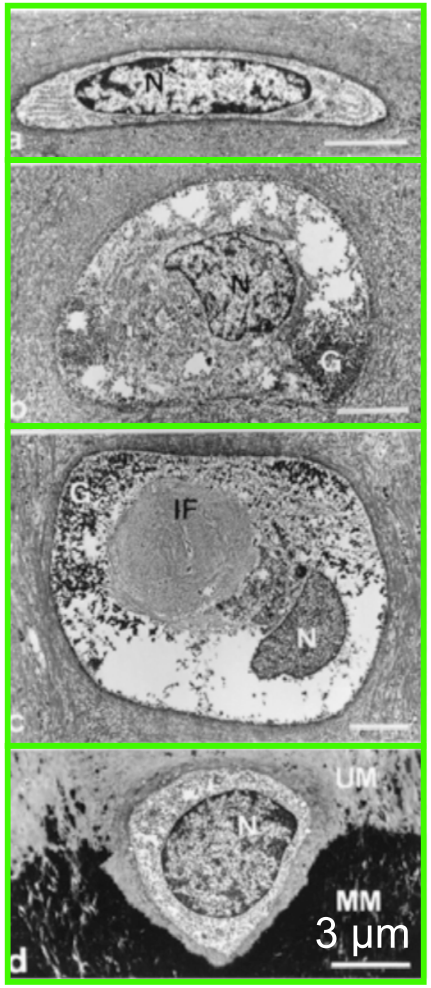
  High [proteoglycan]

  Low [water]

  calcified (C)



Matrix



Chondrocytes

Buckwalter & Mankin 1997 JBJS 79-A, 612-32

Mechanical properties

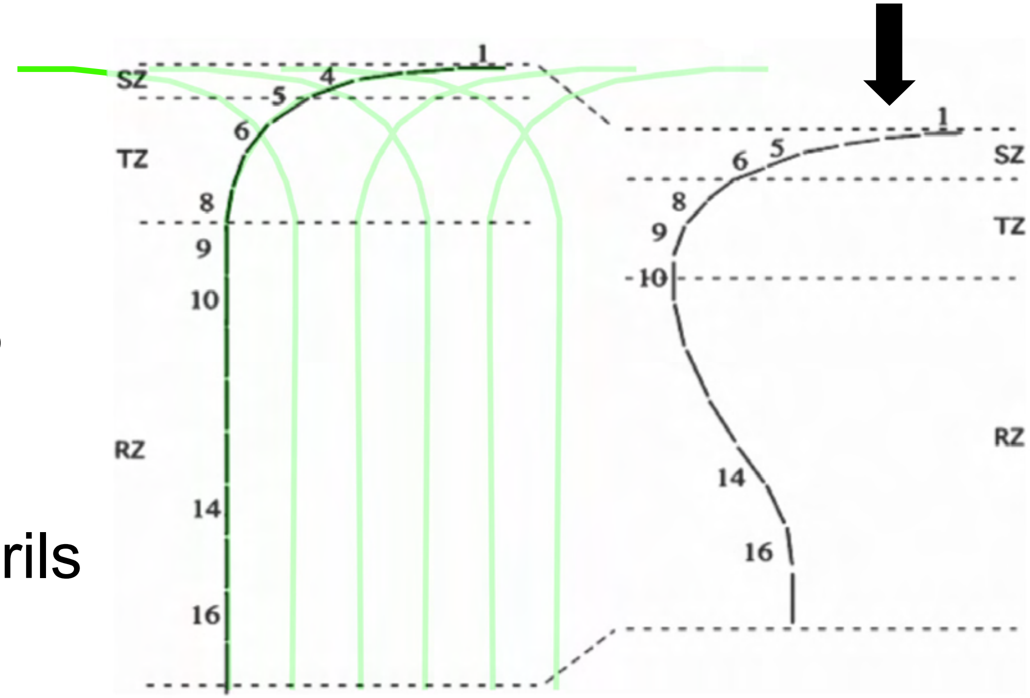
	H_A compressive	H_A tensile	κ, ppd.	κ, parallel
Superficial	low	high	medium	low
Transitional	medium	medium	medium	medium
Deep	high	low	medium	high

- Depth dependent inhomogeneity
  - Fluid pressurization at articular surface
  - Stress & strain non-uniform

Chen et al 2001 J Biomech 34, 1-12
Charlebois et al 2004 J Biomech Eng 126, 129-37
Krishnan et al 2003 J Biomech Eng 125, 569-77

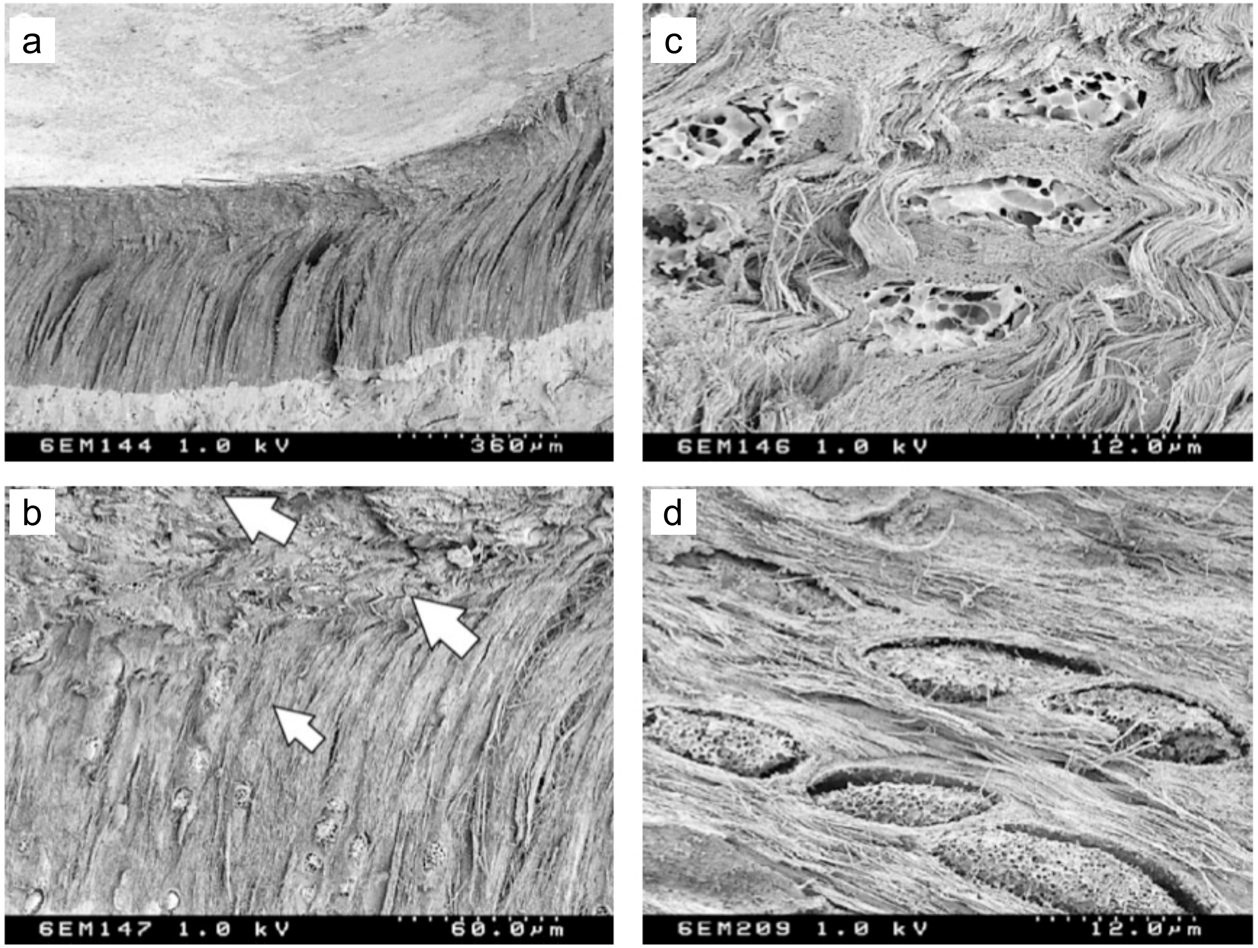
Cartilage structure

- Collagen fibrils
  - "Arcades"
- μMRI in vitro
  - 7 T, T_2 relaxation
  - "magic angle" ~55º
- 20% strain
  - Reorientation of fibrils
  - Change in relative size of zones



Alhadlaq 2004 Osteoarth Cartilage 12, 887-94

Cartilage structure



- Rabbit knee cartilage
  loaded, fast frozen and fractured

  a) tibia articular surface
  b) transitional & deep zone - fibre bending
  c) upper deep zone deformed chondrocytes (ice crystal artefacts)
  d) transitional zone chondrocytes

Kääb et al 2003 Cells Tiss Org 175, 133-9

Cartilage friction

- Coefficient of friction
  - $\mu \sim 0.01$ (dynamic - "start up" ~ 0.2)
- Lubrication regimes:
  - Boundary (surfaces in contact)
    - Hyaluronan, Lubricin / PRG4
  - Hydrodynamic / elastohydrodynamic
    - Fluid layer separating surfaces
    - Enhanced by elastic deformation of surfaces
  - "boosted" / "weeping"
    - Enhanced by pressurisation of tissue fluid

Krishnan et al 2004 J Orthop Res 22, 565-70
Schmidt and Sah 2007 Osteoarth Cartilage 15, 35-47

Cartilage mechanosensitivity

- Paraplegia, immobility (MRI)
  - Reduced tissue thickness - as early as 7 weeks
  - Stiffness may be reduced
    - Gadolinium contrast for glycosaminoglycan content
- Continuous passive motion - lubricin increased
- Chondrocytes in 3D culture
  - Changes in cytoskeleton organization
  - Cell signaling activated
  - Changes in matrix molecule synthesis

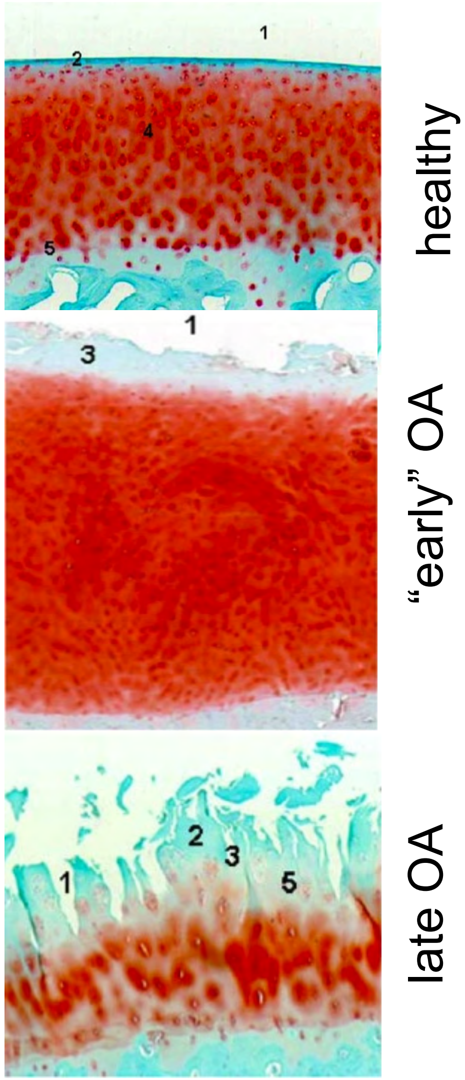
Eckstein et al 2006 J Anat 208, 491-512
Nugent-Derfus et al 2006 Osteoarth Cartilage in press
Knight et al 2006 J Biomech 39, 1547-51

Cartilage degeneration

- Osteoarthritis, injury --> degeneration of tissue
  - Loss of microstructure, cracking, fibrillation, loss of matrix
- Matrix synthesis imbalance
- Mechanical properties altered
- Cell mechanical environment altered
- Cell mechanosensitivity altered

Salter et al 2002 Biorheology 39, 97-108
Jones et al 1999 J Biomech 32, 119-27

Cartilage degeneration



- Histological images
  - Safranin orange
    - Proteoglycans (non-quantitative)
  - Light green counterstain
  - Early:
    - Loss of surface smoothness & proteoglycans
    - Increase in water content, permeability
  - Late:
    - Loss of matrix material
    - Clefting, fibrillation

Lorenz et al 2006 Prog Histochem Cytochem 40, 135-63

Fluid flow in musculoskeletal tissues

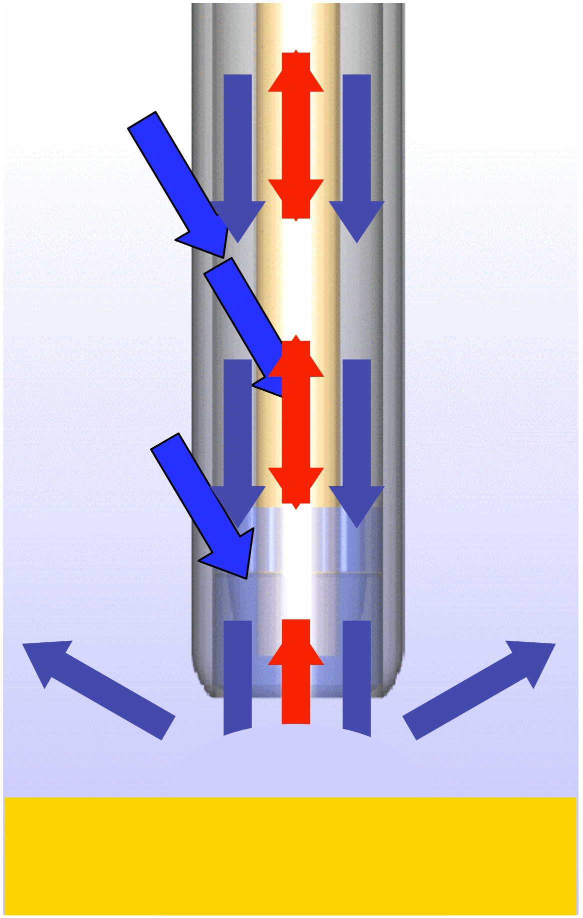
- Bone (cancellous and cortical)
- Cartilage
- Intervertebral disc
- Meniscus
- Tendon, ligament
- Muscle
- …

Summary

- Darcy's Law
  - Permeability in [m^2]
- Biphasic / poroelasticity theory
- Microstructure and function of cartilage
  - Mechanical deformation
  - Lubrication
- Cartilage degeneration

Cartilage degeneration

- Arthroscopic device - tip
  - Tube
  - Fibre optic
  - Nozzle
  - Optical measurement
  - Fluid jet
- Use in conjunction with FE
  - Extract modulus, permeability



Duda et al 2004 Am J Sports Med 32, 693-8