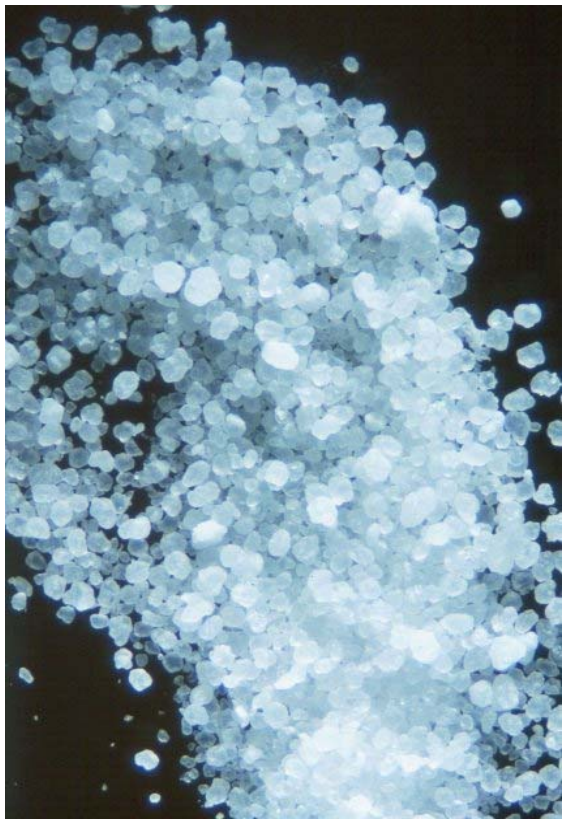
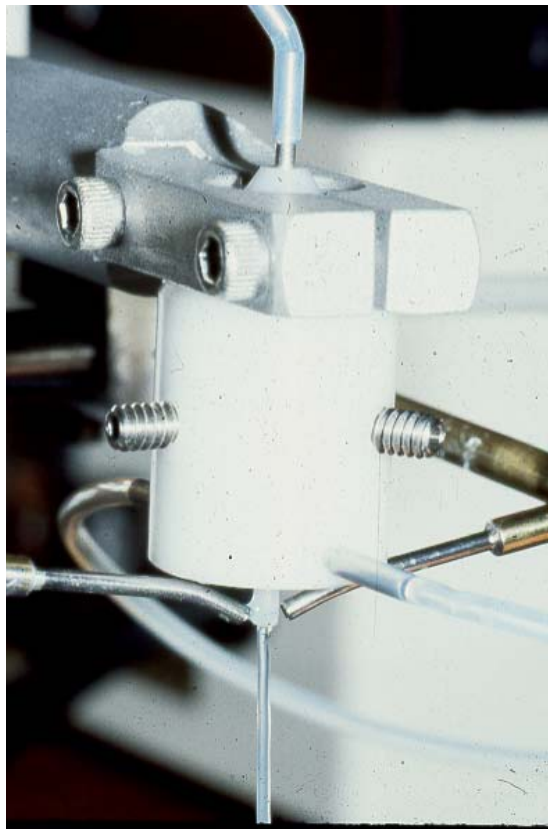
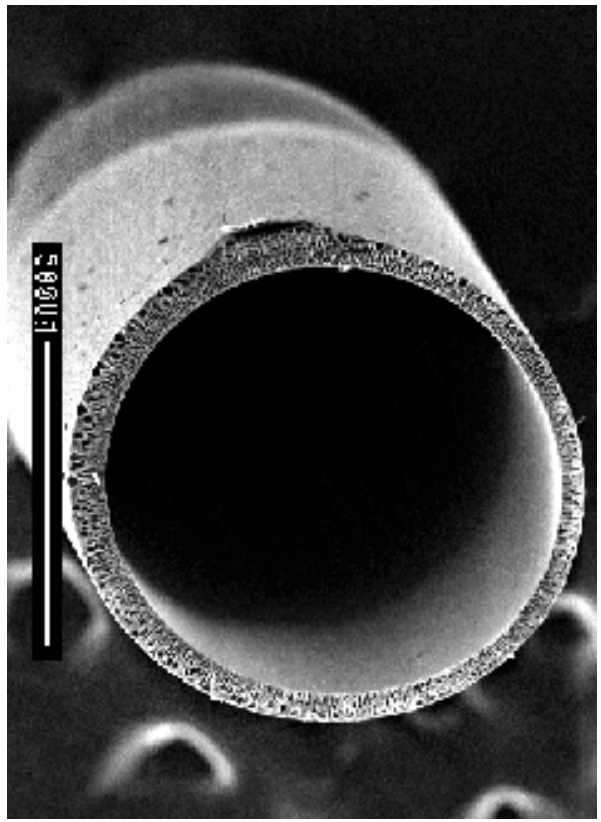
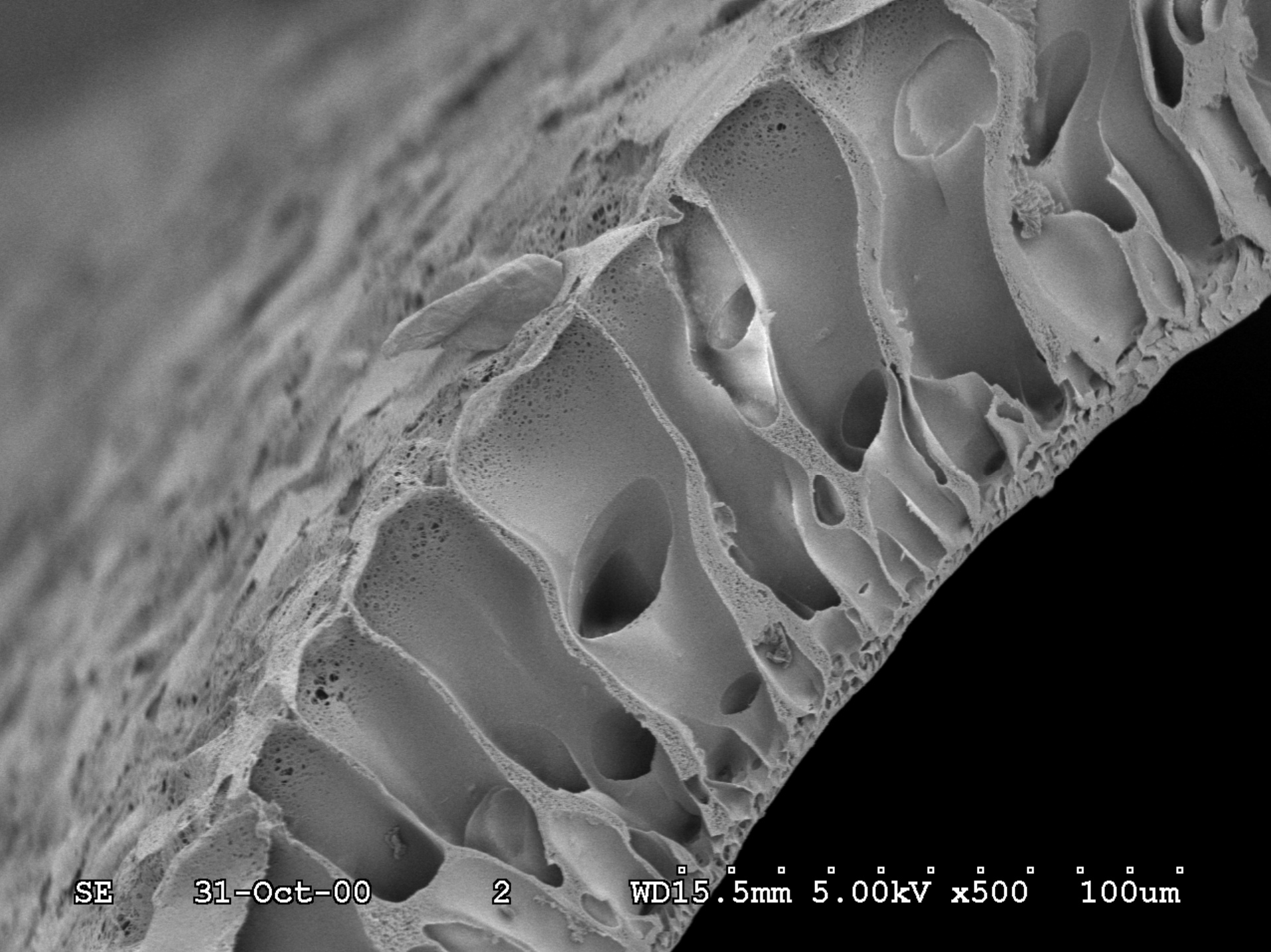
HFM Fabrication

-Fiber Spinning



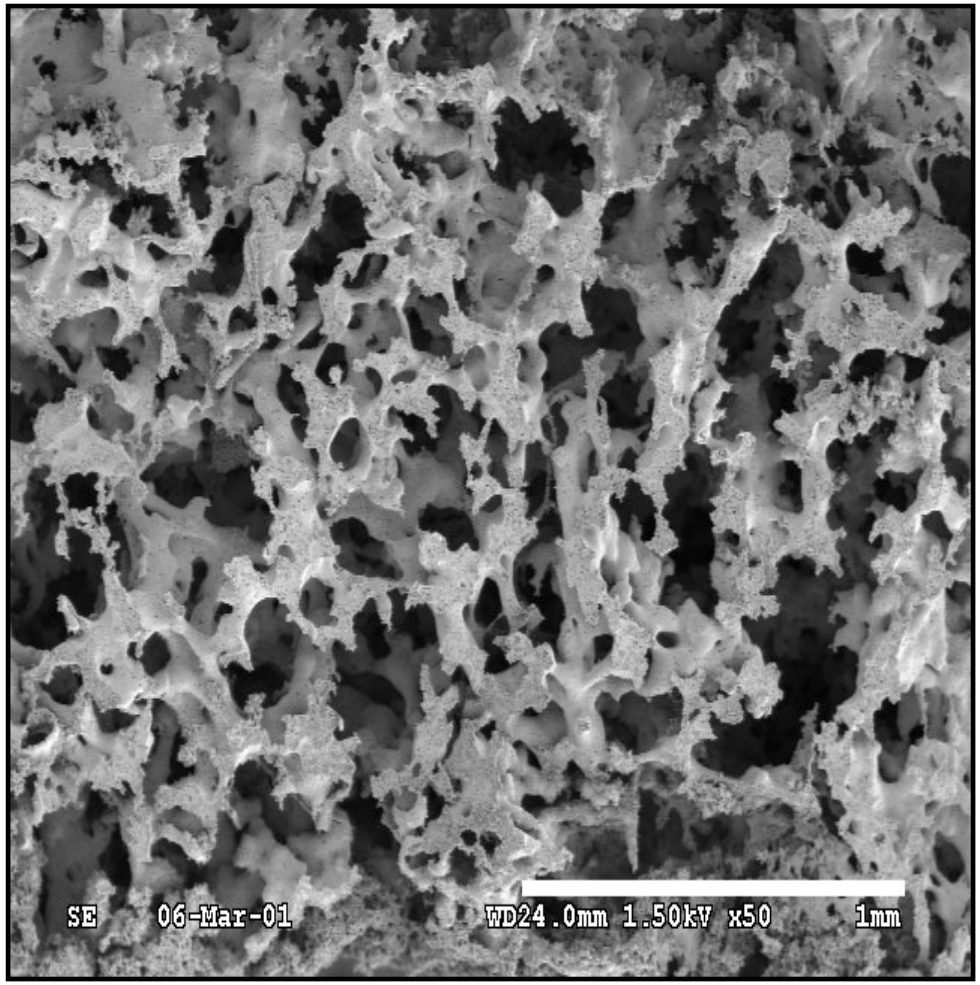




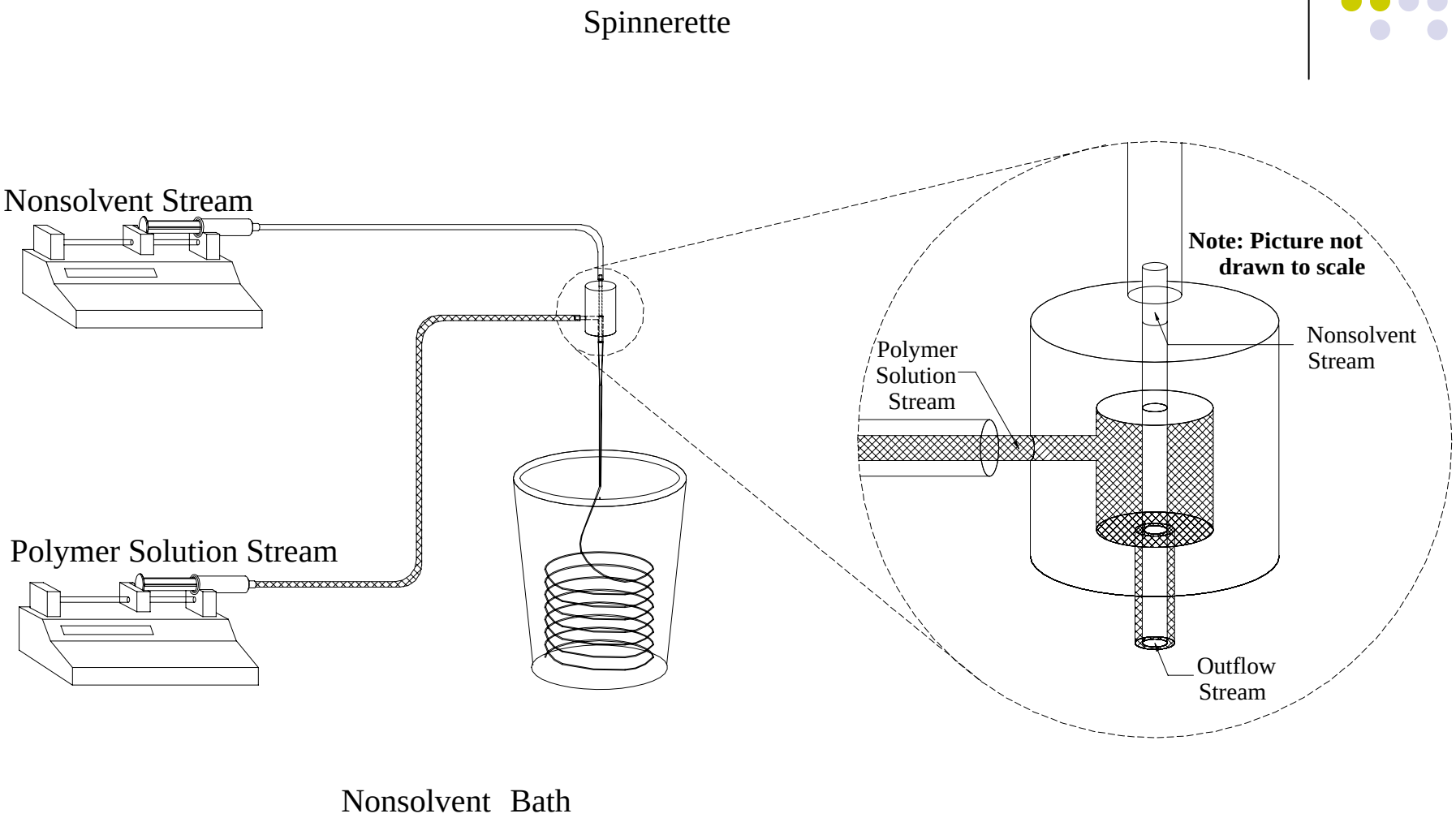

SE 31-Oct-00 2 WD15.5mm 5.00kV x500 100um

Phase Inversion

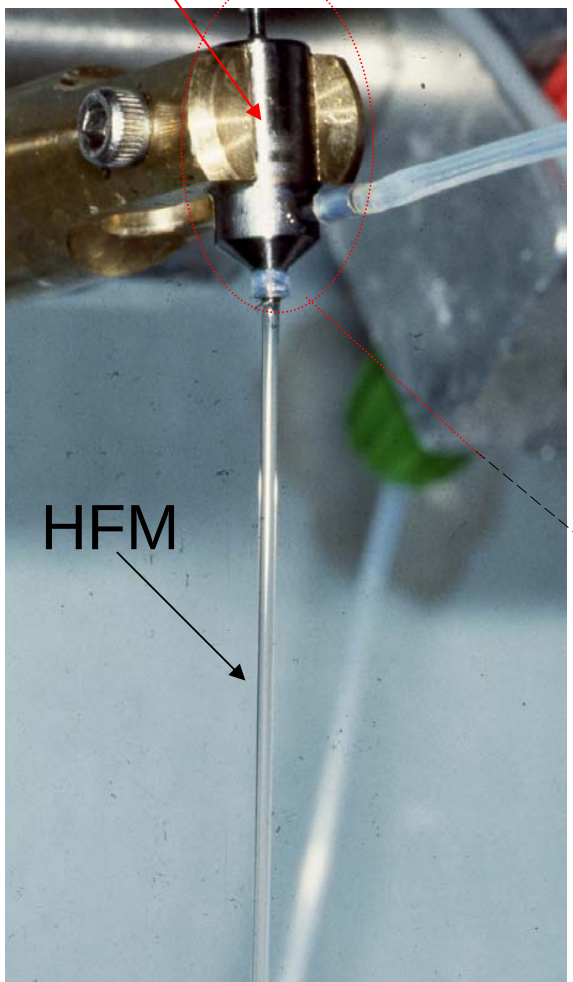
- Controlled precipitation
- Solution--> porous solid that is interconnected and traversed by an interpenetrating pore structure which provides channels across the wall structure

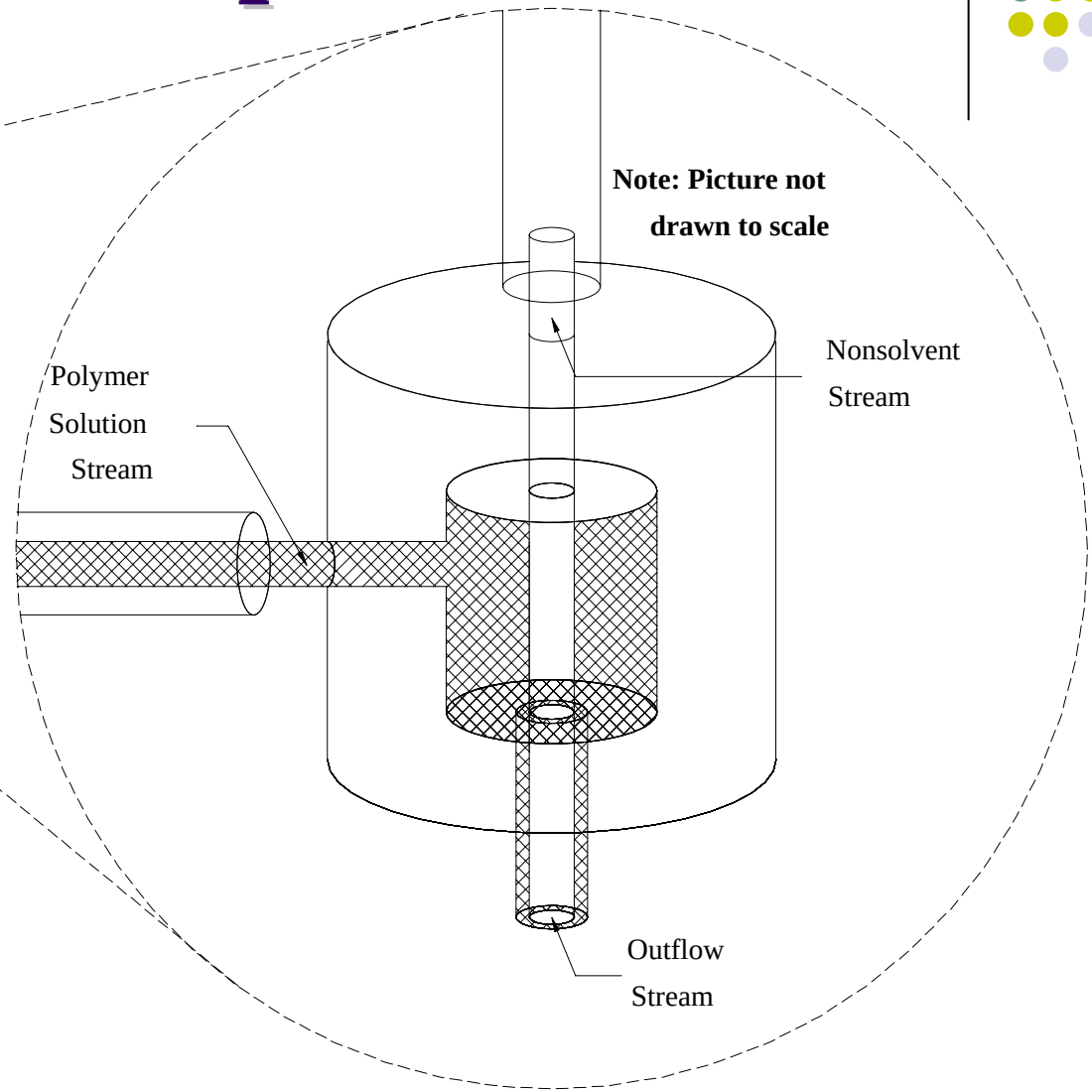


Dry-Jet Wet Spinning



Anatomy of a Spinneret

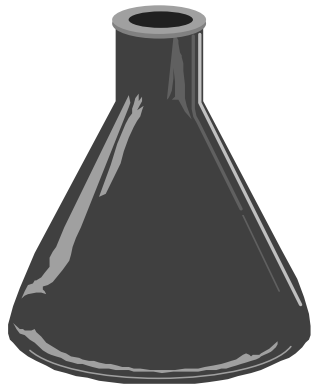




Required Elements

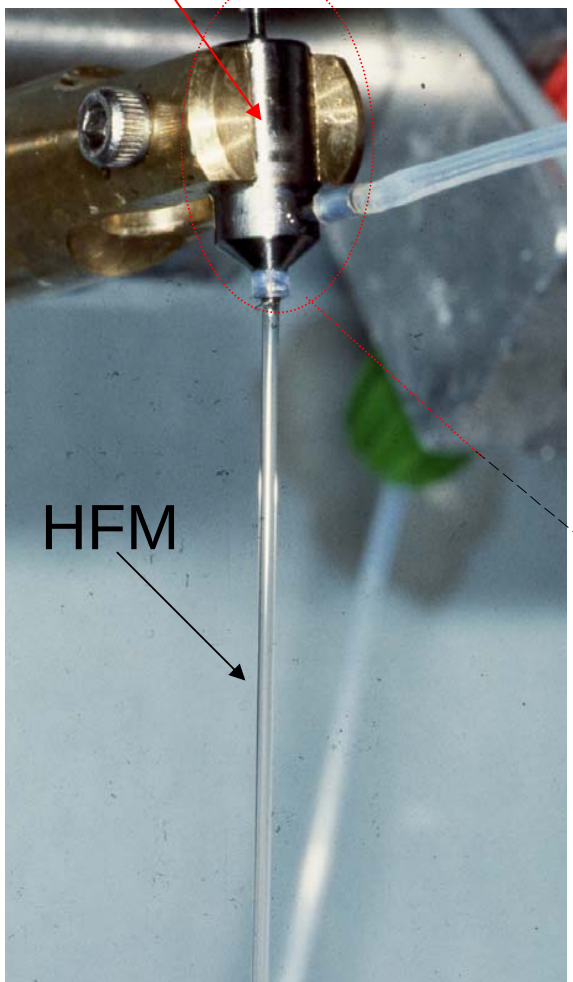
- A polymer of sufficient Mw

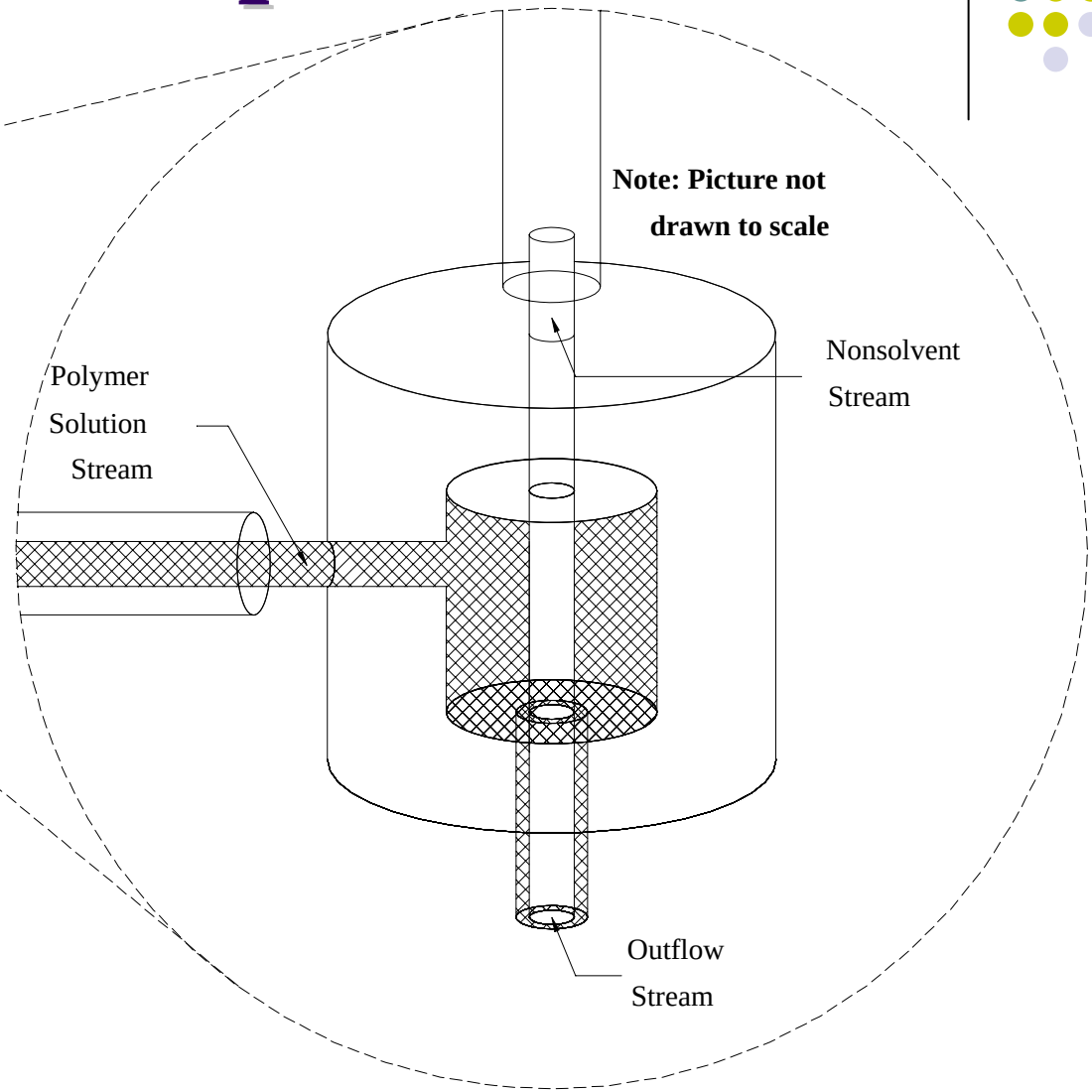
that is, enough length to provide inter chain entanglement following precipitation and adhesive force to provide the appropriate mechanical properties for a particular application



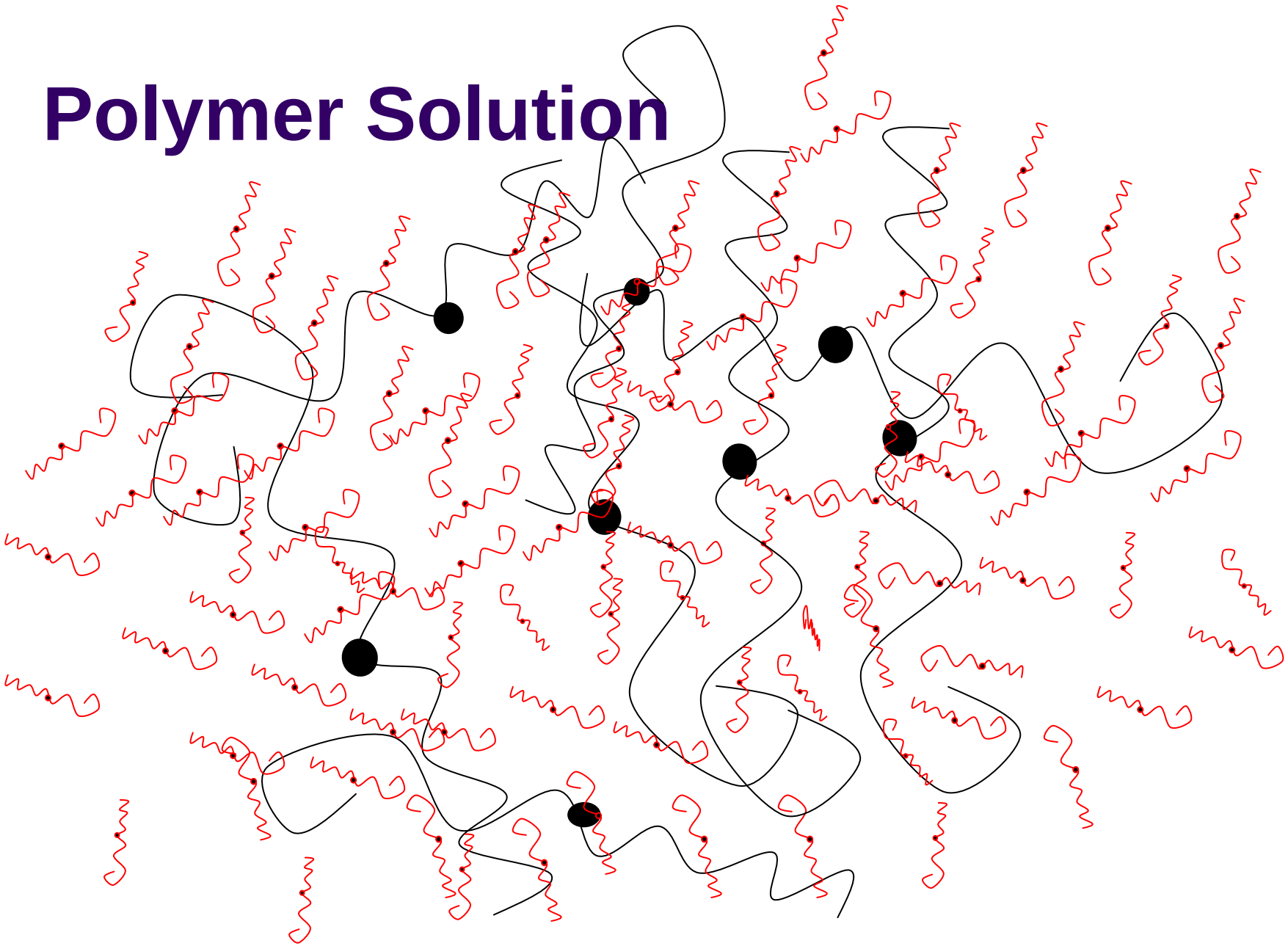
- Polymer & solvent ⟷
- Miscible non-solvent

Anatomy of a Spinneret

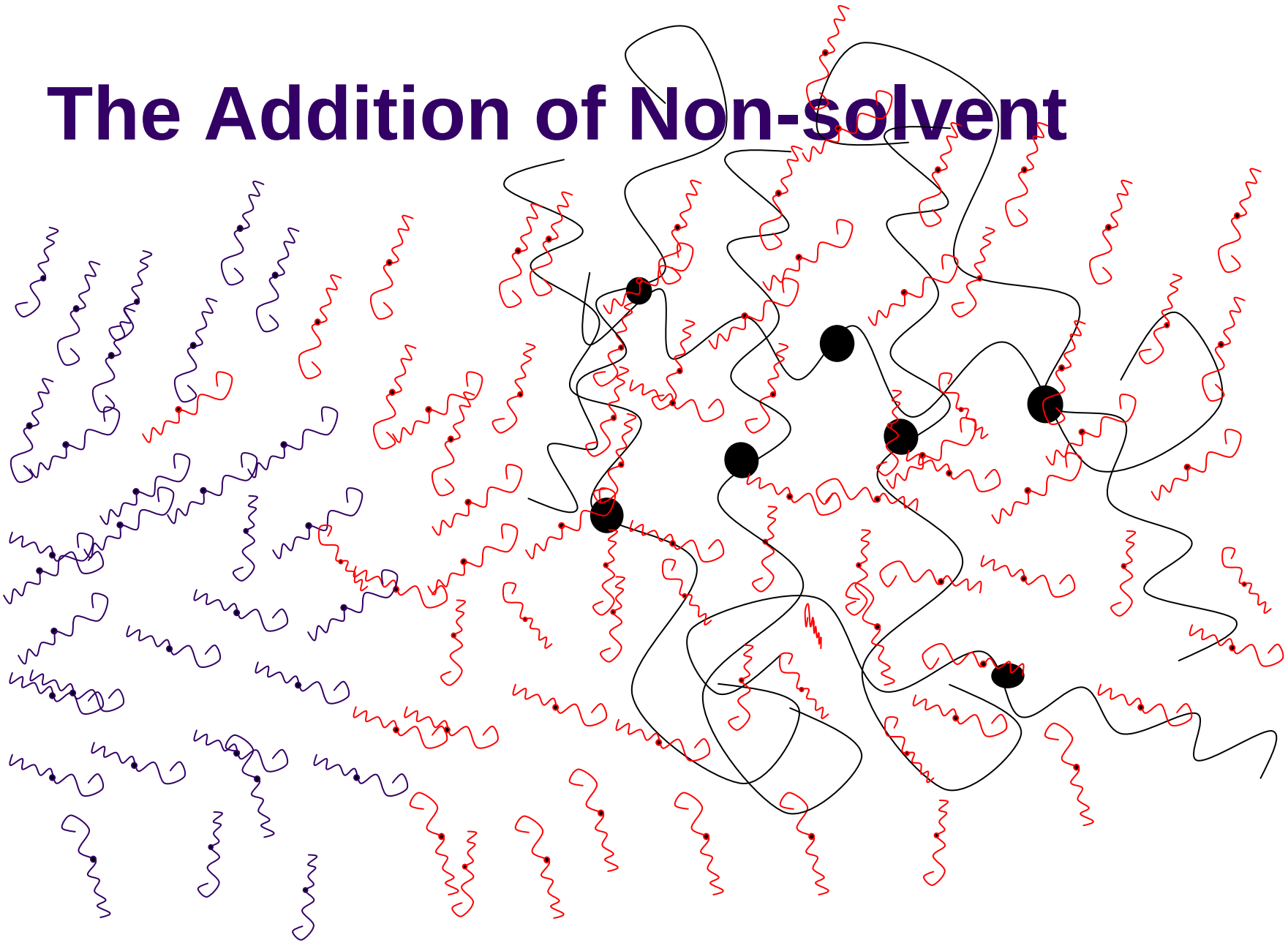




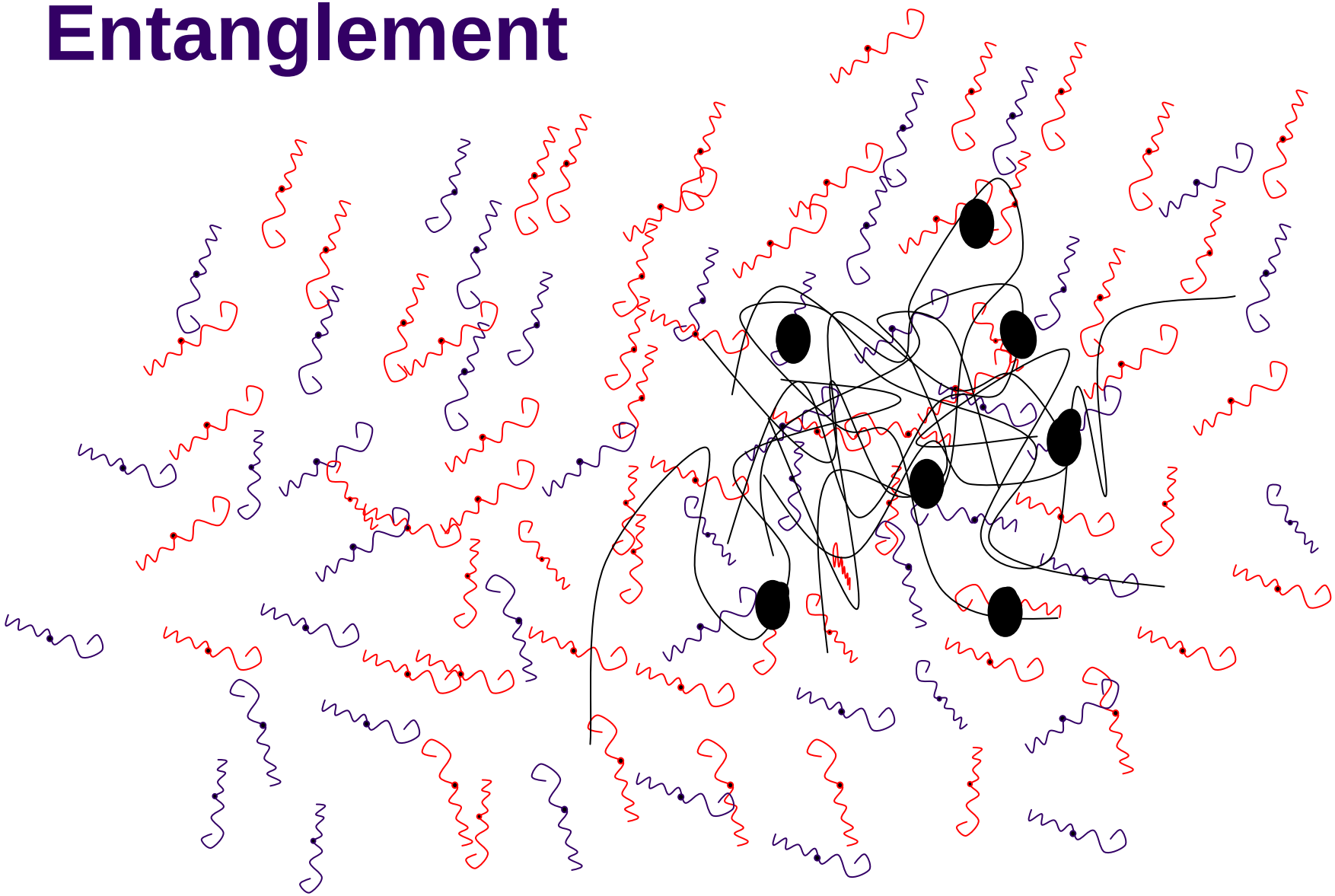
Polymer Solution



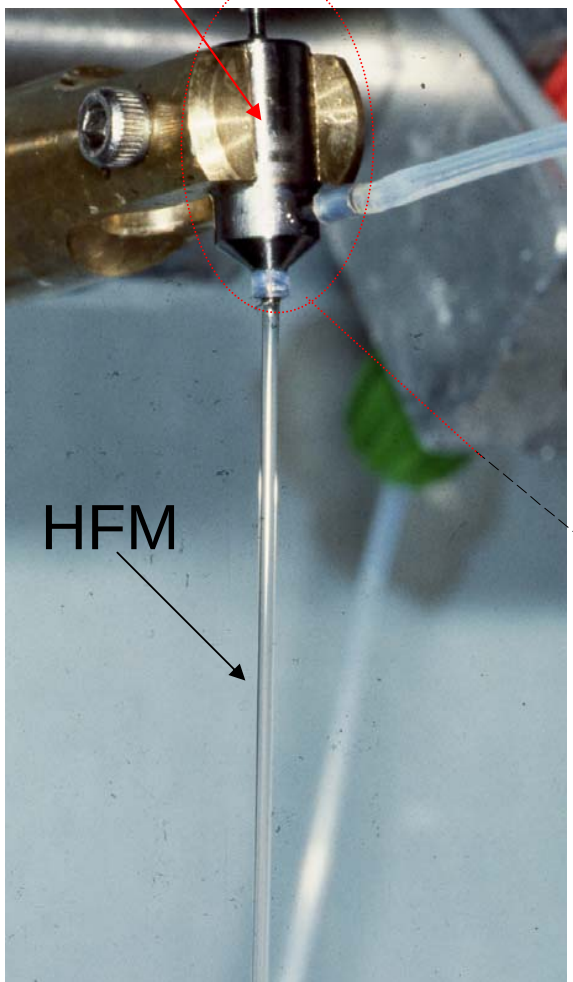
The Addition of Non-solvent

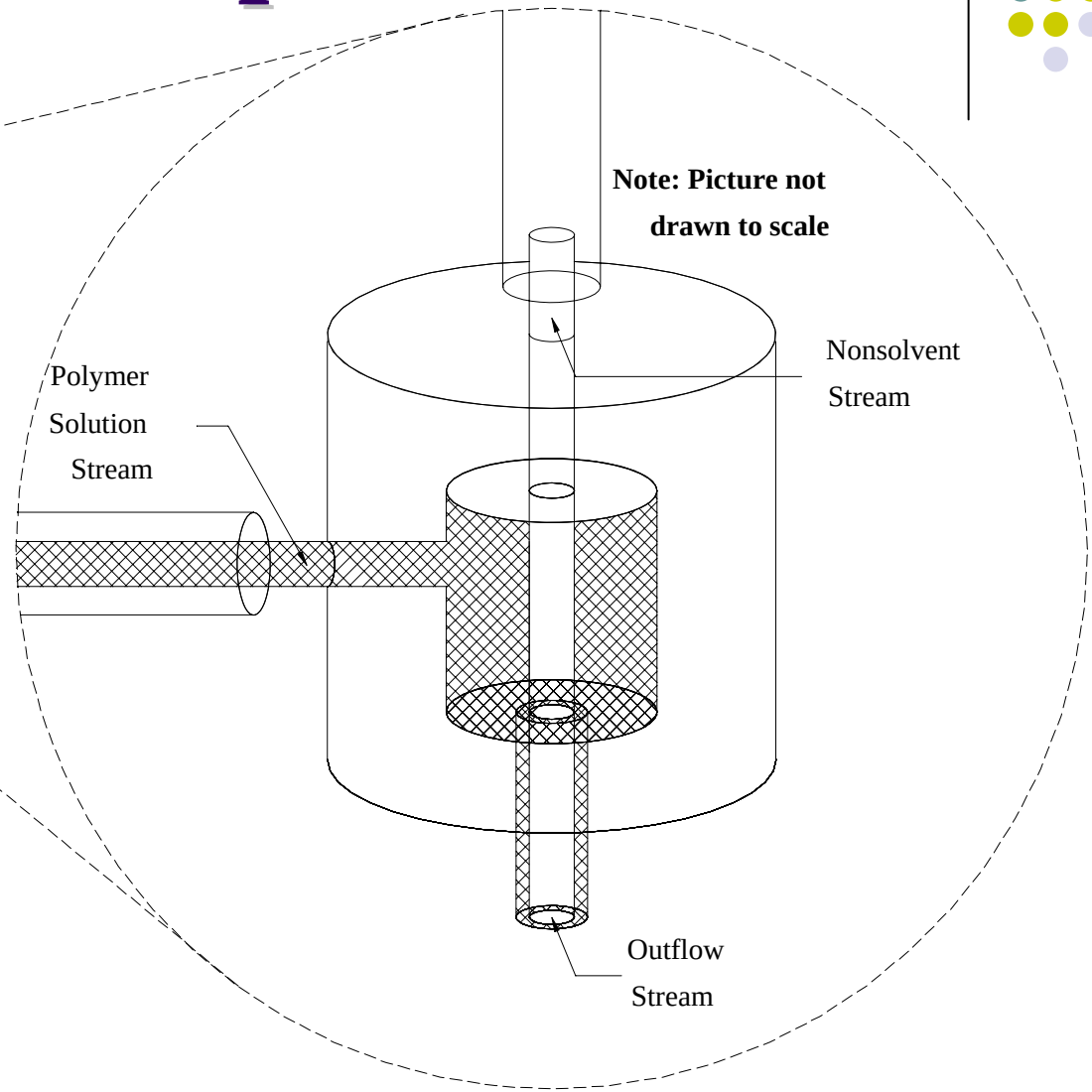


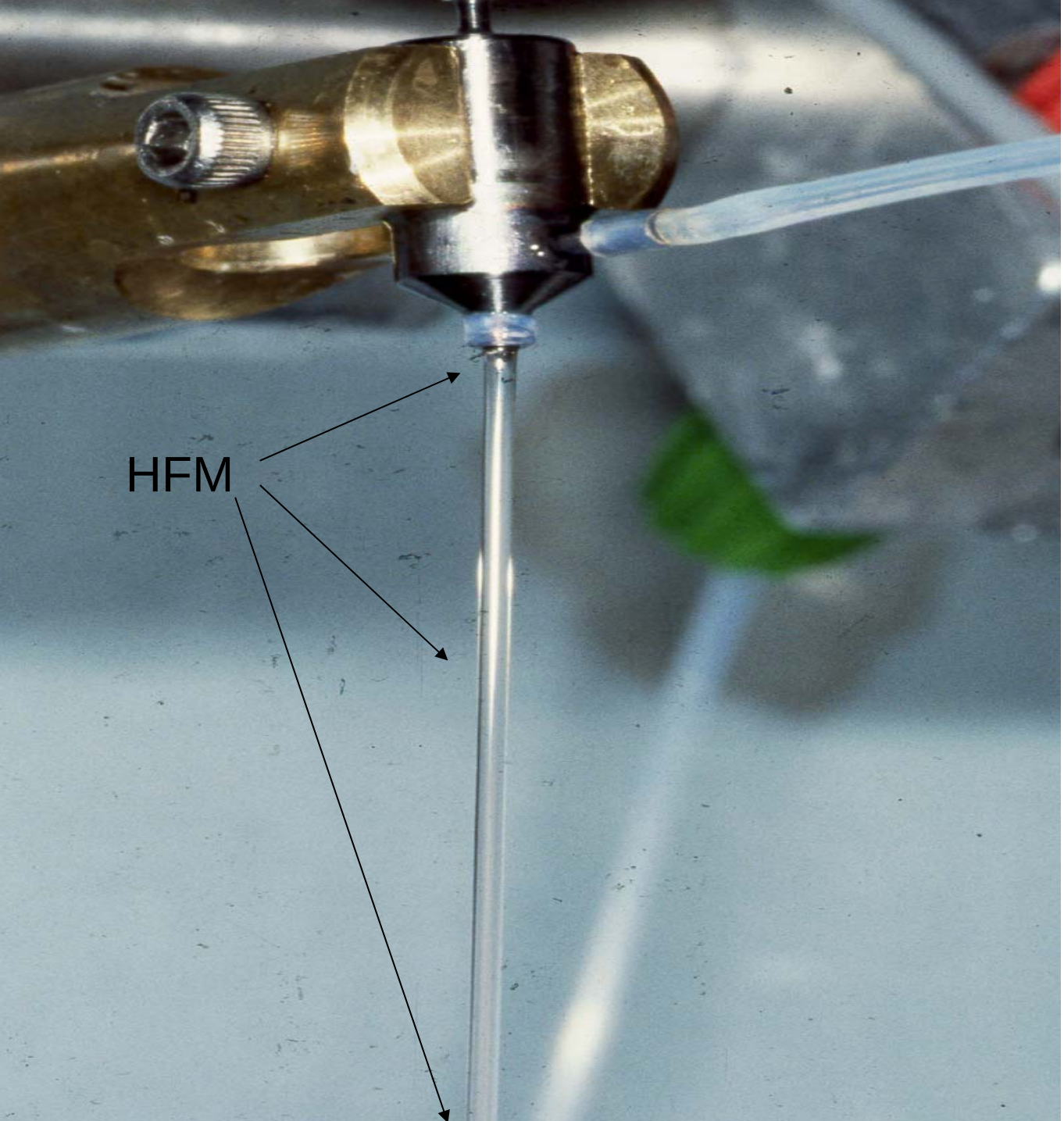
Precipitation with Chain Entanglement



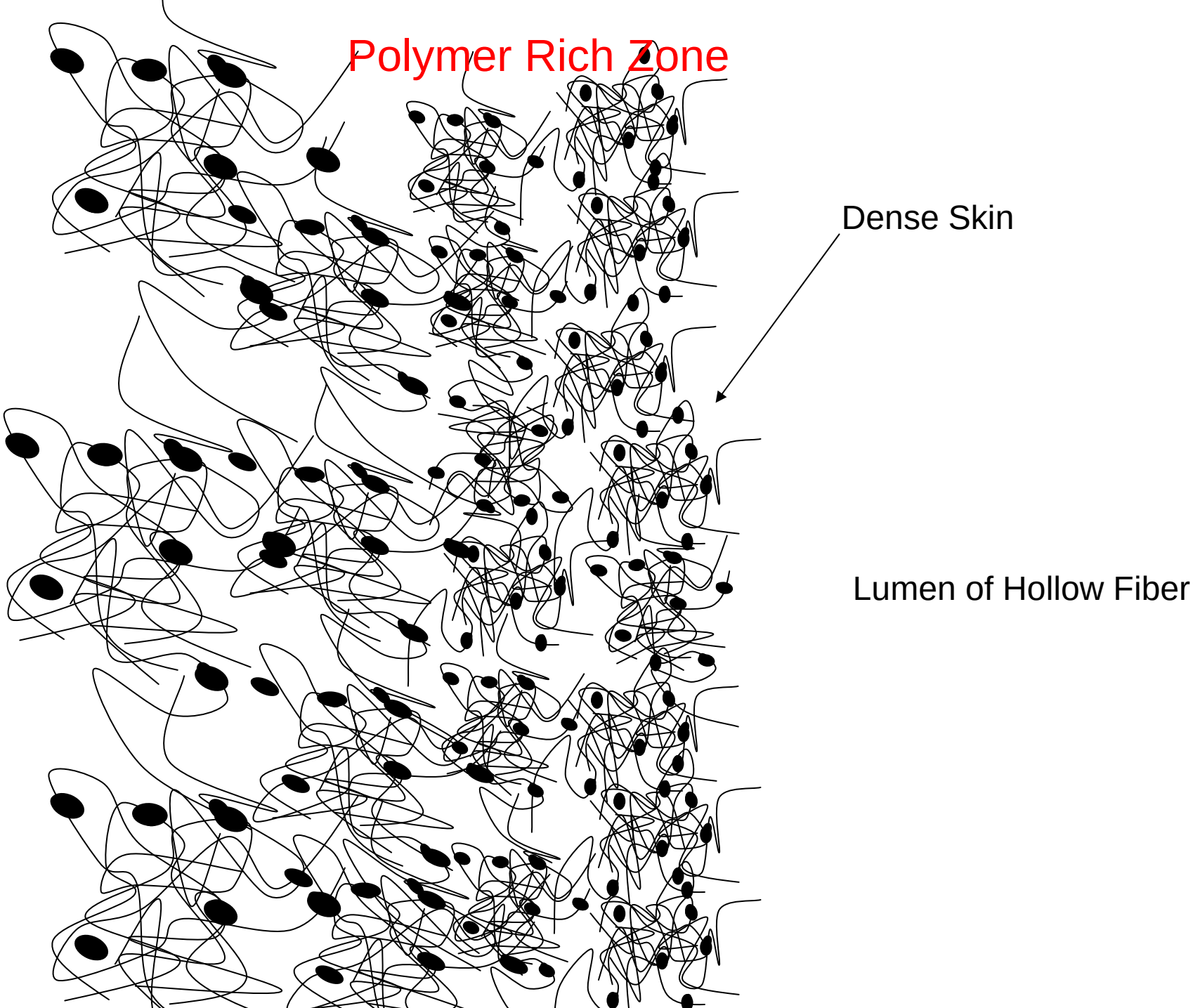
Anatomy of a Spinneret

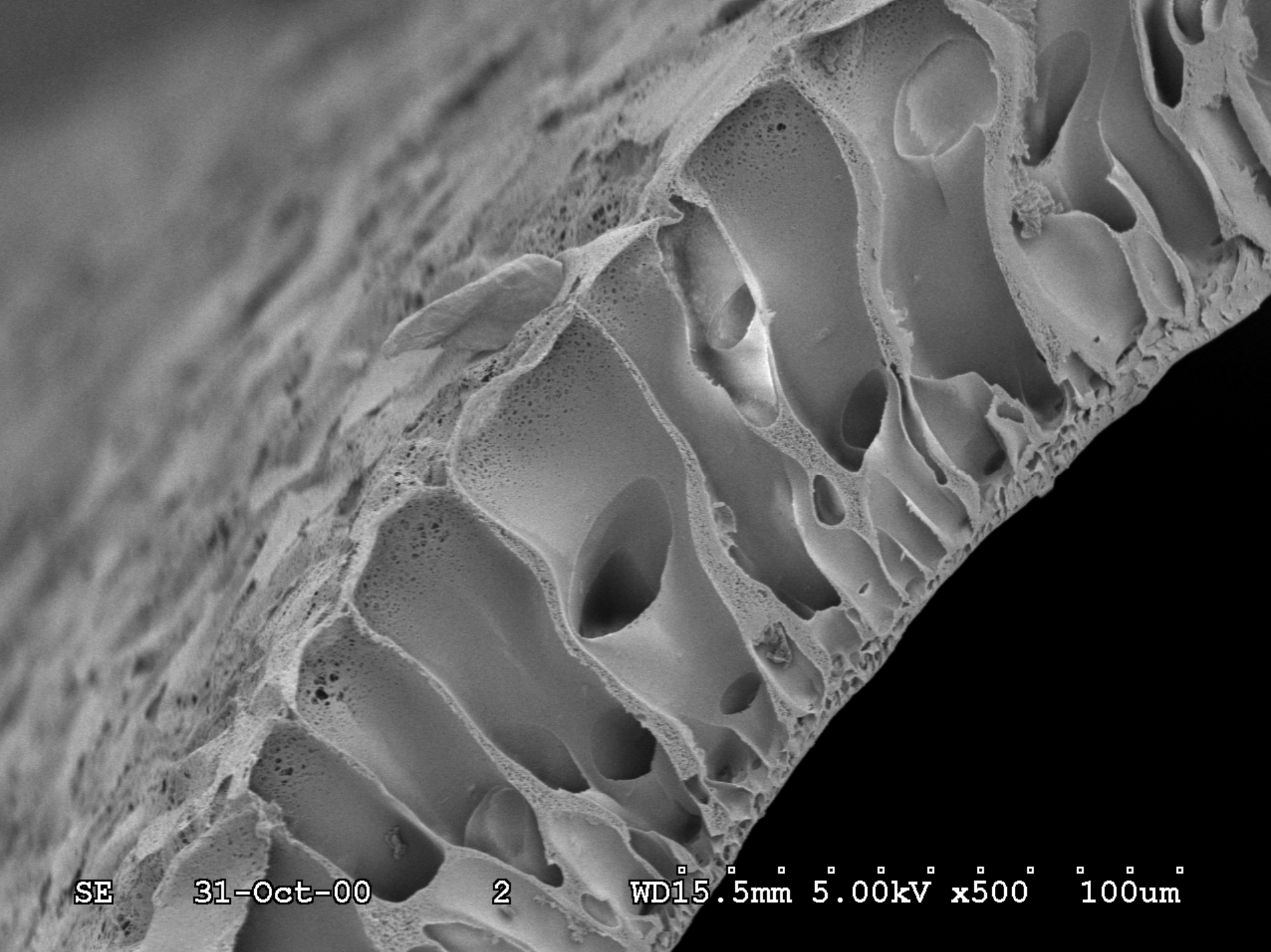




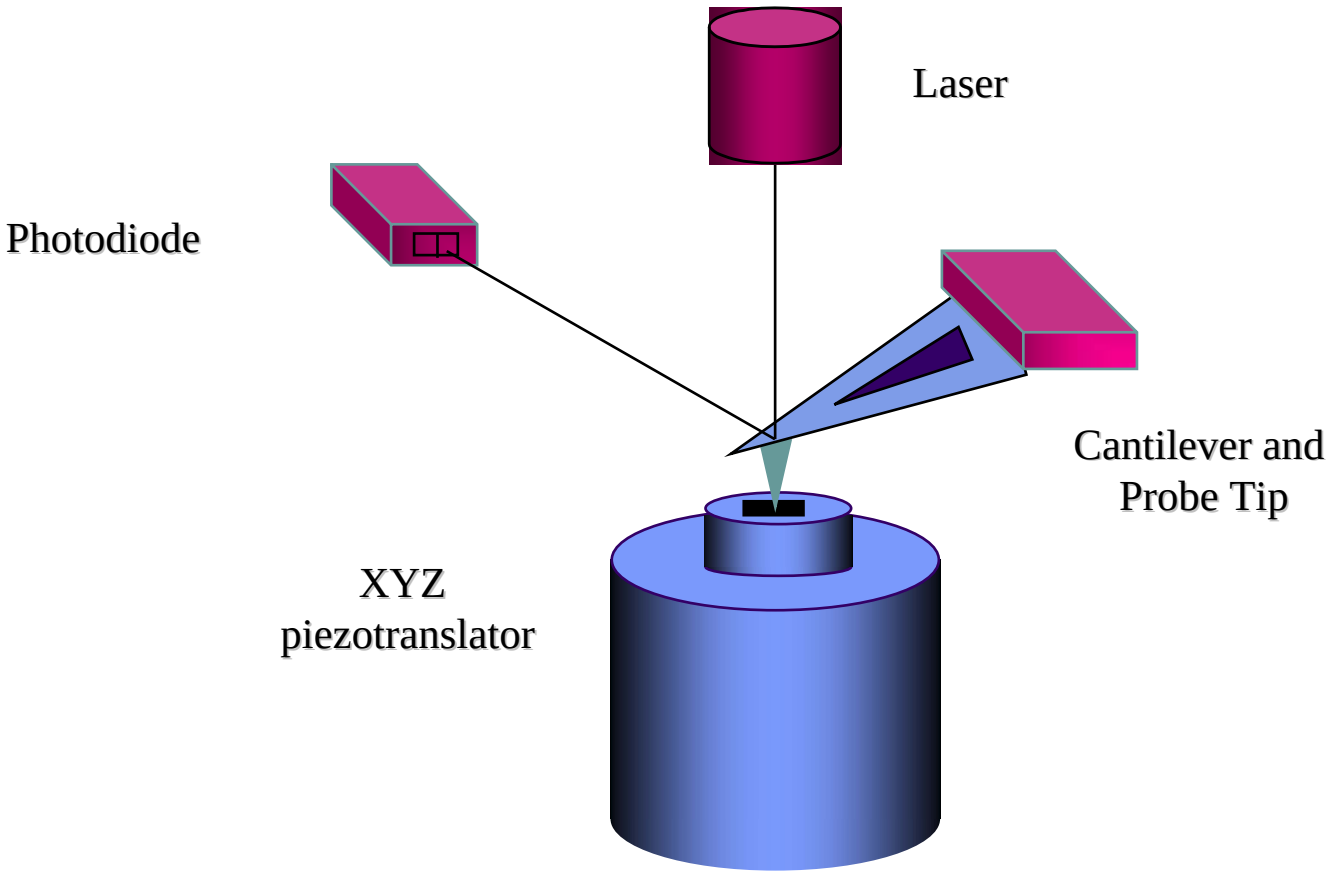


Various Stages in the Early Life of a HFM

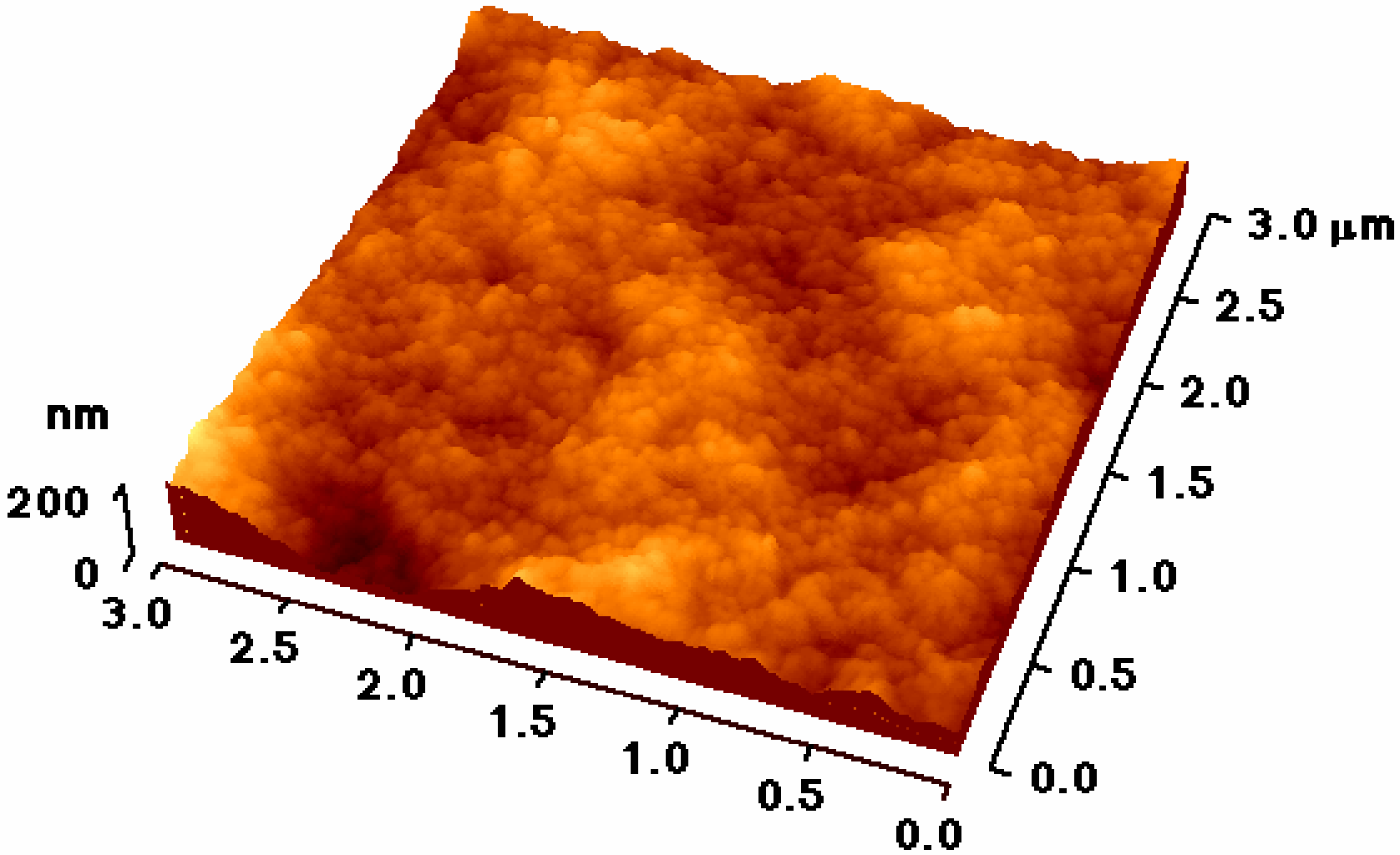

Polymer Rich Zone
Dense Skin
Lumen of Hollow Fiber


SE 31-Oct-00 2 WD15.5mm 5.00kV x500 100um

Topography of Selective Skin Layer

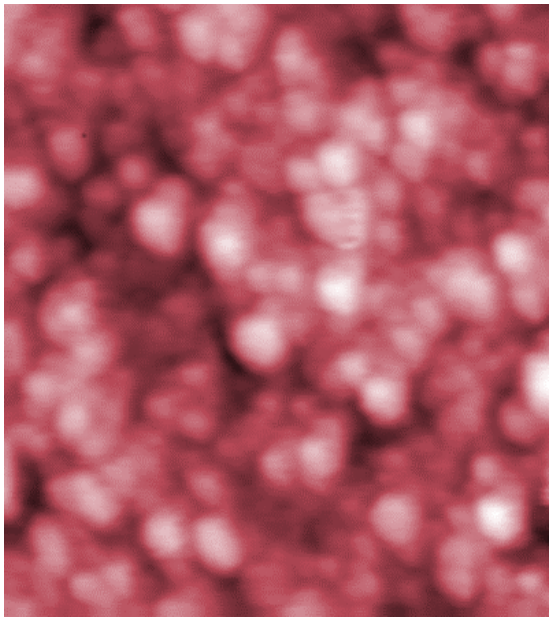


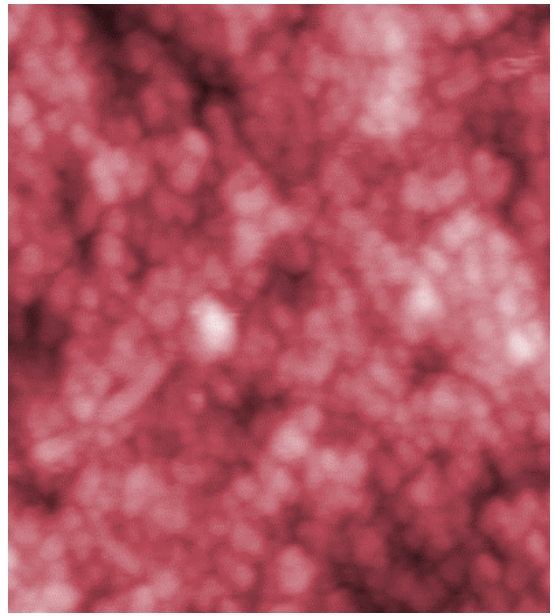
Inner Skin Ultra-topography



4° C - 100% H_20 Quench

22° C - 100% H_20 Quench

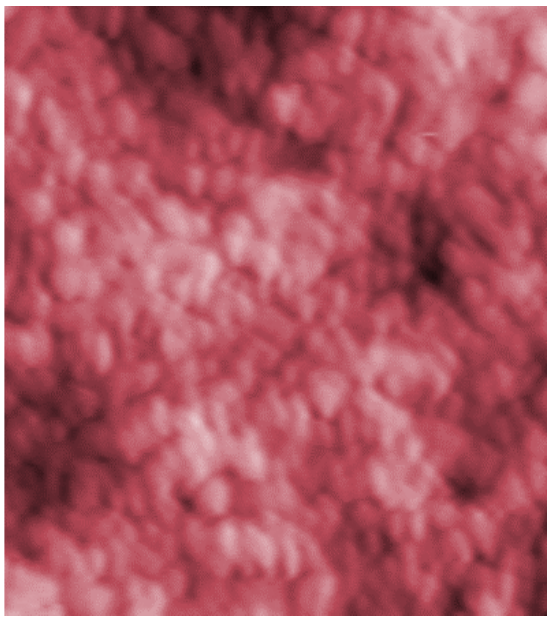


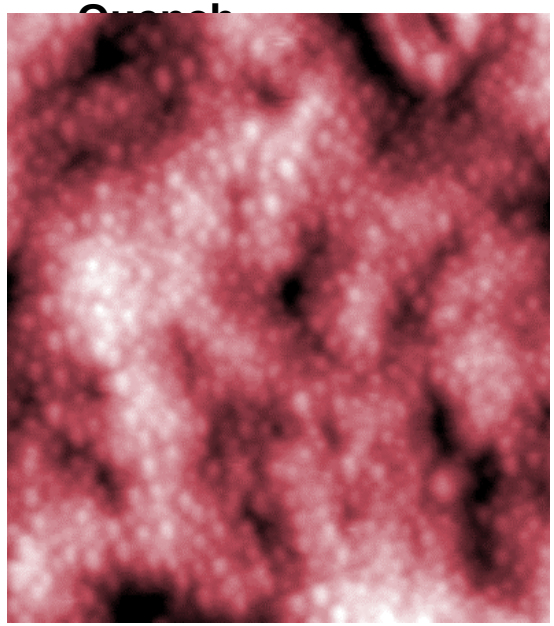


1000 x 1000 nm

54° C - 100% H_20 Quench

54° C - 50/50 DMF/H_20 Quench

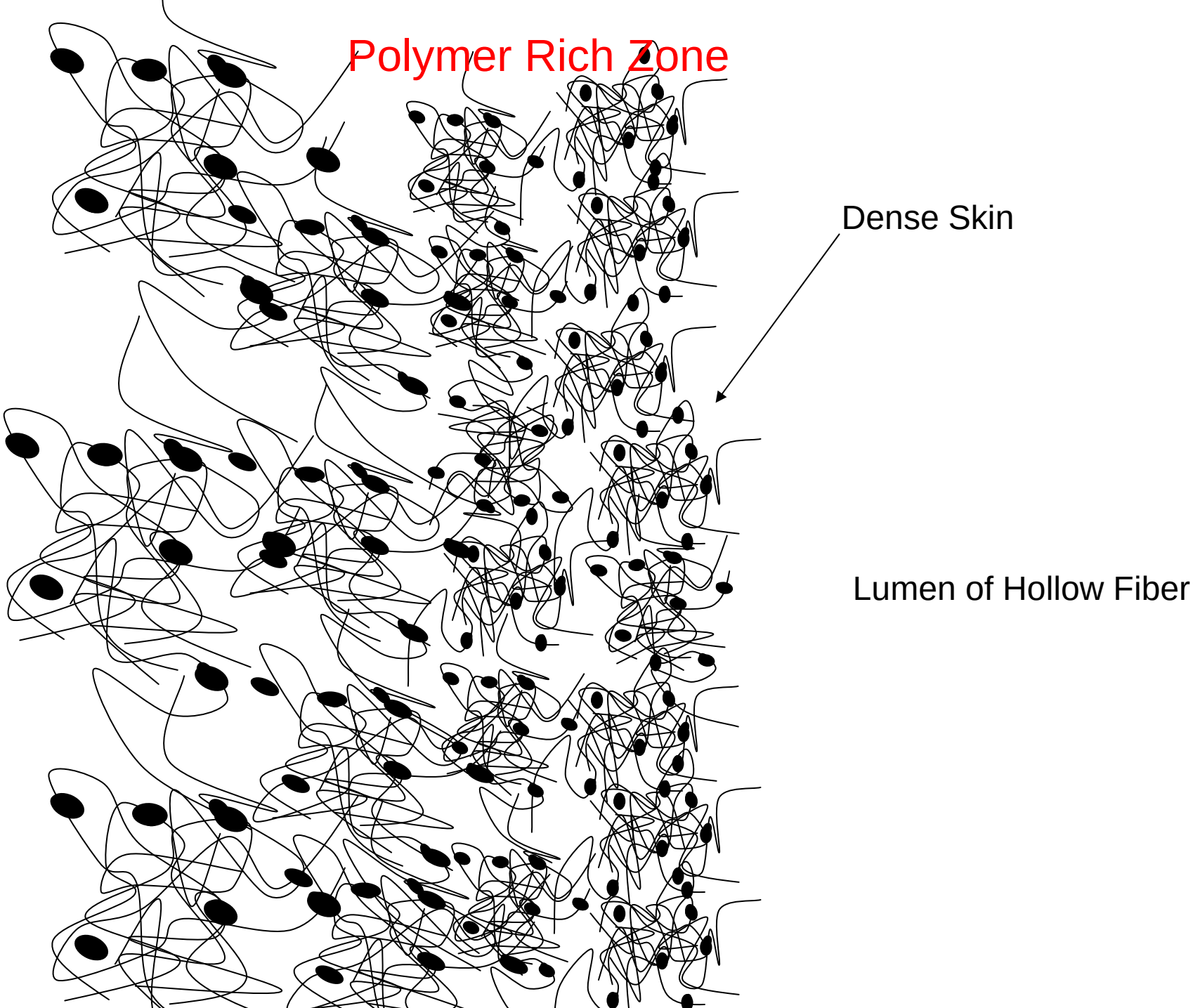




35

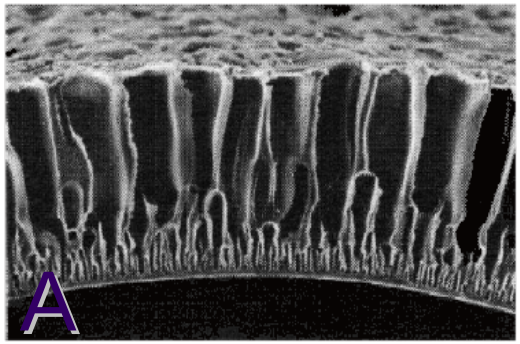
nm

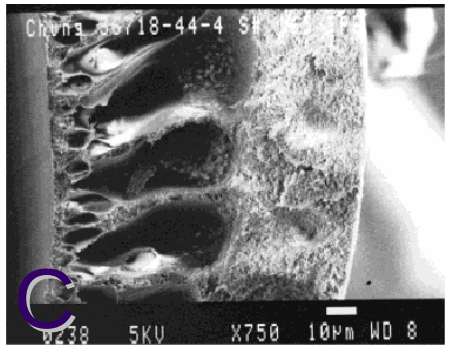
0

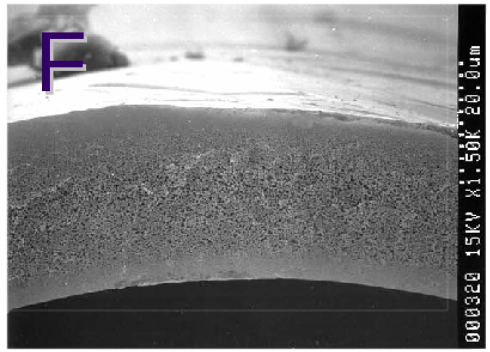

Polymer Rich Zone
Dense Skin
Lumen of Hollow Fiber

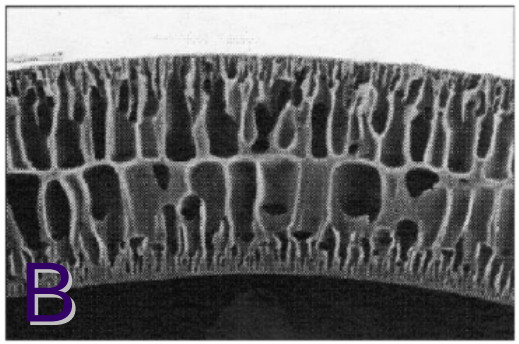
Production Spinning Line

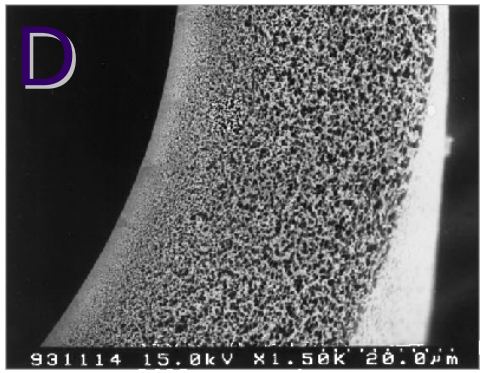
On a Larger Scale Various Structures are Apparent and can be controlled by changing Fabrications conditions

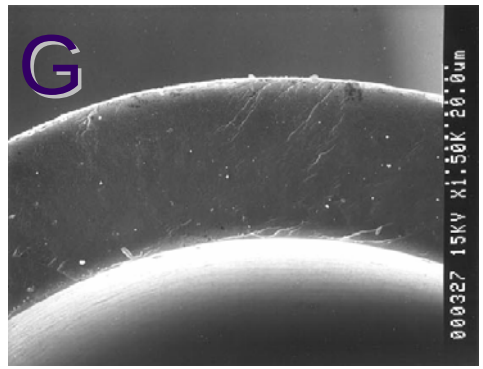




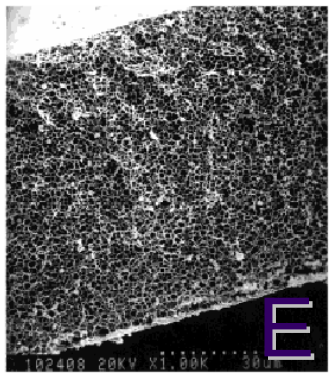


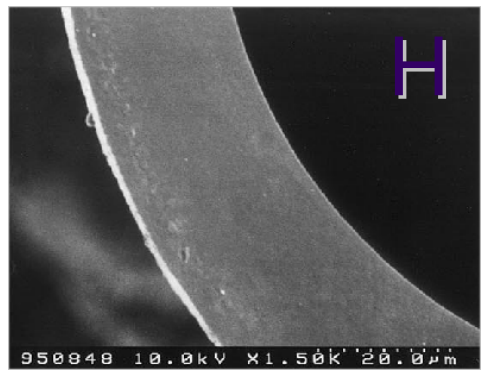




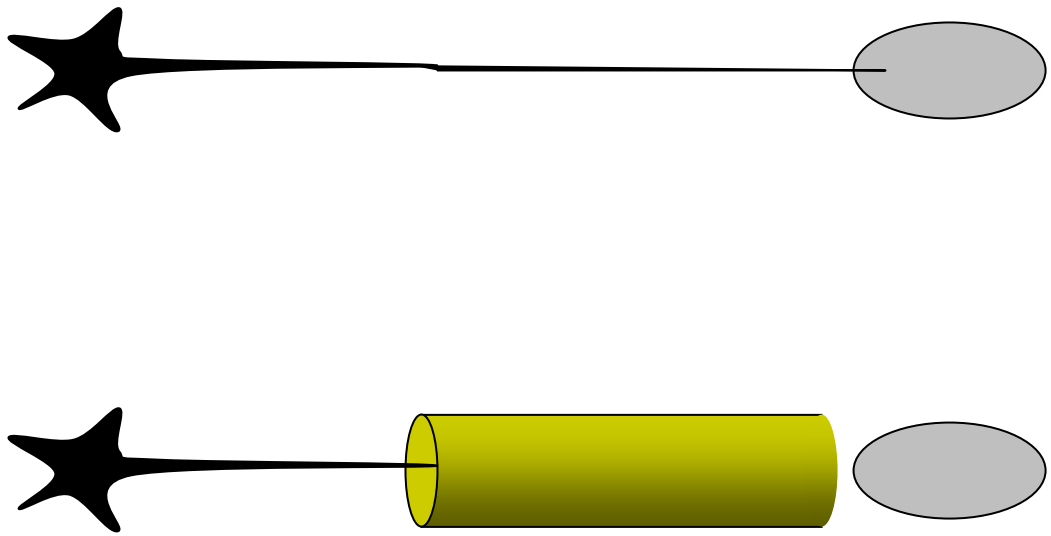


A	PAN-PVC	Li et al. 1998
B	PAN-PVC	Li et al. 1998
C	Polyimide	Chung et al. 1992
D	Polysulfone	Valette et al.1999
E	Cellulose acetate	Hao et al. 1996
F	PAN copolymer	Valette et al.1999
G	AN69	Valette et al.1999
H	PMMA	Valette et al.1999

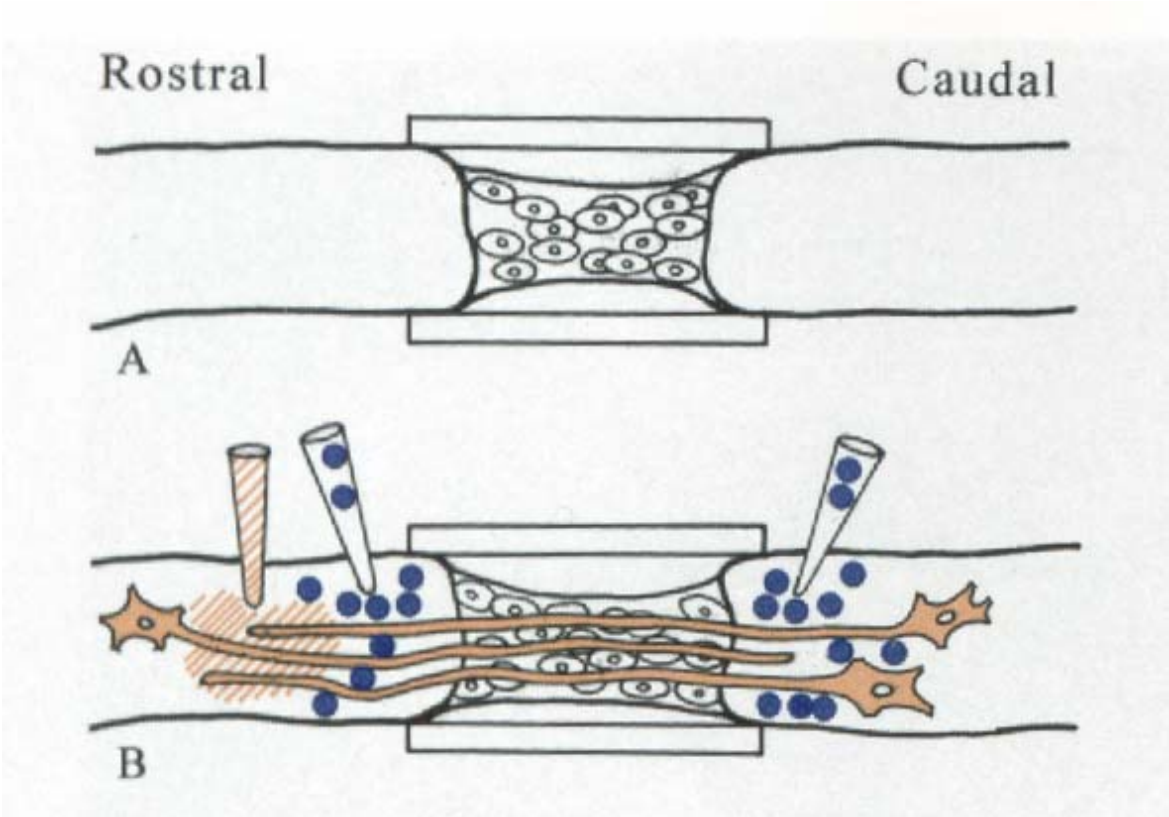




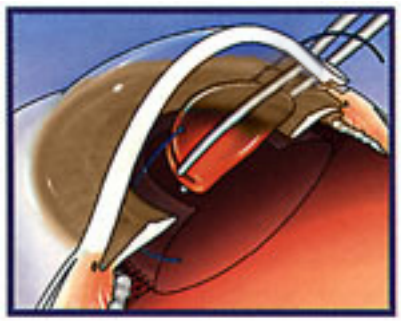
Nerve Track Repair: Bridging Substrates

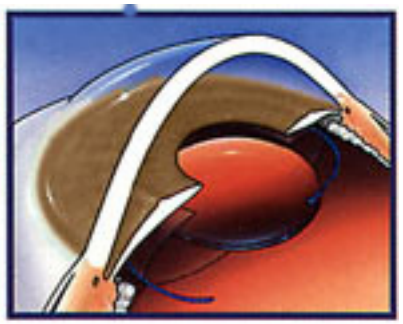


Nerve Repair-Entubulation



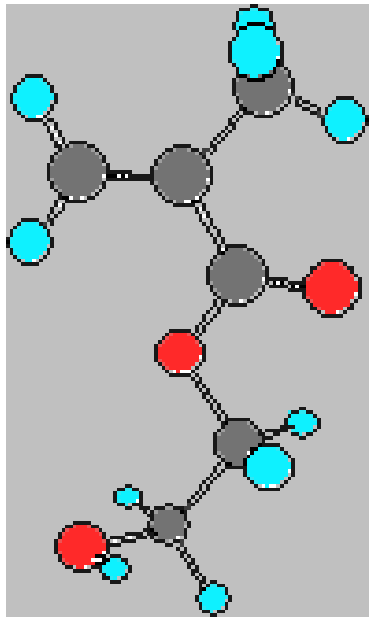
Hydrogels





Folded Lens in Incision

Unfolded in the Eye



Definition

-water insoluble, three dimensional network of polymeric chains that are crosslinked;

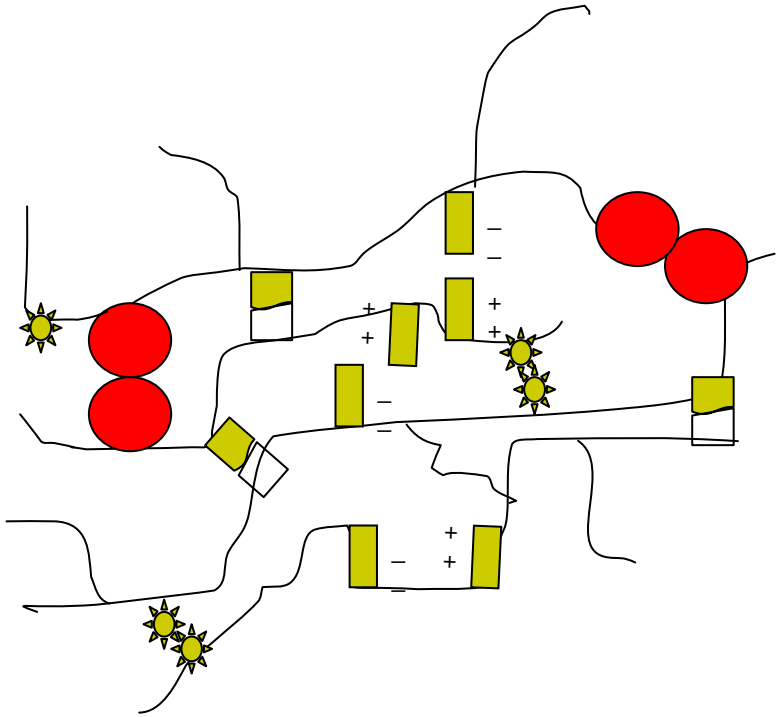
-polymers capable of swelling substantially in aqueous conditions (eg hydrophilic)

-polymeric network in which water is dispersed throughout the structure

-typically in the swollen state the mass fraction of water is much higher than the mass fraction of polymer.

The Cross-links may be physical or chemical:

- by reaction of one or more monomers with pendant functional groups
- Electrostatic, hydrogen or van der Waals interactions (physical), heating creates a solution;
- Covalent bonds (chemical)



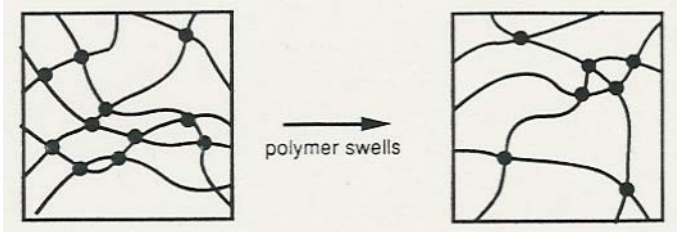
Hydrogels

- One or more highly electronegative atoms which results in charge asymmetry favoring hydrogen bonding with water;
- hydrophilic nature -dry materials absorb water;
- By definition, water must constitute at least 10% of the total weight (or volume) for a materials to be a hydrogel;
- When the content of water exceeds 95% of the total weight (or volume), the hydrogel is said to be superabsorbant;

Hydrogels: Swelling

- Degree of swelling can be quantified by:
  - ratio of sample volume in the dry state to sample volume in the swollen state;
  - weight degree of swelling: ratio of the weight of swollen sample to that of the dry sample

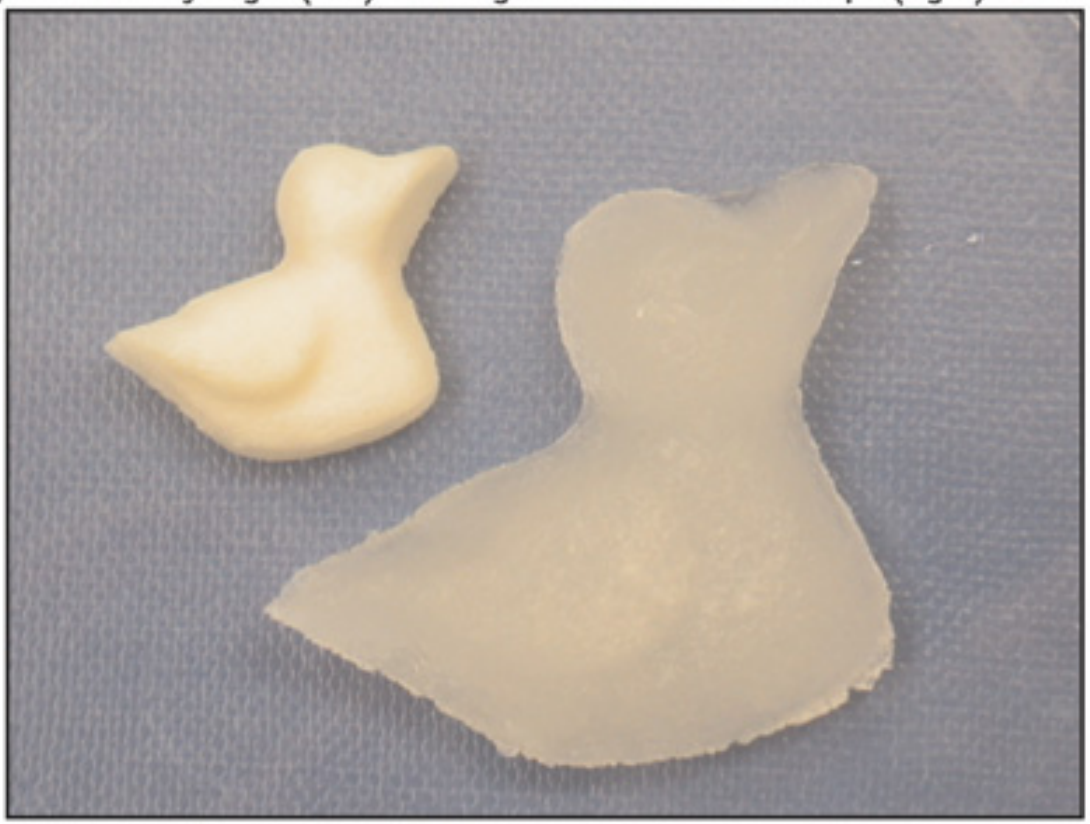
Hydrogels:



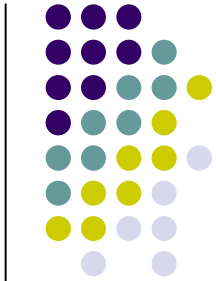
- In a chemically cross-linked hydrogel, all of the polymer chains are connected by covalent bonds to form a network; and, thus
- The material can be viewed as one molecule of large size or supramacromolecule;
- The thermodynamically driven swelling force is counterbalanced by the retractive force of the crosslinked structure;
- The unique property of these gels is there ability to maintain their original shape during and after swelling;
- Two forces become equal at some point and equilibrium is reached

FIGURE 1

Swelling of a dried hydrogel (left) to a larger size of the same shape (right) in water.



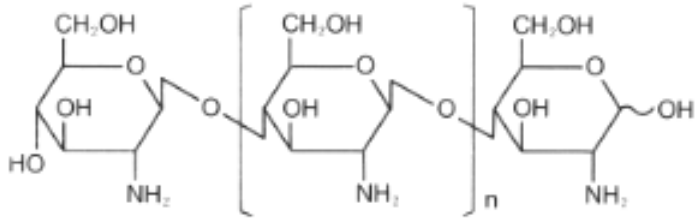
Xerogels



- Dried hydrogels;
- Usually clear and swelling in water takes a long time;
- The swelling behavior is due to slow diffusion of water through the compact polymer chains;
- A useful property in controlled drug delivery;

Chitosan

Sample: Chitosan

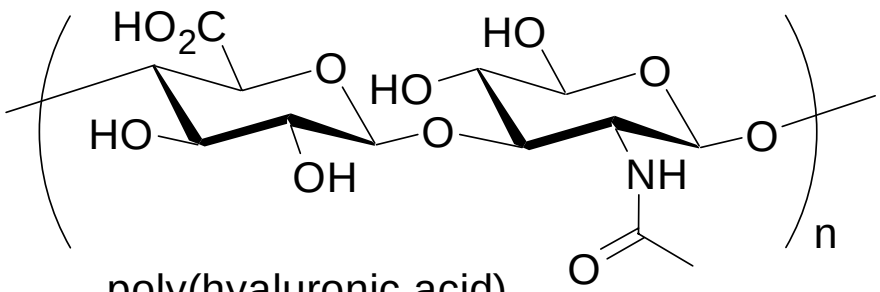


Hydrogels: Swelling

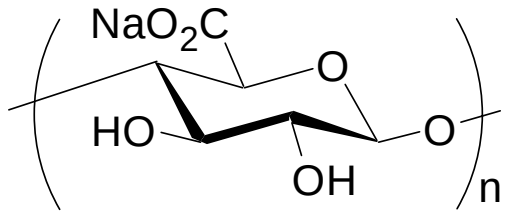
- Why is the degree of swelling important?
  - solute diffusion coefficient through the hydrogel
  - surface properties and surface mobility
  - optical properties (particularly for contact lens applications)
  - mechanical properties

Hydrogel Forming Polymers

Natural

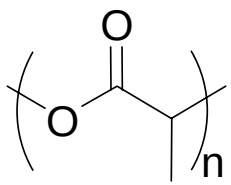


poly(hyaluronic acid)

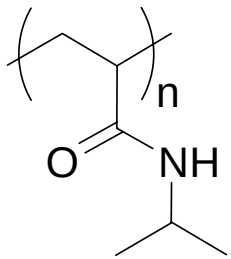


poly(sodium alginate)

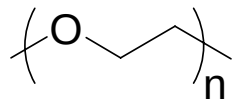
Synthetic



poly(lactic acid)

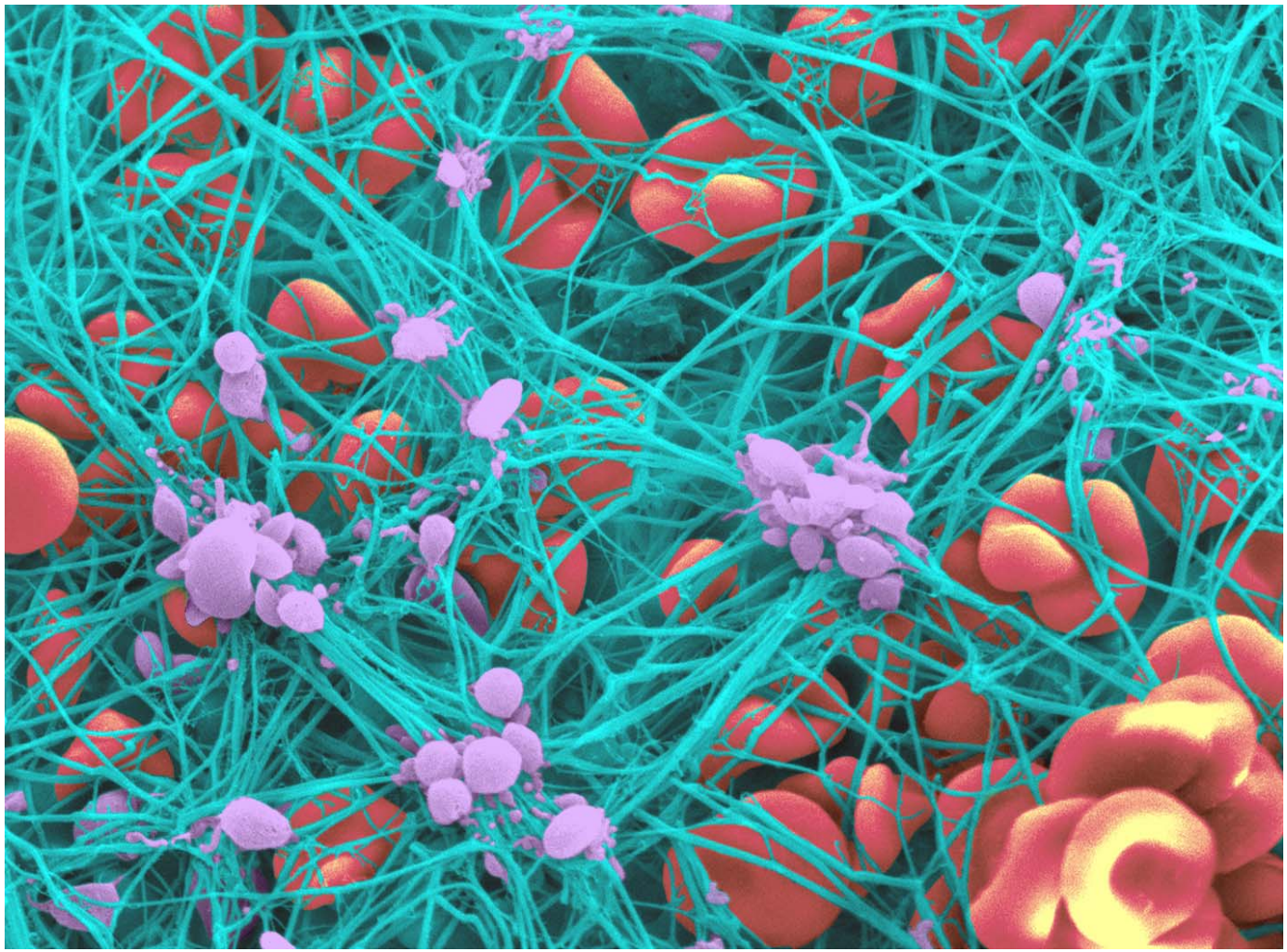


poly(N-isopropyl acrylamide)



poly(ethylene glycol)

Fibrin Hydrogel (Blood Clot)



Hydrogels

Highly swollen hydrogels:

- cellulose derivatives
- poly(vinyl alcohol)
- poly(N-vinyl 2-pyrrolidone), PNVP
- poly(ethyleneoxide)

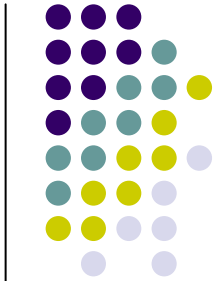
Moderately or poorly swollen hydrogels:

- poly(hydroxyethyl methacrylate), PHEMA and derivatives

One may copolymerize a highly hydrophilic

monomer with other less hydrophilic monomers to achieve desired swelling properties

Examples of biological hydrogels:

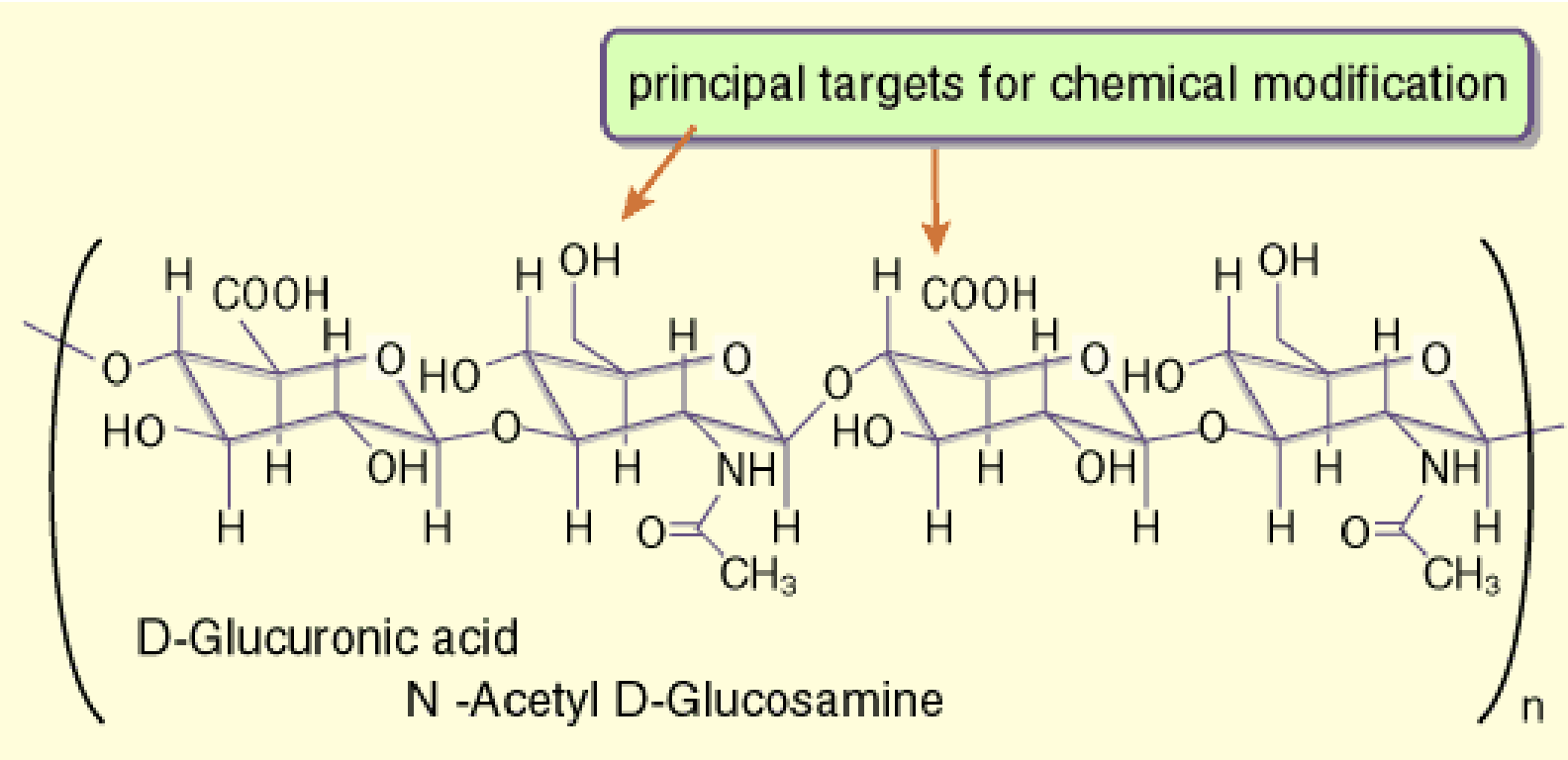


- Jello (a collagen gel ~ 97% water)
- Extracellular matrix components
- Polysaccharides
- DNA/RNA
- Blood clot
- Mucin - lining the stomach, bronchial tubes, intestines
- Gycocalyx - lining epithelial cells of blood vessels
- Sinus secretions

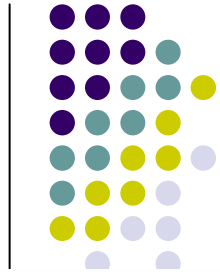
Function of a biological hydrogel

- Decreased permeability to large molecules
- Structural strength (for epithelial cell walls)
- Capture and clearance of foreign substances
- Decreased resistance to sliding/gliding
- High internal viscosity (low washout)

Hylauronic Acid



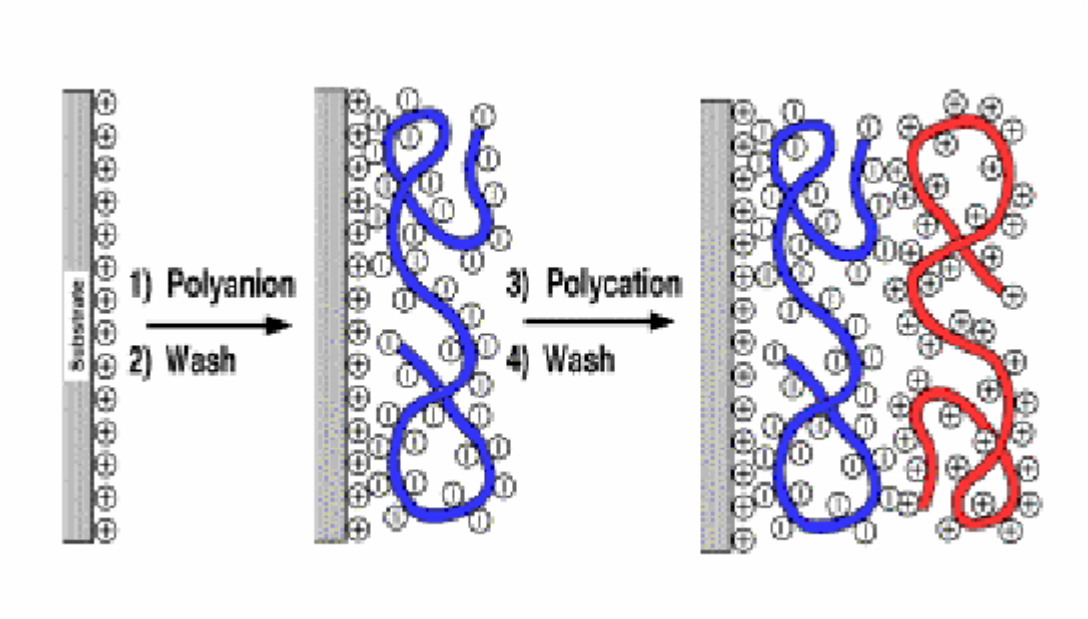
Polyelectrolyte Hydrogels



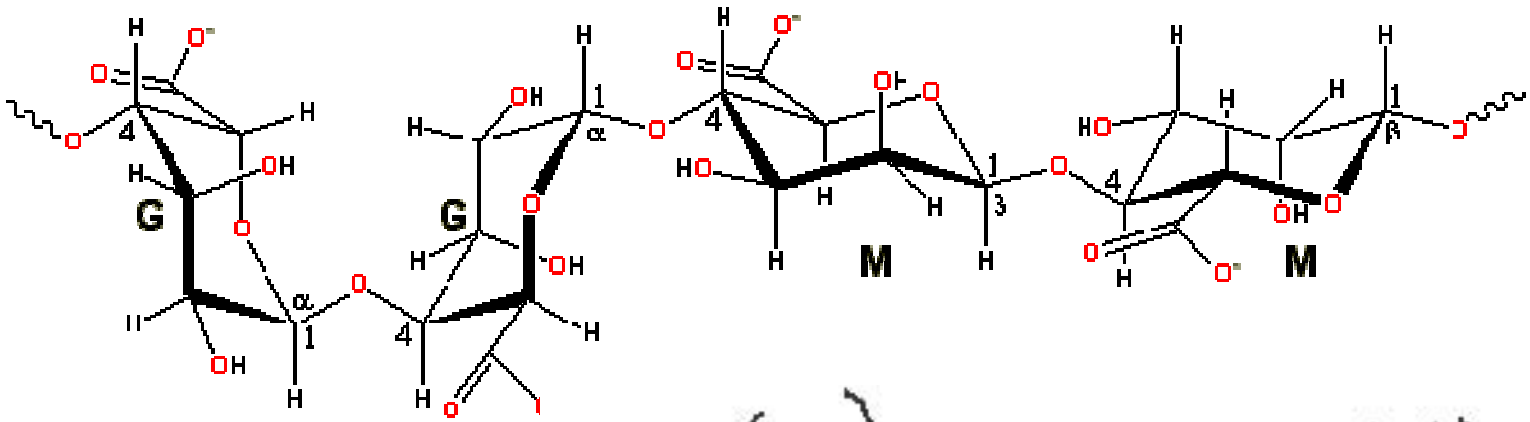
- Polyelectrolytes studied as coacervates for biomaterials:[4]
  - Polyanions
    - Carboxymethylcellulose
    - Alginate
    - Dextran sulfate
    - Carboxymethyl dextran
    - Heparin
    - Carrageenan
    - Pectin
    - xanthan
  - Polycations
    - Chitosan (derived from crab shells)
    - Polyethyleneimine
    - Poly(4-vinyl-N-butylpyridinium) bromide
    - Quarternized polycations
    - Poly(vinylbenzyltrimethyl)ammonium hydroxide

Polyelectrolyte Multilayers

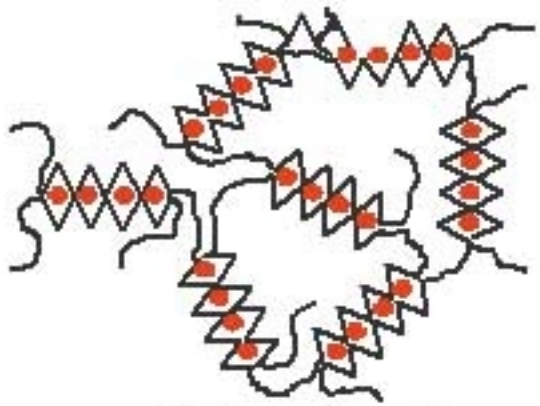
Layer by layer deposition



Alginate gels



M-rich network

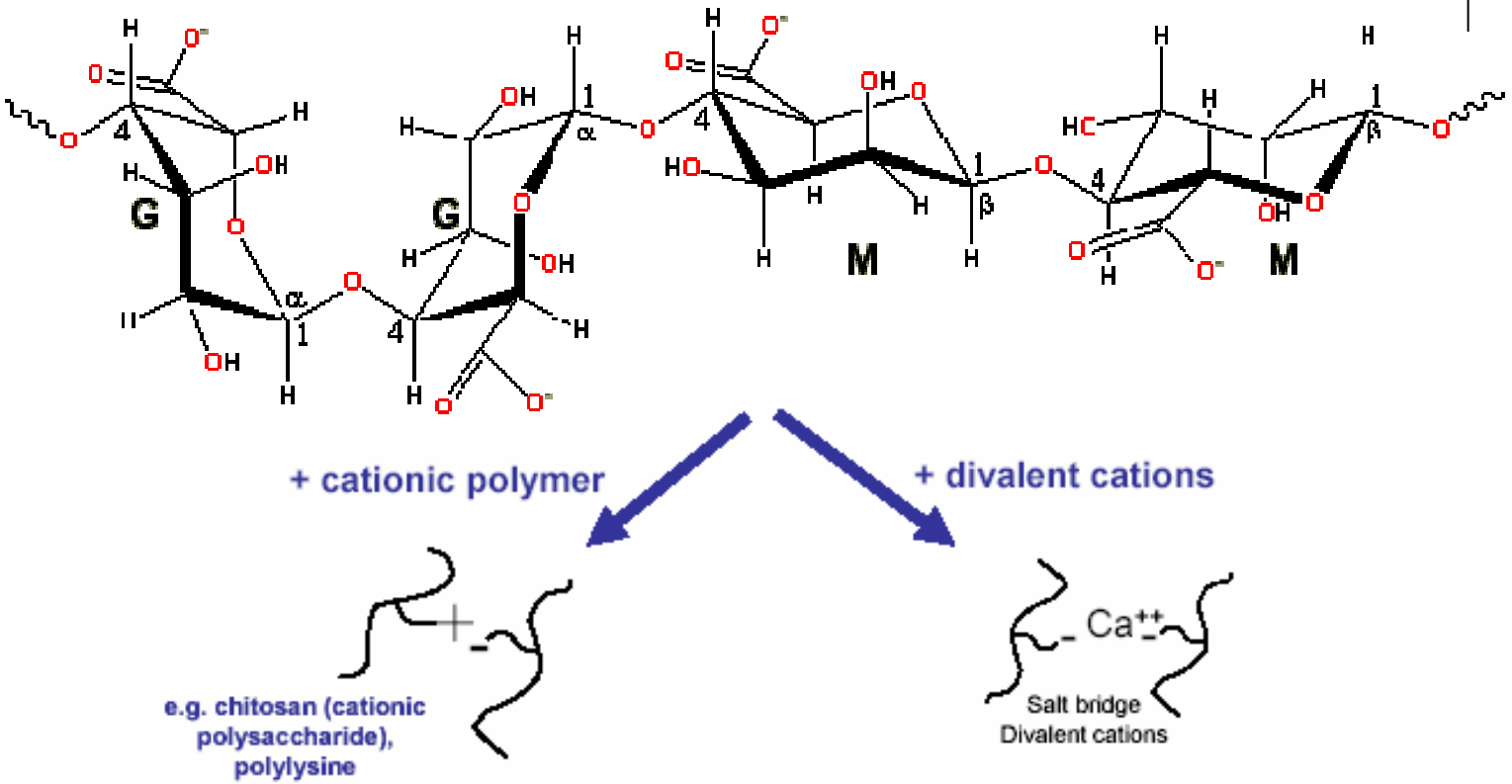


G-rich network

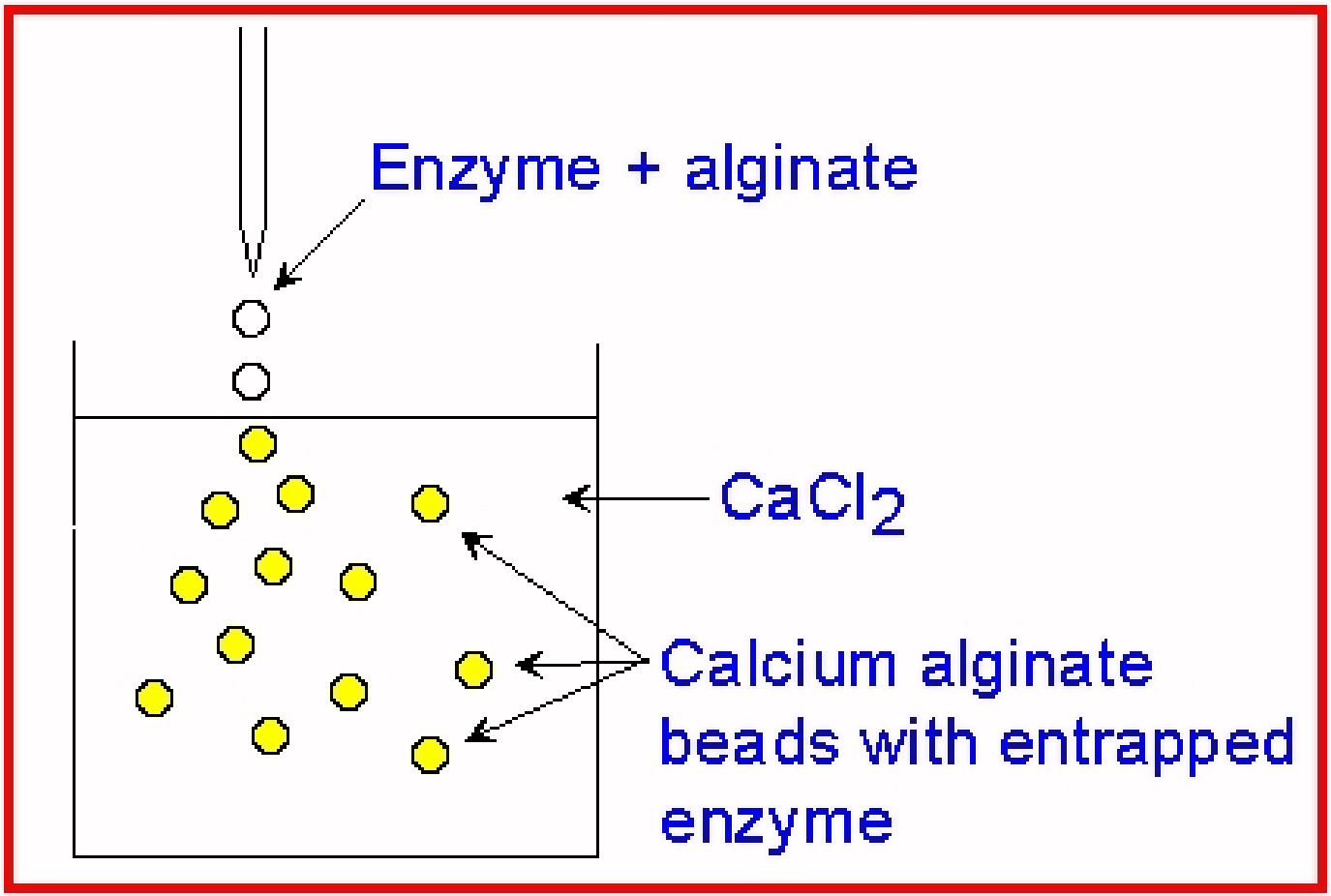
represents M-fractions

represents cross-linked G-fractions

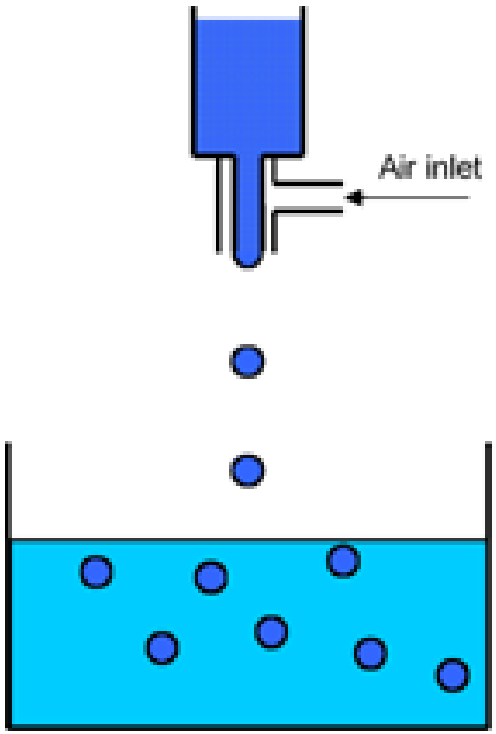
Alginate gels

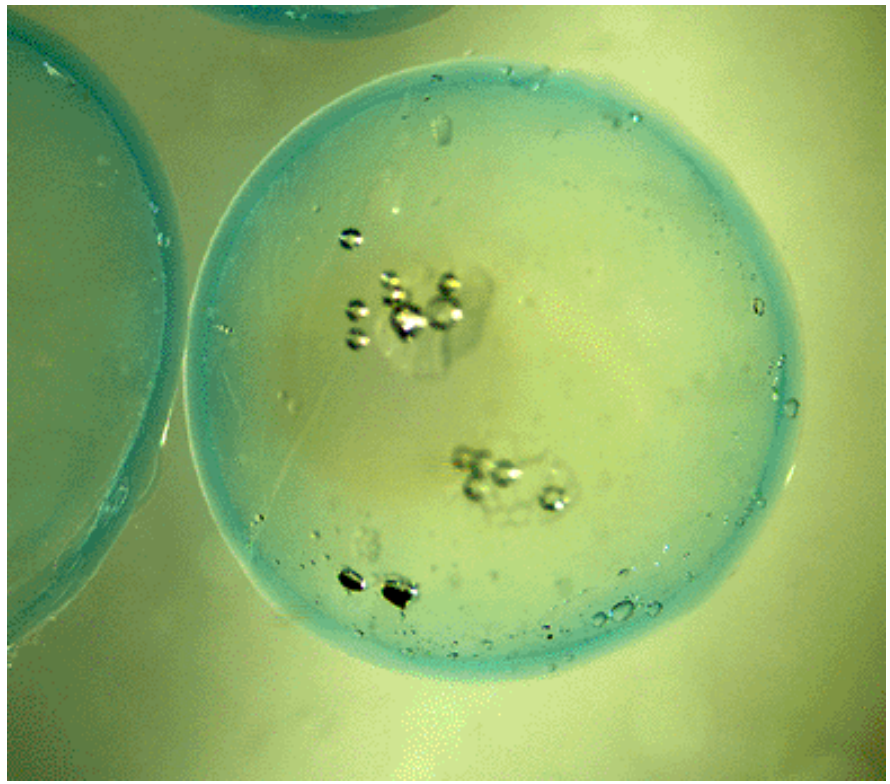


Enzyme Immobilization

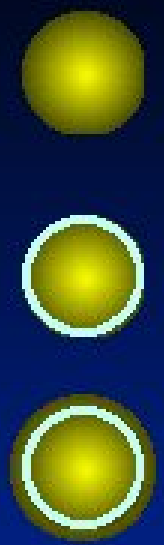


Cell Encapsulation





Microencapsulation Method



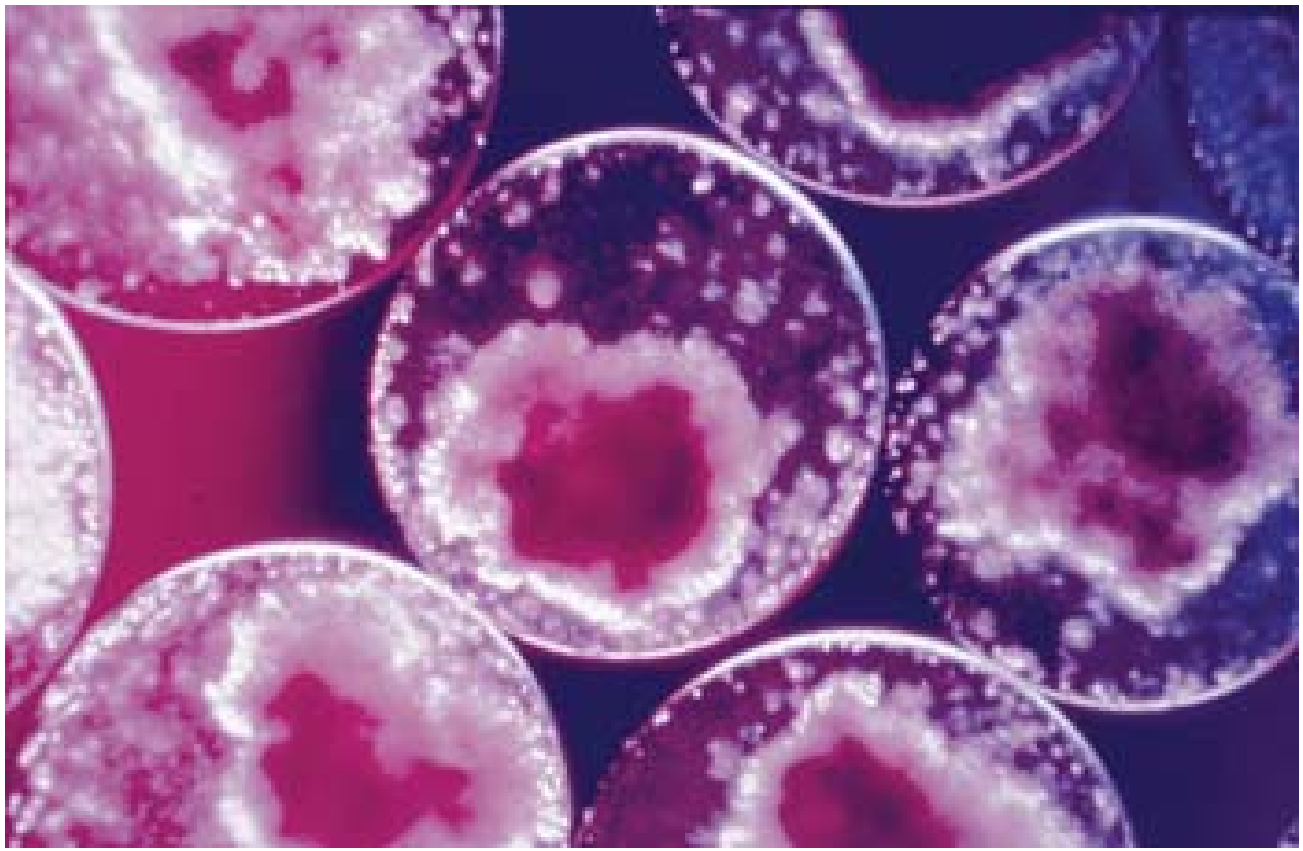
Cells in Alginate Beads

Poly-L-Lysine layer Added

Second Layer of Alginate Added

Encapsulated Cells maintained in regular tissue culture

APA CAPSULES



Applications

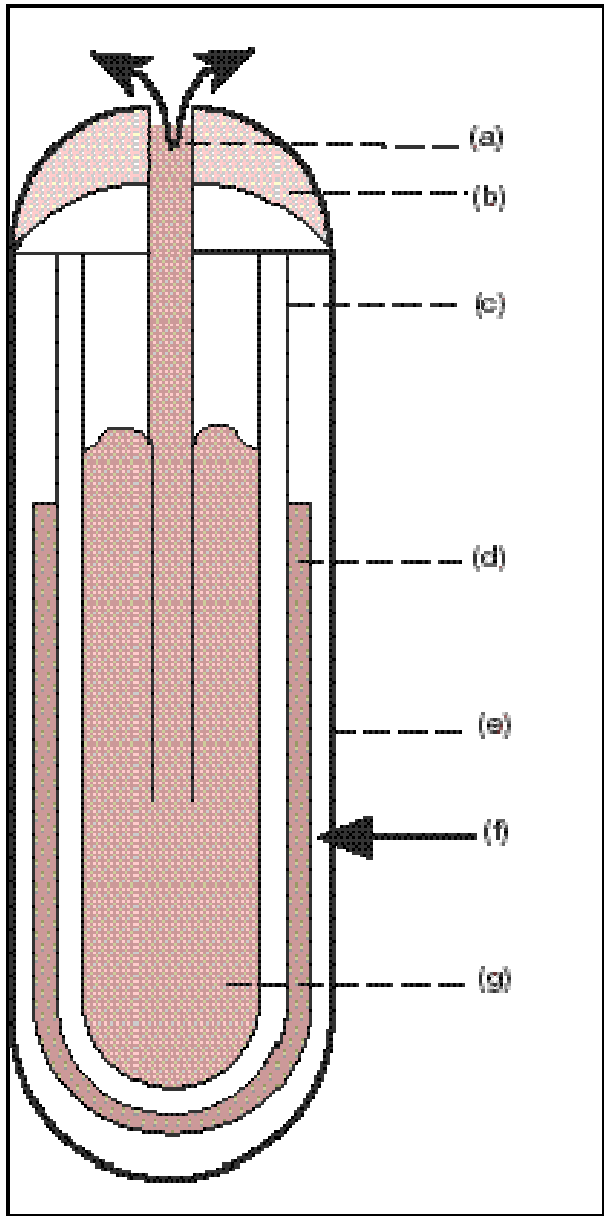
Pharmaceutical applications

- monomer composition and relative amounts of multi-polymer hydrogels can be varied to alter the diffusion characteristics; and
- permeability of the gel containing pharmaceutical agents

Delivery

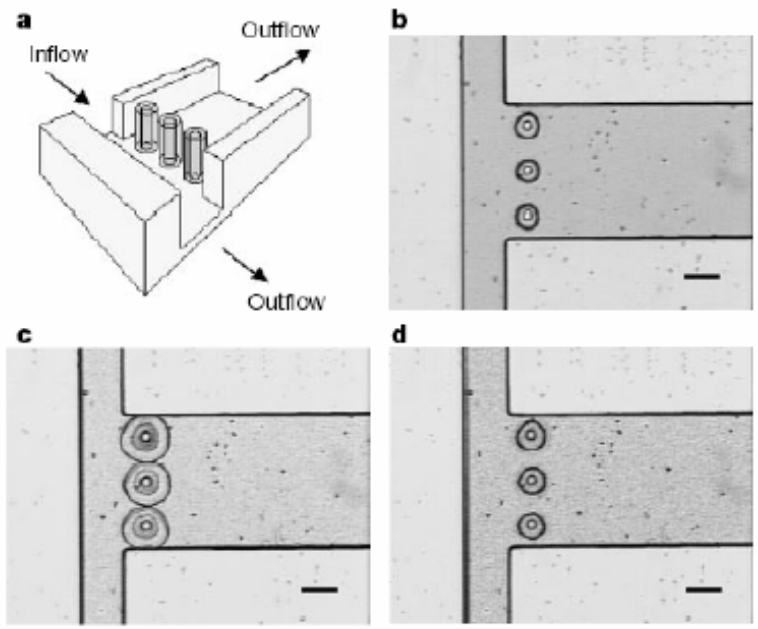
- drug gets trapped in the hydrogel during polymerization
- drug introduced during swelling in water
- Release occurs by outflow of drug from the gel and inflow of water to the gel

Drug delivery

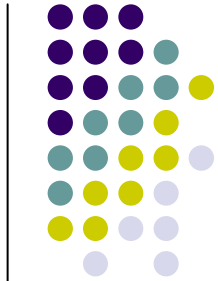


Applications in Biomaterials and Tissue Engineering

- Cell Encapsulation
- Drug delivery
- Surface modification
- Enzyme Immobilizatic
- Biosensors
- Lab on a chip



Hydrogels: Applications



- Biomedical use due to bio- and blood-compatibility
- Pharmaceutical use due to hydrophilicity (controlled/sustained drug release)
- Earliest biomedical application contact lenses
  - good mechanical stability
  - favorable refractive index
  - high oxygen permeability
  - needs hygienic maintenance
  - unable to correct for astigmatism
- lubricating surface coating
  - used with catheters, drainage tubes and gloves
  - non-toxic

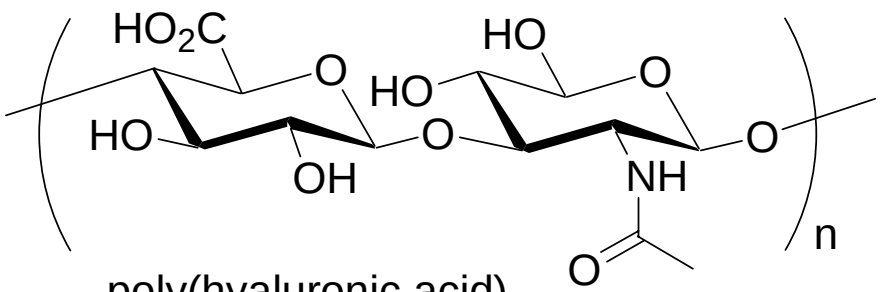
Corning® Ultra Low Attachment Products
Unique hydrogel surface inhibits cell attachment

Important features of hydrogels

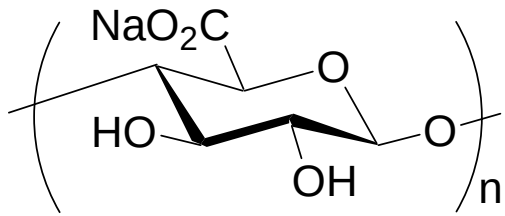
- Usually comprised of highly polyionic polymers
- Often exhibit large volumetric changes eg. Highly compressed in secretory vessicle and expand rapidly and dramatically on release
- Can undergo volumetric phase transitions in response to ionic concentrations (Ca++, H+), temperature, ..
- Volume is determined by combination of attractive and repulsive forces:
  - repulsive electrostatic, hydrophobic
  - attractive, hydrogen binding, cross-linking

Hydrogel Forming Polymers

Natural

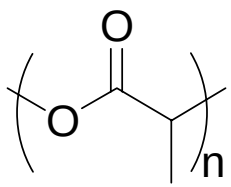


poly(hyaluronic acid)

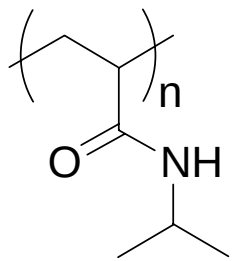


poly(sodium alginate)

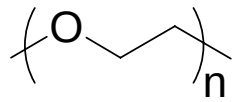
Synthetic



poly(lactic acid)

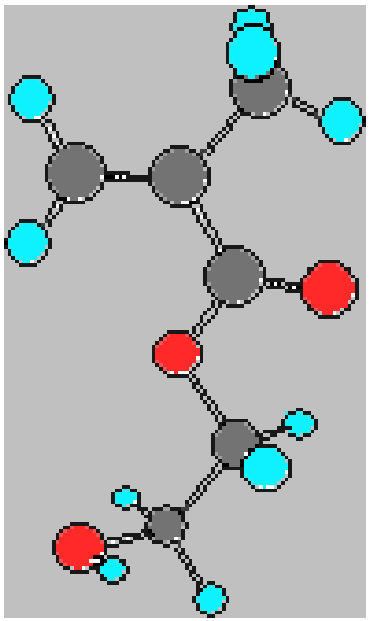


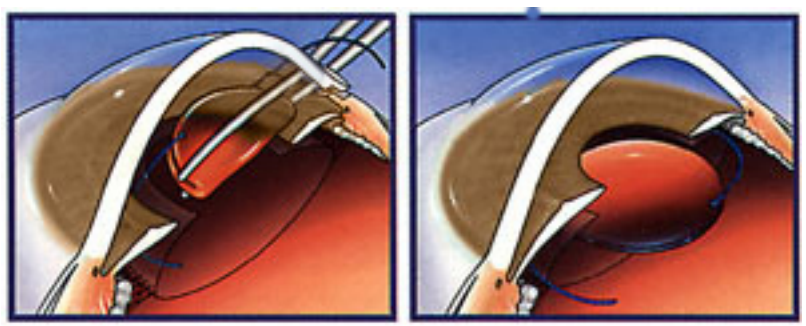
poly(N-isopropyl acrylamide)



poly(ethylene glycol)

Hydrogels / Applications in Opthamology





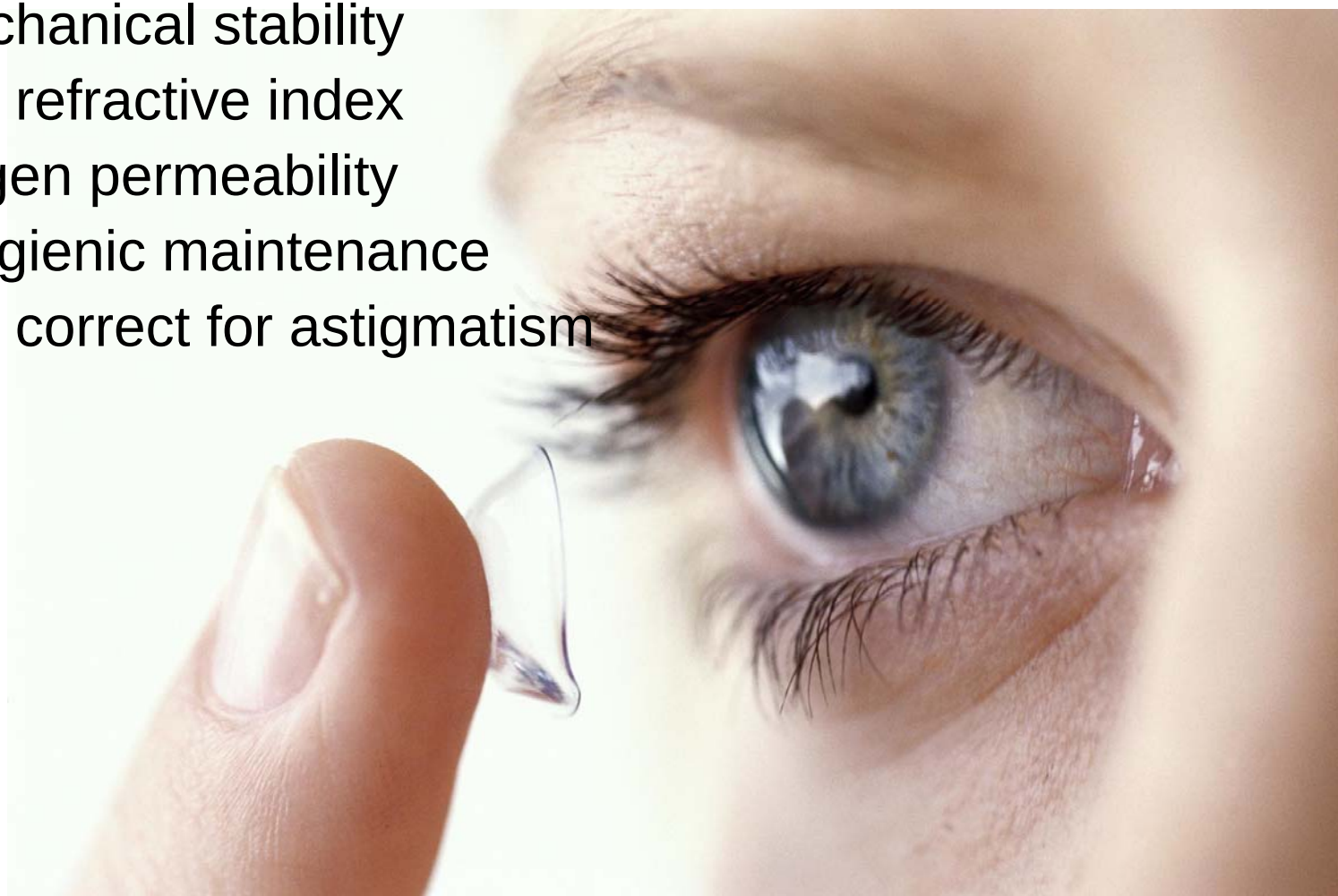
Folded Lens in Incision

Unfolded in the Eye

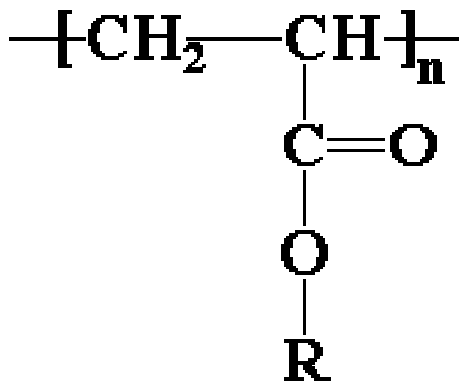
Hydrogels: Applications

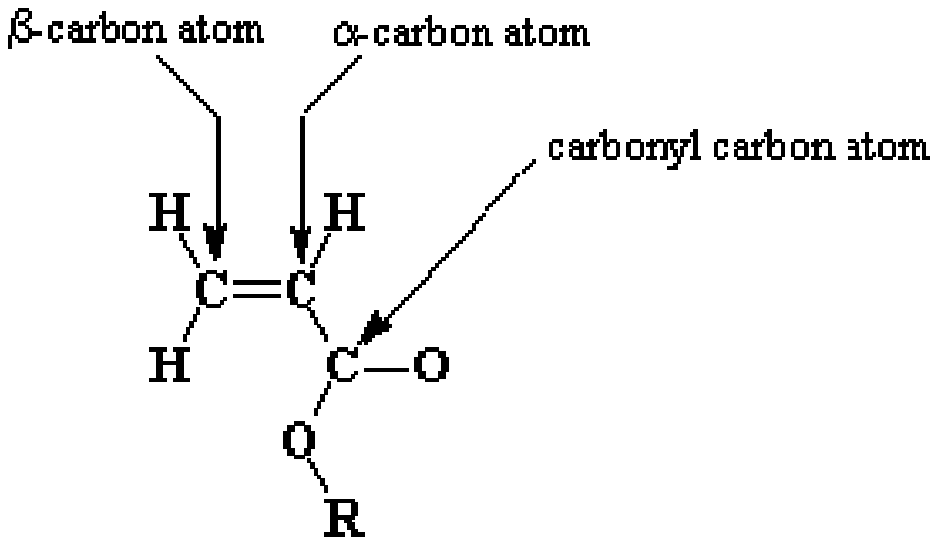
Earliest biomedical application contact lenses

- good mechanical stability
- favorable refractive index
- high oxygen permeability
- needs hygienic maintenance
- unable to correct for astigmatism

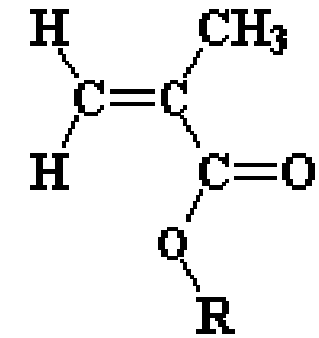


Acrylates


CH2
CH
n
C
O
O
R

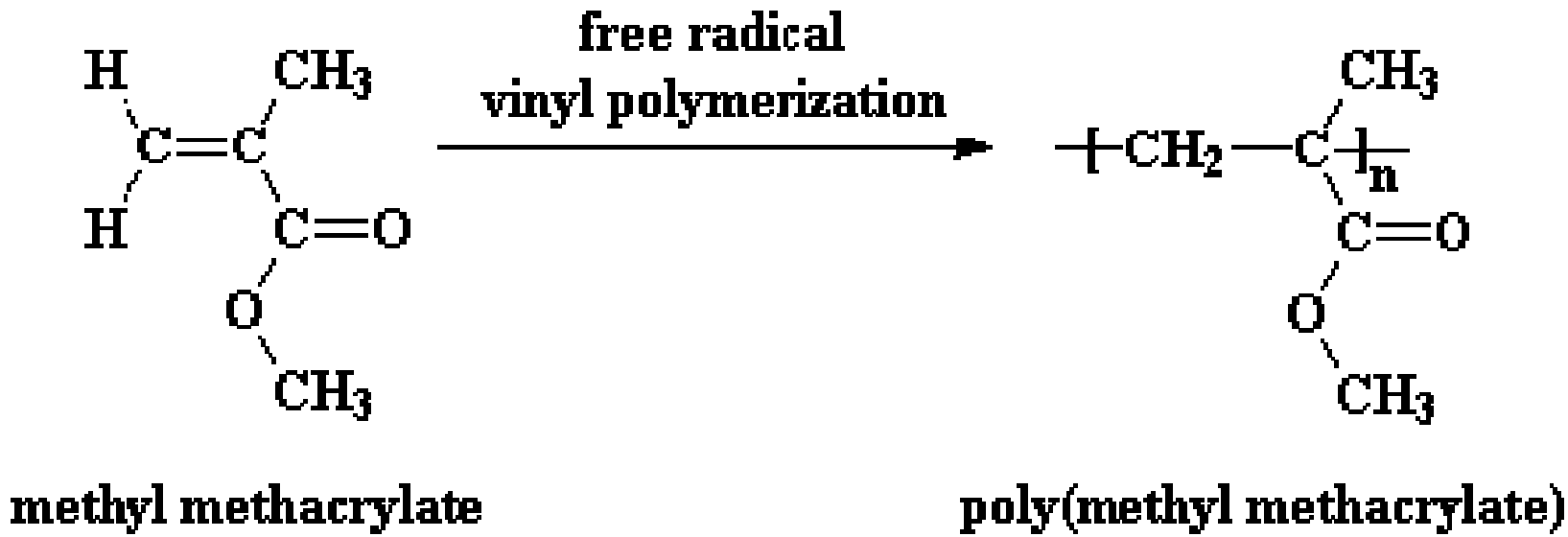

β-carbon atom
α-carbon atom
carbonyl carbon atom
H
H
C
C
H
C
O
O
R

Methacrylates



a methacrylate

Poly(methyl methacrylate)



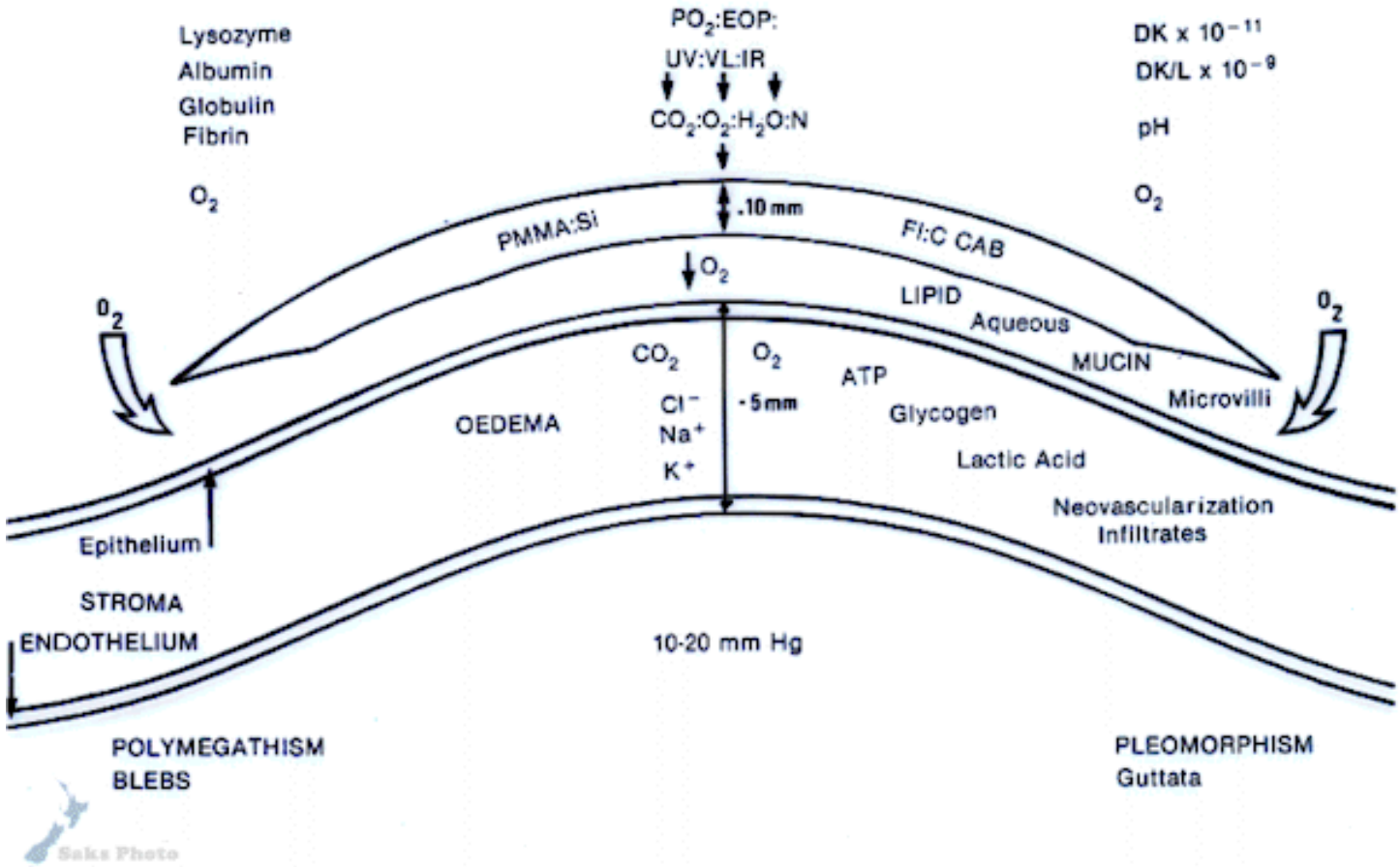
methyl methacrylate

poly(methyl methacrylate)

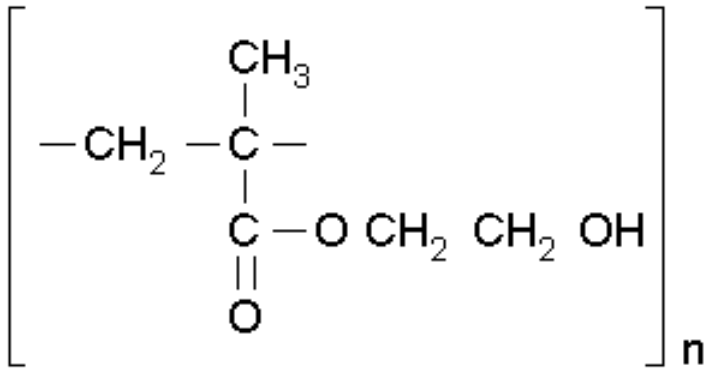
Table 1.—Summary of the Historical Development of Contact Lenses

Year	Individual(s)	Development
1508	Leonardo da Vinci	Described glass contact lens
1636	René Descartes	Tube of water used to neutralize the cornea
1801	Thomas Young	Used Descartes' principle to study the eye
1827	John Herschel	Described how a contact lens could be ground; concept of molding the eye
1887	F. A. Muller	Fitted a glass blown lens for a patient to protect the eye
1888	A. E. Fick	Described first glass lens to be worn to correct vision
1888	E. Kalt	Designed and fitted glass corneal lenses; Used ophthalmometer to fit lenses
1936	W. Feinbloom	Made lens with glass central optic and plastic surround (first plastic used in contact lens)
1938	Mullen and Obrig	First all-plastic (PMMA) contact lens
1947	N. Bier	Fenestrated minimum-clearance haptic lens
1947	K. Tuohy	All-plastic corneal lens
1950	Butterfield	Designed corneal lens to parallel the cornea; used peripheral curves
1960	Wichterle and Lim	Hydrogel polymers for contact lenses
1968		U.S. FDA became involved in regulating contact lenses
1971	Bausch & Lomb	First hydrogel lens approved in United States
1970s	J. DeCarle	Extended wear with high water content hydrogel lenses
1970s	Rynco Scientific	Use of CAB polymer for contact lenses
1970s		First clinical marketing of soft silicone lenses
1978	Danker Laboratories	U.S. FDA approval of CAB lenses
1979	Syntex Ophthalmic	U.S. FDA approval of a PMMA-silicone copolymer lens

SOURCE: G. E. Lowther, Contact *Lenses: Procedures and Techniques* (Boston, MA: Butterworths, 1982)


Lysozyme
Albumin
Globulin
Fibrin
O_2
PO_2:EOP:
UV:VL:IR
CO_2:O_2:H_2O:N
DK x 10^{-11}
DK/L x 10^{-9}
pH
O_2
PMMA:Si
.10 mm
FI:C CAB
O_2
LIPID
Aqueous
MUCIN
Microvilli
O_2
O_2
CO_2
O_2
ATP
Cl^-
Na^+
K^+
.5mm
OEDEMA
Glycogen
Lactic Acid
Epithelium
Neovascularization
Infiltrates
STROMA
ENDOTHELIUM
10-20 mm Hg
POLYMEGATHISM
BLEBS
PLEOMORPHISM
Guttata

Poly(2-hydroxyethylmethacrylate pHEMA



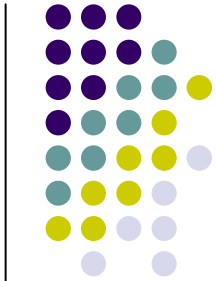
Hydrogels: PHEMA

- The most widely used hydrogel
- water content similar to living tissues
- inert to biological processes
- shows resistance to degradation
- permeable to metabolites
- not absorbed by the body
- withstands sterilization by heat
- prepared in various shaped and forms

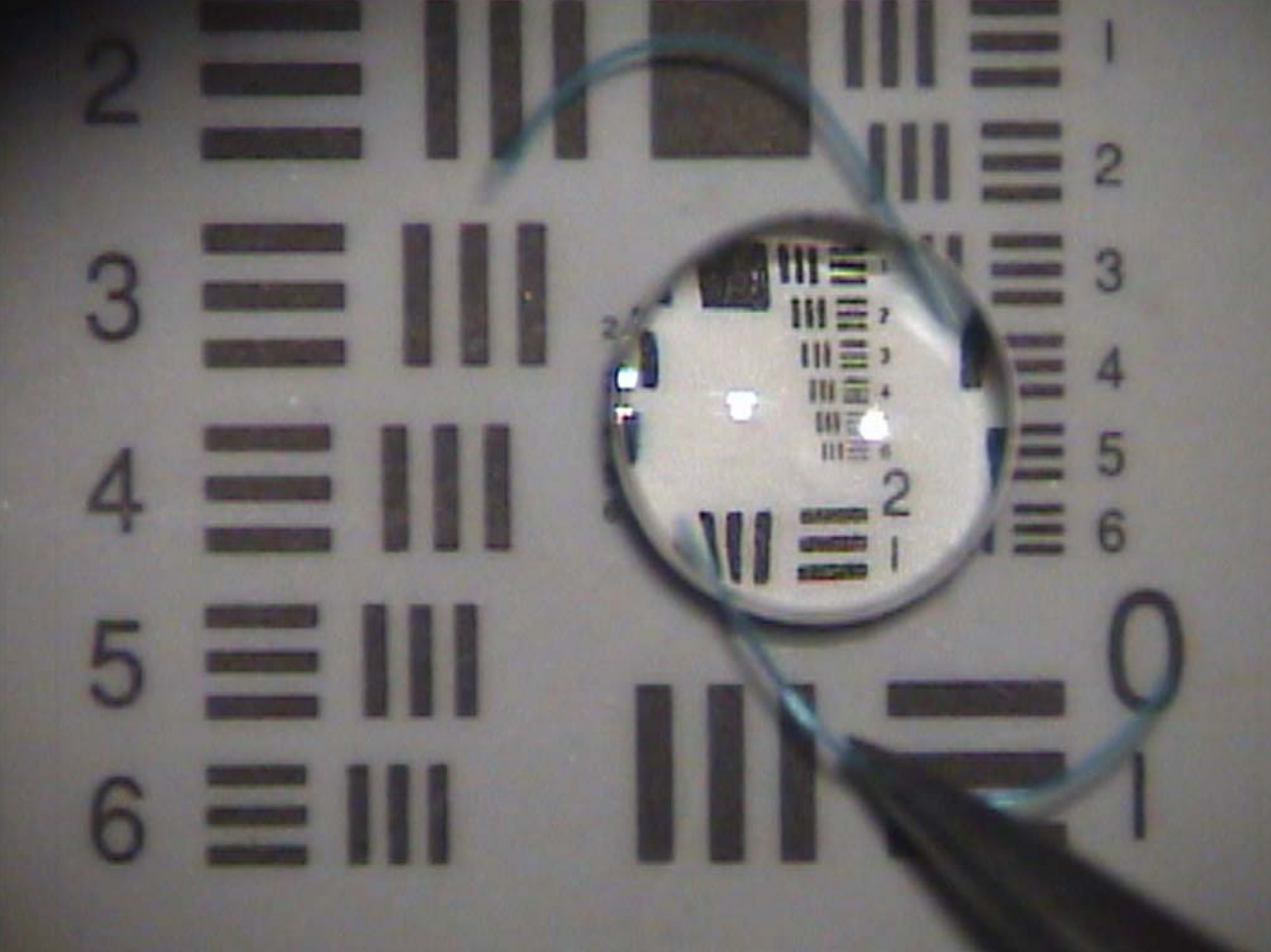
Contact lens

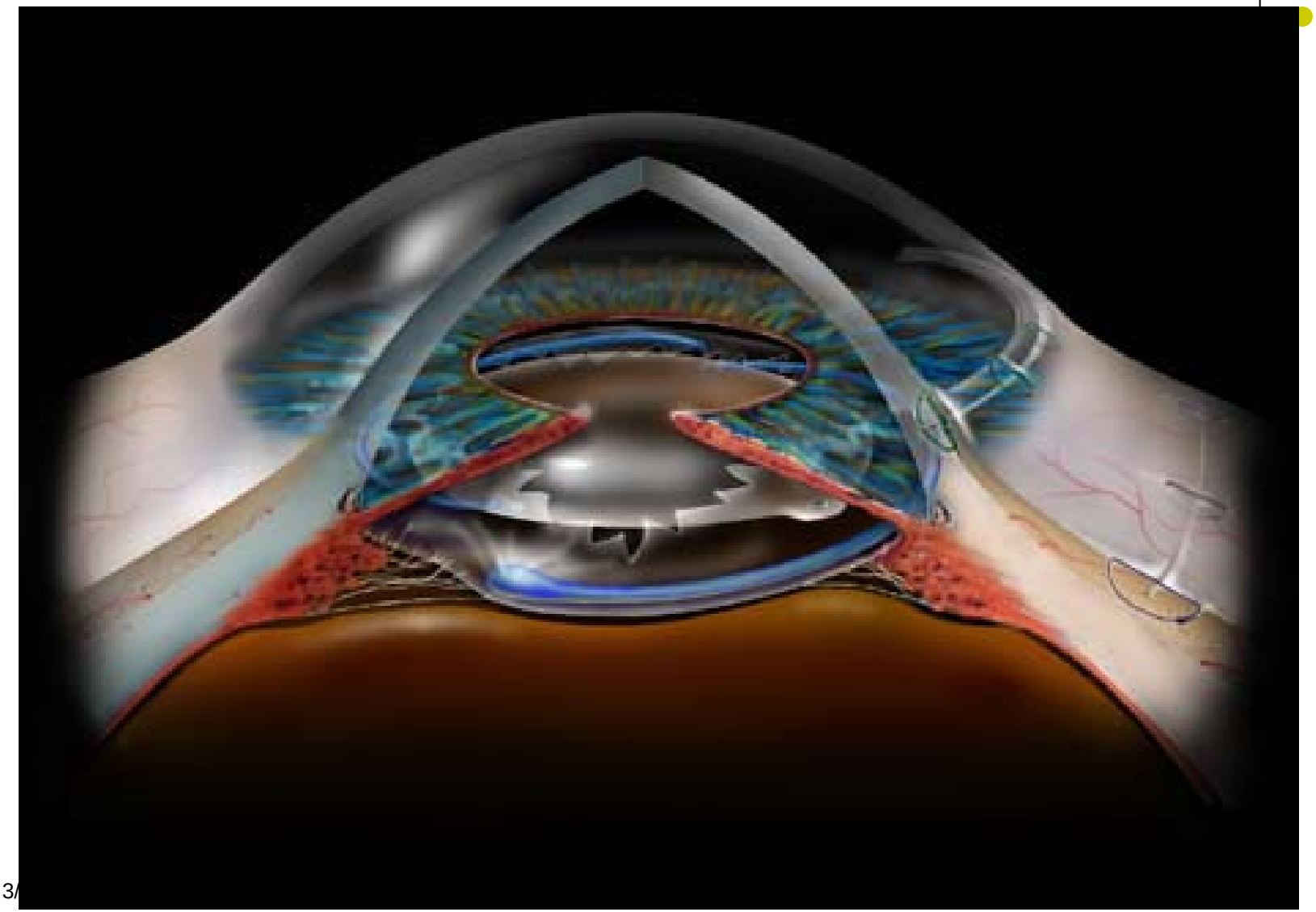
- PMMA
- HEMA
- Fabrication methods
  - Computer assisted cutting (lathe)-PMMA rods
  - Spin casting-polymerization
  - Molding-polymerization

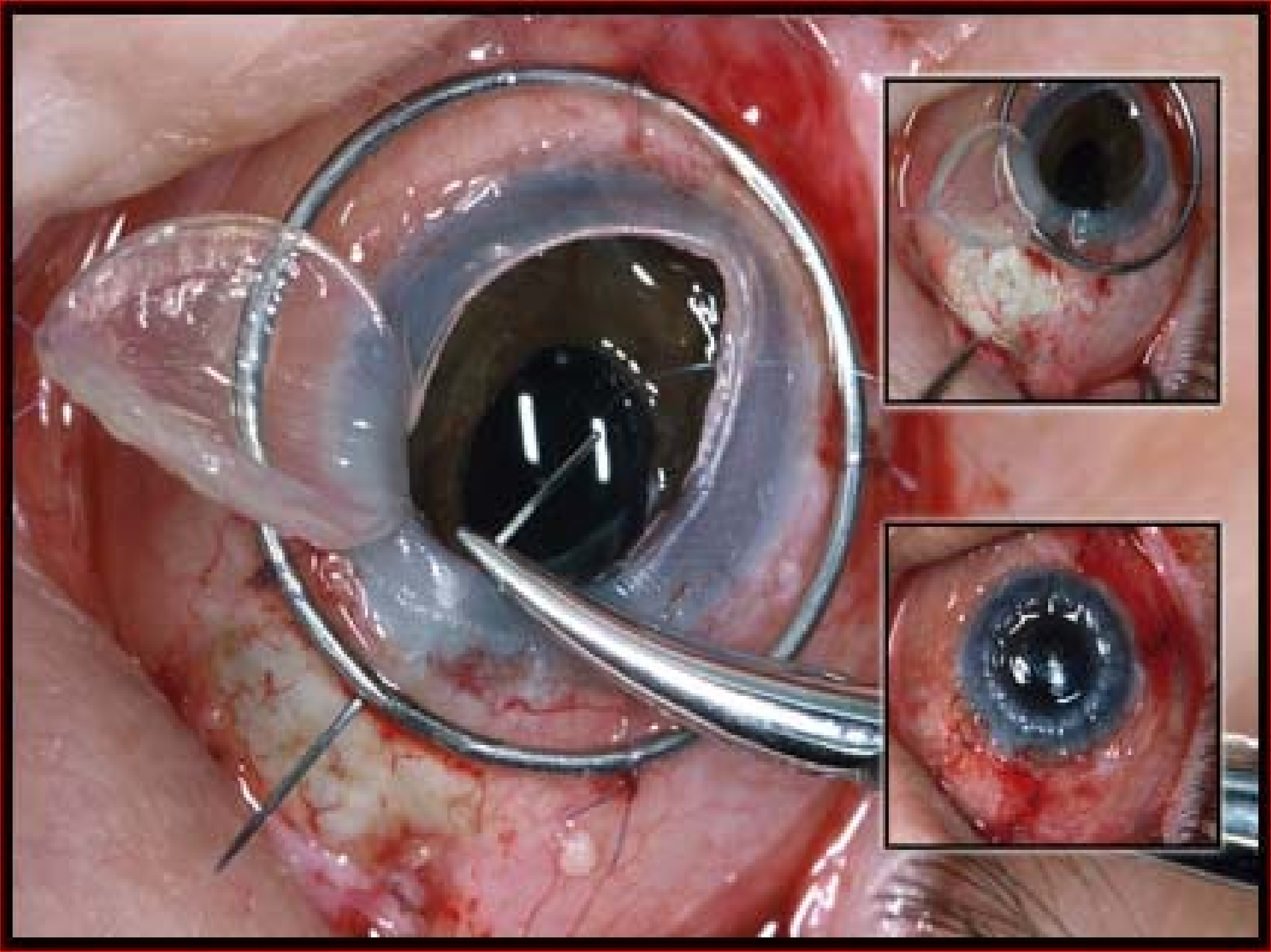
Intraocular lens

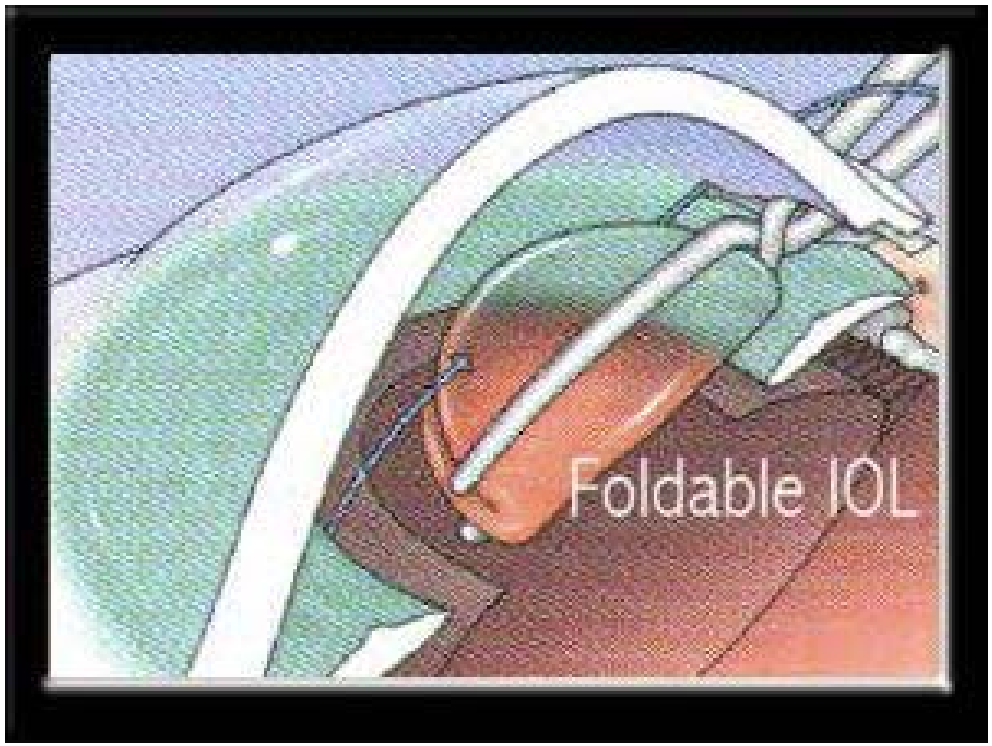


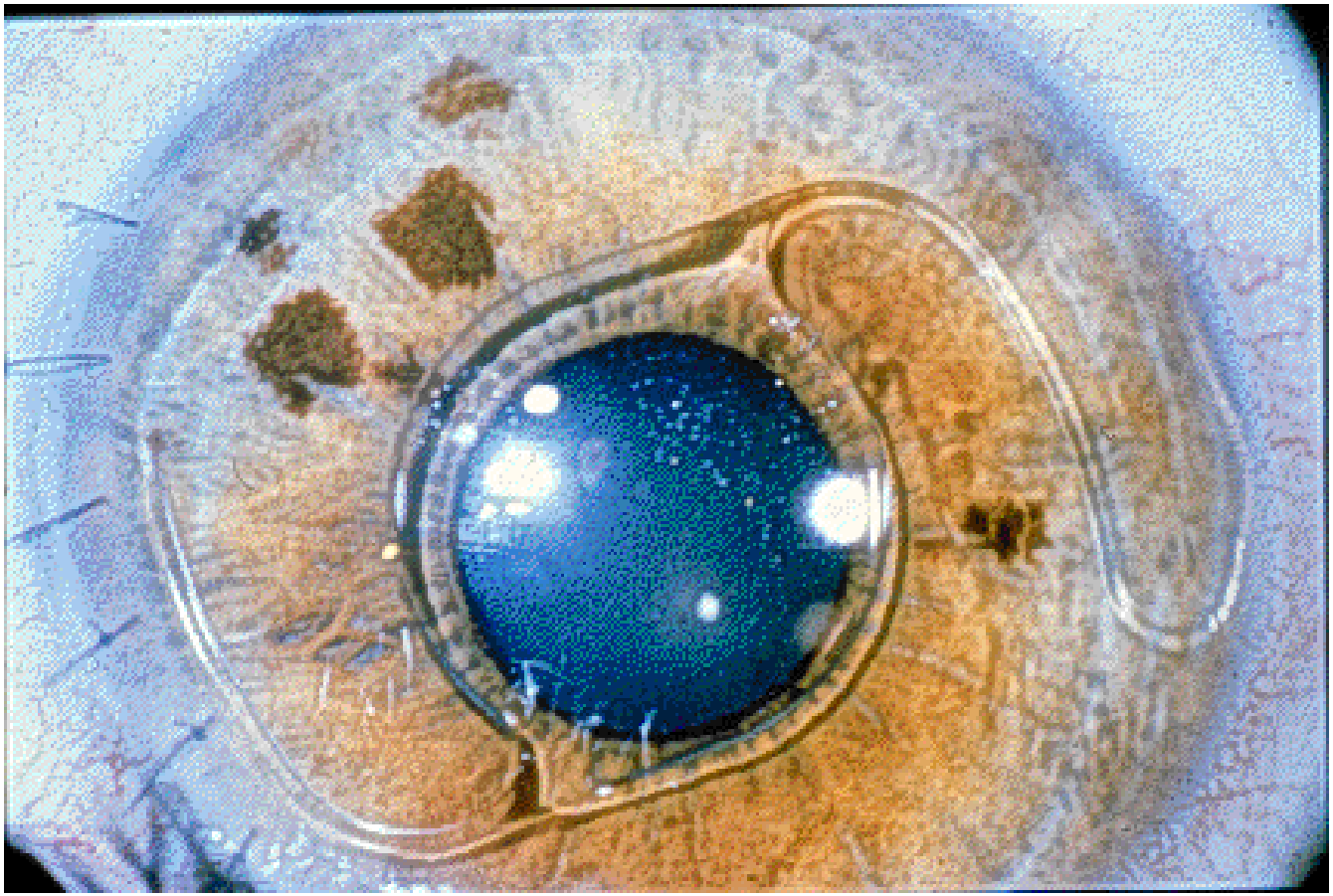
- PMMA
- HEMA
- Polymer backbone - mixture of PMMA and PHEMA
- Varying water contents
- Additives such as UV blockers

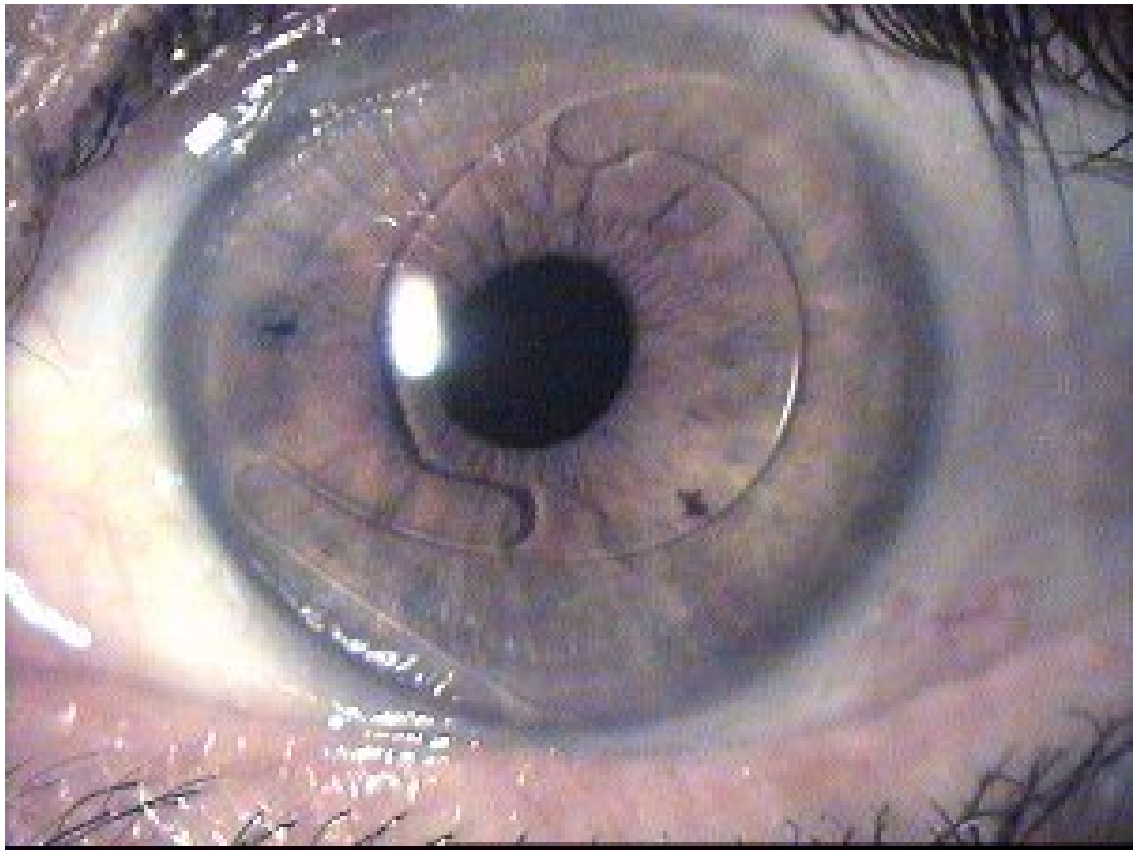

2
3
4
5
6
1
2
3
4
5
6
0
1
2
1



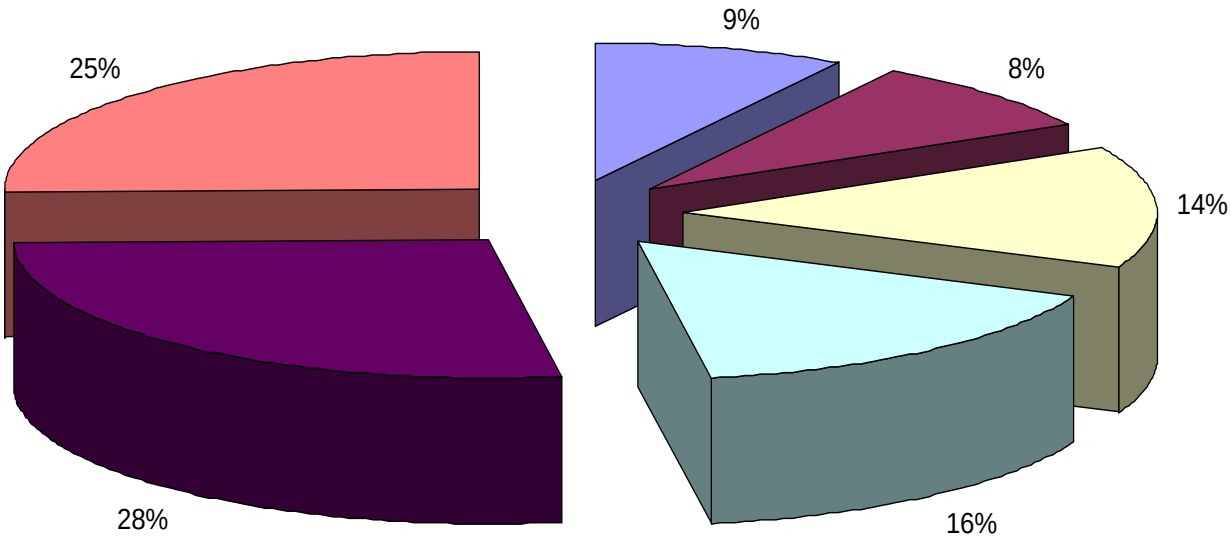



Foldable IOL

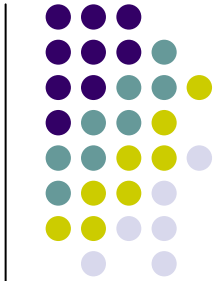




Foldable IOL complications/explantations - Survey Lens Totals 2001

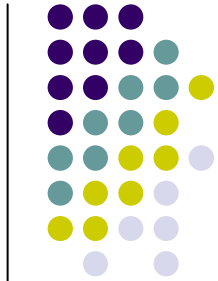


Reasons for Revision Surgery

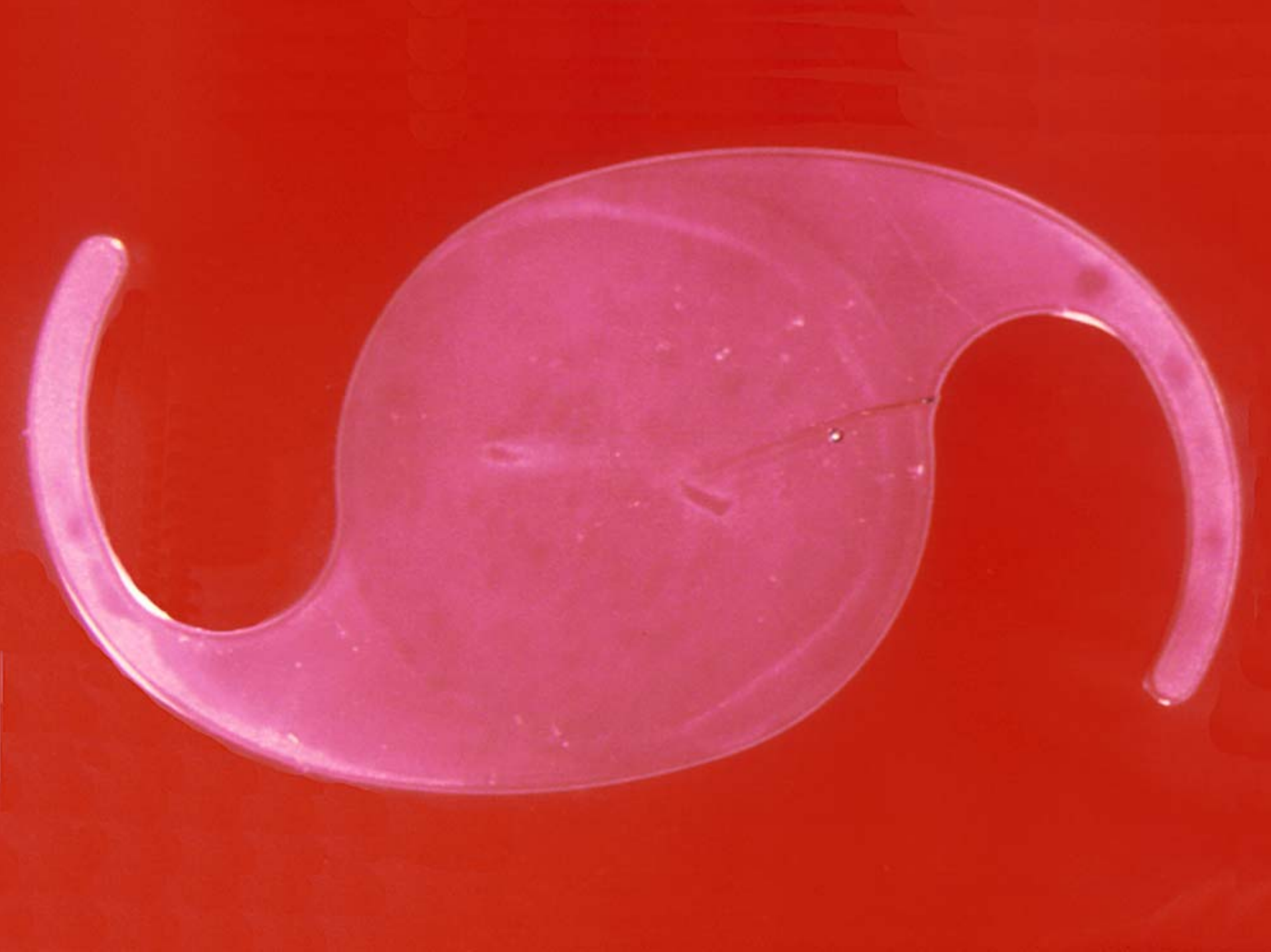


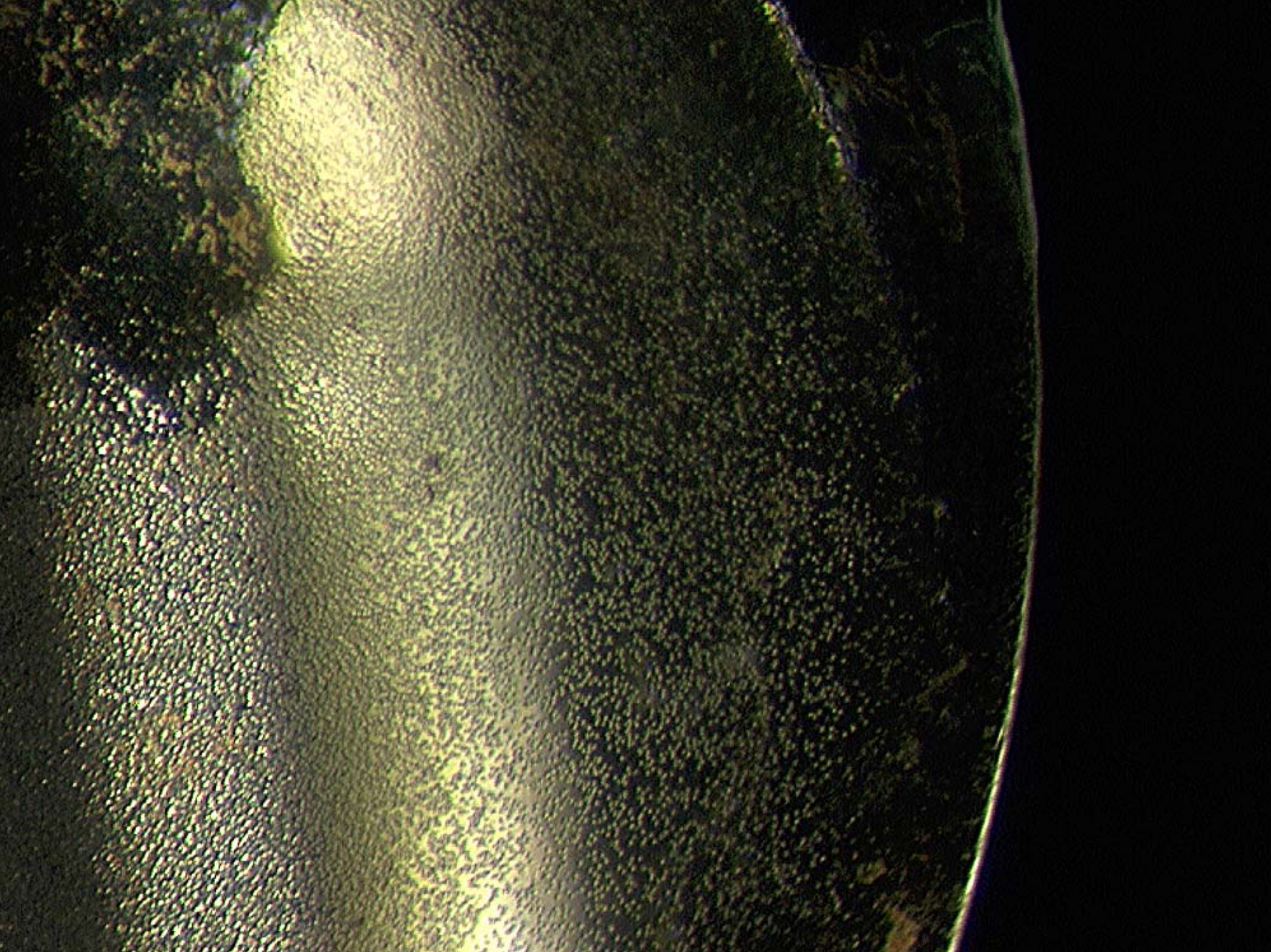
- Incorrect lens power seen most commonly
- Glare/optical aberrations
- Dislocation/decentration
- Late postoperative opacification

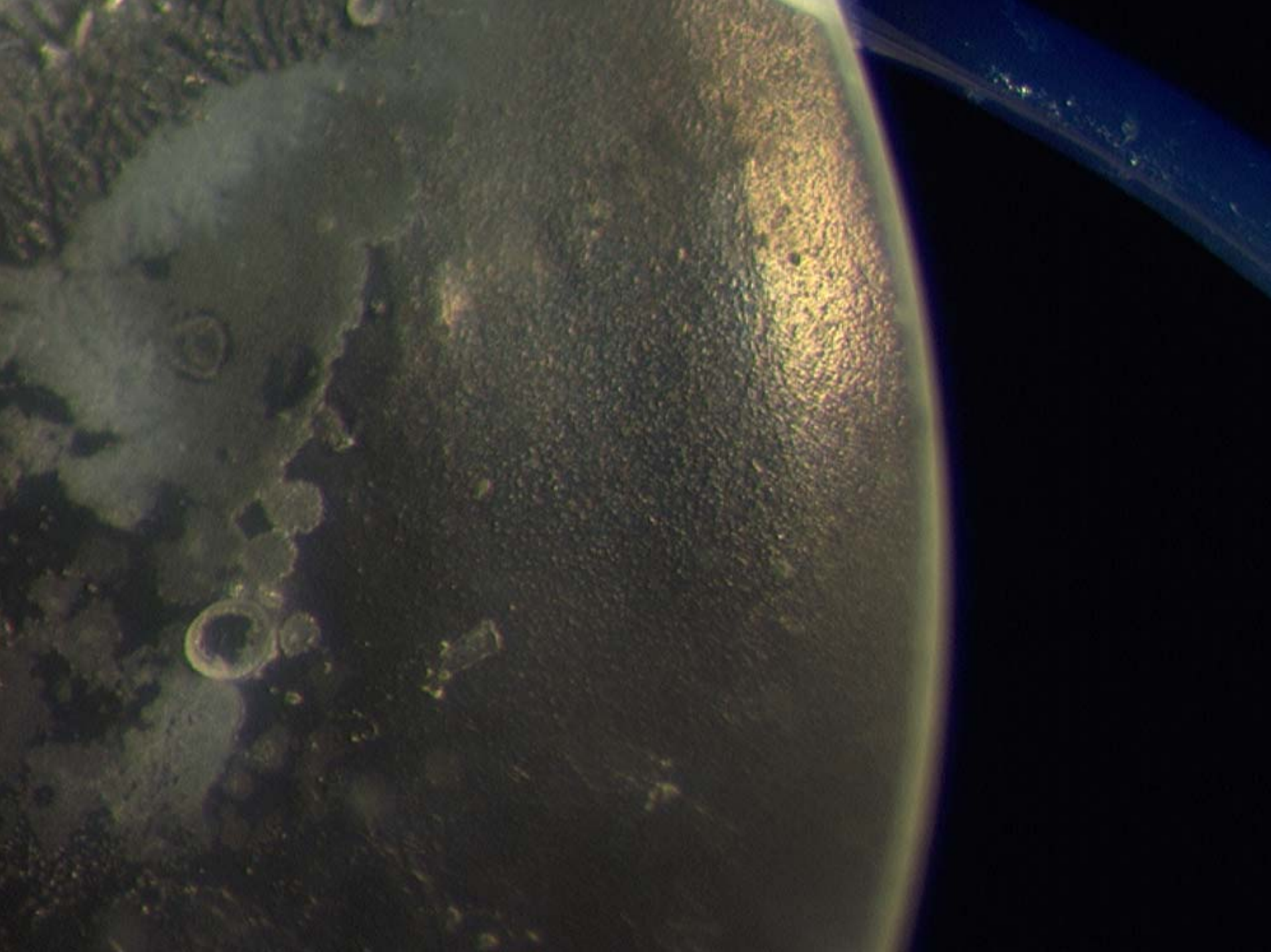
IOL Optic Opacification



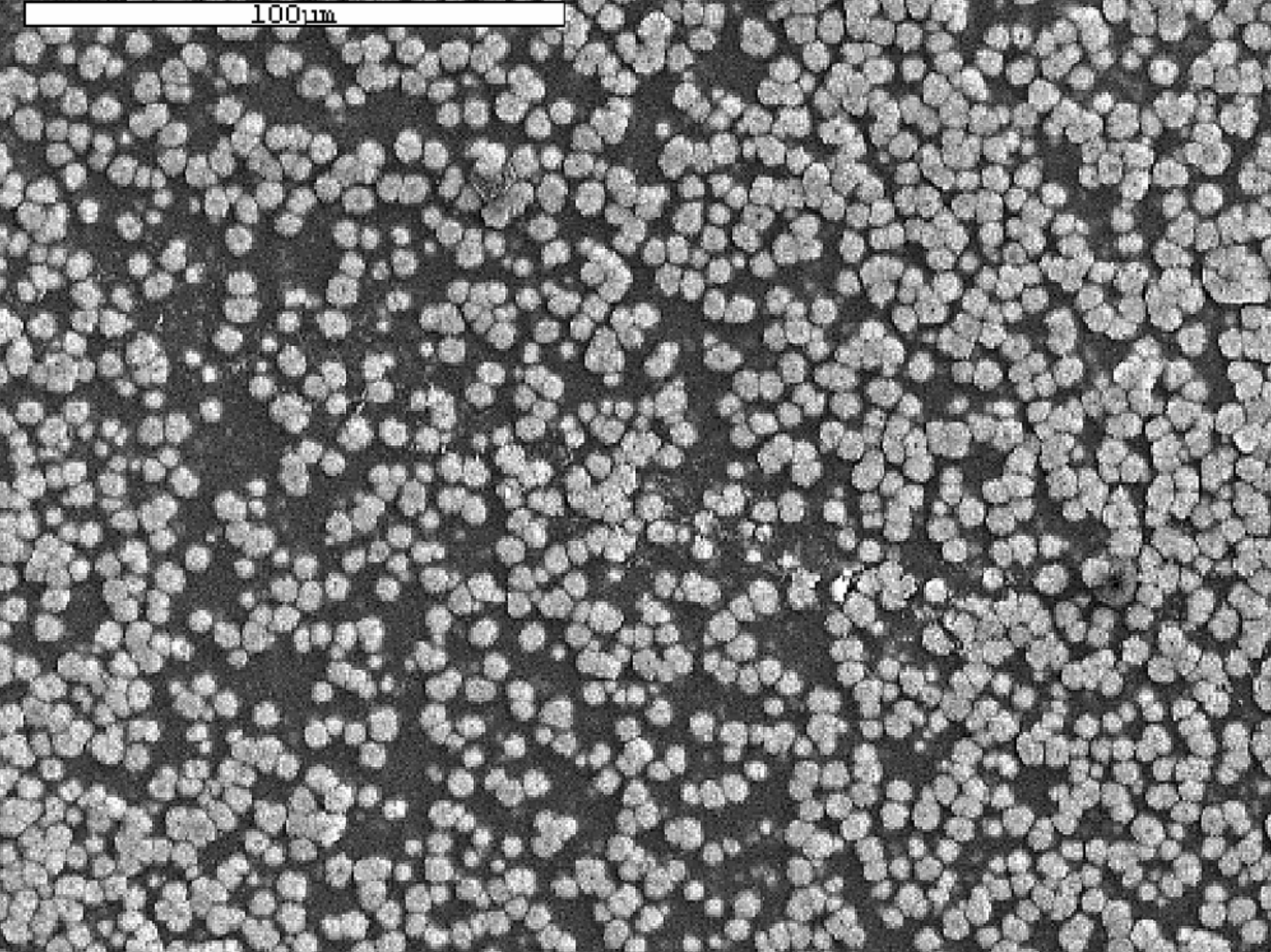
- Surface opacification
- Opacification within the substance of the optic
- Analysis of opacifications reveals presence of calcium
- Calcium staining
- Scanning electron microscopic analysis

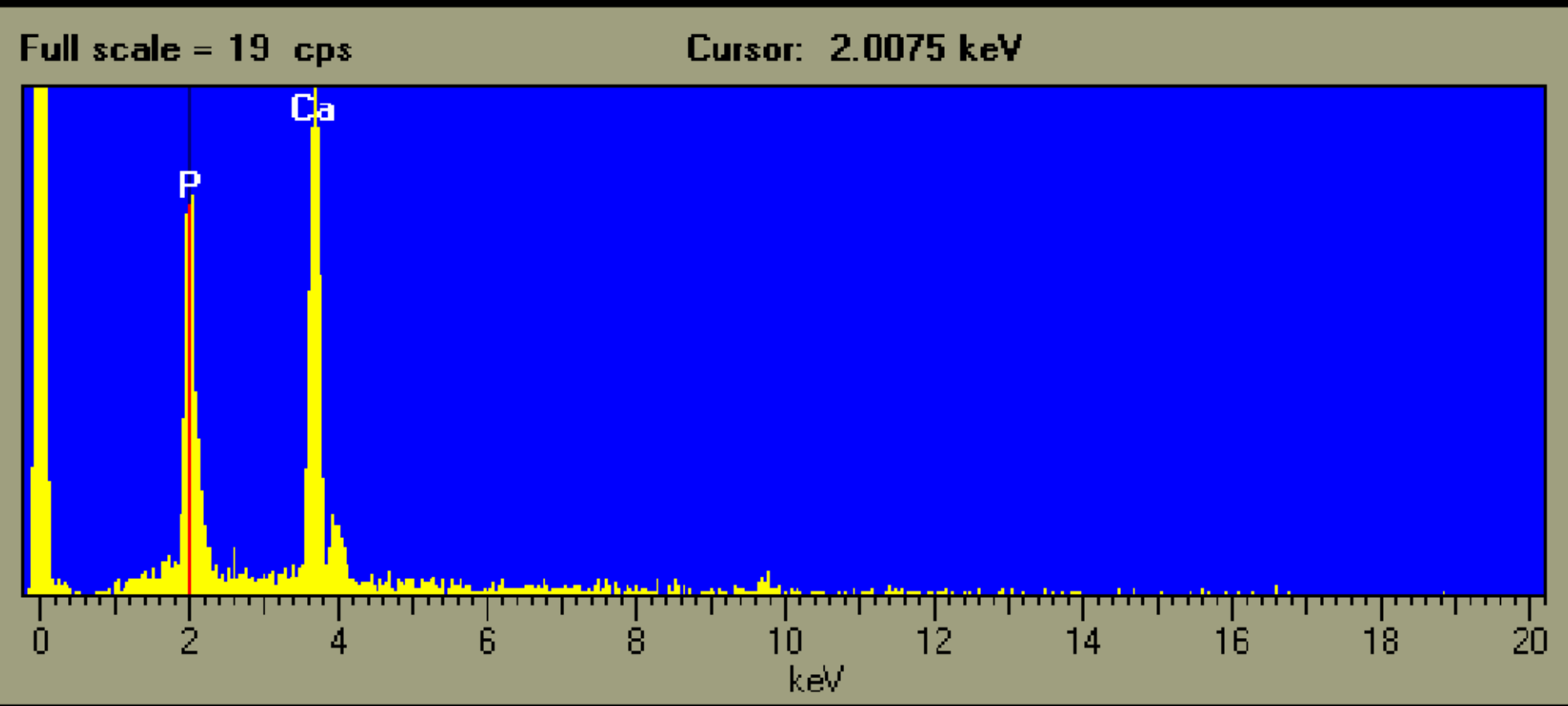







500μm


100μm


Full scale = 19 cps
Cursor: 2.0075 keV
Ca
P
0
2
4
6
8
10
12
14
16
18
20
keV

Accommodative IOL: 1CU (HumanOptics)

Total diameter: 9.7 mm