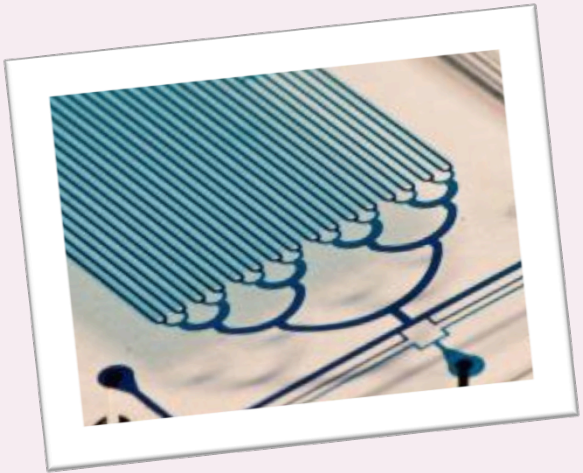
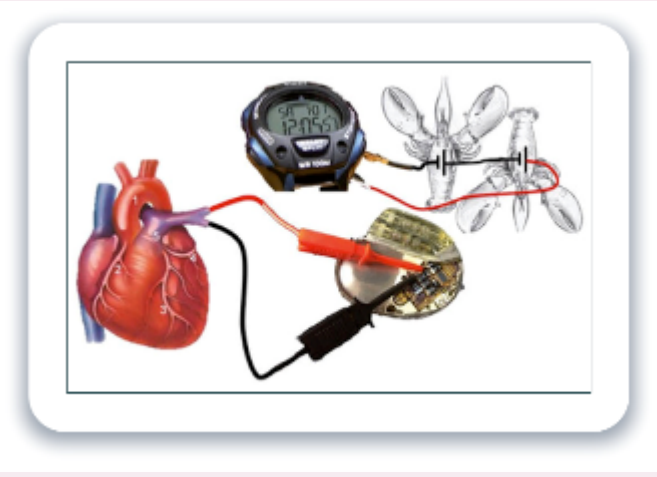
Santa Clara University
School of Engineering

Department of Bioengineering

http://www.scu.edu/engineering/bioengineering/index.cfm





Milestones in History of Biotechnology

- Antiquity : Yeast/Bacteria Fermentation (Sugar to Ethanol), natural vaccines and antibiotics in Mesopotamia .
- 1860: Lactic Acid Fermentation /experimental proof (Sugar to Lactic acid).
- WW1: Conversion of Corn Starch to acetone in the presence of *Clostridium acetobubutylicum*.
- Late 1960's: Single Cell protein production (*Candida tropicalis* and *C. lipolytica*) from gas oil and n-alkanes by molecular sieve filtration.
- Late 1970's: Production of first synthetic insulin (pancreatic enzyme) using Recombinant DNA technology in *E. coli* fermentation.

Milestones in History of Biomedical Engineering

- 3,000-year-old mummy from Thebes with a wooden prosthetic tied to its foot to serve as a big toe.
- Egyptians (Antiquity) used hollow reeds to look and listen to the internal goings on of the human anatomy (stethescope).
- 1800's and birth of *Electrophysiology*: DuBois Reymond / Hermann von Helmholtz application of engineering principles to a problem in physiology and identifying the resistance of muscle and nervous tissues to direct current.
- 1895: Wilhelm Roentgen : Discovery of *X-Ray*
- WW1 and WW2: Birth of *Biophysics*
- Post WW2: Integration into academic programs and formation of multiple professional societies.
- 1970s: Shell research sponsorship of SCP research for water contamination purpose.
- Early 1980s: Use of HFCS in food and soft drinks in the US.
- Late 1980's: Commercialization of *Health Technology*

What is Bioengineering?

Definition from NIH

- Integrates physical, chemical, mathematical, computational sciences and engineering principles to study biology, medicine, behavior, and health

- Advances fundamental concepts and creates knowledge from the *molecular* to the *organ systems* levels;

- Develops innovative biologics, materials, processes, implants, devices, and informatics approaches for the prevention, diagnosis and treatment of disease, for patient rehabilitation, and for improving health

Biomedical Engineering Job Listings

- Bio-Imaging Engineer
- Validation Engineer
- Vaccine Development Scientist
- Manufacturing Development Engineer
- Regulatory Affair Specialist
- Biostatistician
- Bioinformatics programmer
- Stent Engineer
- Fermentation Engineer
- Biomedical Engineer
- Membrane Scientist
- Bio-MEMS researcher
- Environmental Bio-safety
- Engineer
- Automation Engineer
- Tissue Engineer
- Formulation Scientist
- And Many Others……..

Projected Biotechnology Jobs by Economic Region, 2010–2020

Industries with Projected Biotechnology Jobs

- Pharmaceutical and Medicine Manufacturing
- Navigational, Measuring, Electromedical, and Control Instruments Manufacturing
- Medical Equipment and Supplies Manufacturing
- Professional and Commercial Equipment and Supplies Merchant Wholesalers
- Chemical and Allied Products Merchant Wholesalers' Management
- Scientific and Technical Consulting Services
- Scientific Research and Development Services
- Postsecondary Colleges, Universities, and Schools
- Medical and Diagnostic Laboratories
- Federal, State, and Local Government

This map will be updated as projections are completed for additional counties.

Greater Sacramento does not include projections for Sutter County or Yuba County.

Bay Area does not include projections for Napa County, Santa Cruz County, or Solano County.

San Joaquin Valley does not include projections for Madera County, Merced County, or Tulare County.

Southern California does not include projections for Ventura County.

Southern Border does not include projections for Imperial County.

EDD Employment Development Department State of California

LaborMarketInfo

Data Source:
Occupational Research Group
Labor Market Information Division
California Employment Development Department

Cartography by:
Labor Market Information Division
California Employment Development Department
June 2013

Biotechnology Occupations at a Glance: Employment Change and Job Openings

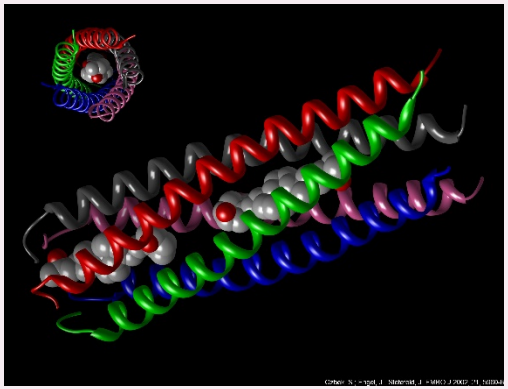
Key Occupation	Annual Average Employment		Employment Change		Average Annual Job Openings			Percent of Occupation in designated Biotech Industry [5]
	2010	2020	Numerical [1]	Percent	New Jobs [2]	Replace-ment Needs [3]	Total Jobs [4]	
Biochemical Engineers [6]	--	--	--	--	--	--	--	--
Biochemists and Biophysicists	6,400	8,800	2,400	37.5	250	140	390	87.5
Biological Technicians	11,400	13,300	1,900	16.7	180	390	570	84.2
Biologists [7]	--	--	--	--	--	--	--	--
Biomedical Engineers	4,000	6,700	2,700	67.5	270	90	360	96.3
Chemical Engineers	1,900	2,200	300	15.8	30	60	90	66.7
Chemical Technicians	6,200	7,100	900	14.5	90	90	180	22.2
Chemists	10,900	12,100	1,200	11.0	120	360	480	41.7
Compliance Officers	25,900	30,000	4,100	15.8	410	310	720	36.6
Electrical Engineers	21,000	23,200	2,200	10.5	230	510	740	13.5
Environmental Scientists and Specialists, Including Health	13,000	16,000	3,000	23.1	290	390	680	80
Epidemiologists [8]	--	--	--	--	--	--	--	--
Management Analysts	82,800	101,400	18,600	22.5	1,870	1,350	3,220	60.2
Market Research Analysts and Marketing Specialists	53,700	78,300	24,600	45.8	2,450	1,430	3,880	30.9
Medical and Clinical Laboratory Technicians	16,900	19,400	2,500	14.8	250	330	580	72
Medical and Clinical Laboratory Technologists	11,800	13,200	1,400	11.9	140	230	370	71.4
Medical Scientists, Except Epidemiologists	27,800	39,300	11,500	41.4	1,150	170	1,320	76.5
Microbiologists	3,600	4,400	800	22.2	80	80	160	75
Natural Sciences Managers	8,800	10,300	1,500	17.0	150	530	680	93.3
Statisticians	3,000	3,600	600	20.0	50	180	230	50
Technical Writers	6,400	7,700	1,300	20.3	120	130	250	38.5

http://www.calmis.ca.gov/SpecialReports/Biotechnology_in_CA_2013.pdf#page=10

EXAMPLE OF PRODUCTS ON THE MARKET OR IN DEVELOPMENT

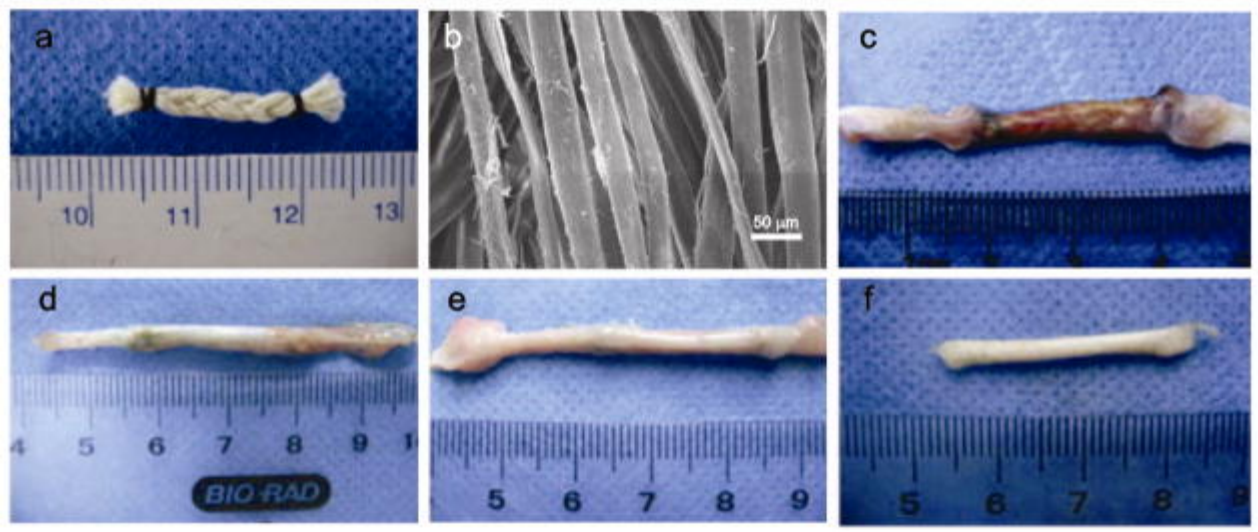
Biomaterials

SMART POLYMERS



http://engineering.nyu.edu/files/pressrelease/COMPcc_blackBG_color_600dpi_4inx3in.jpg

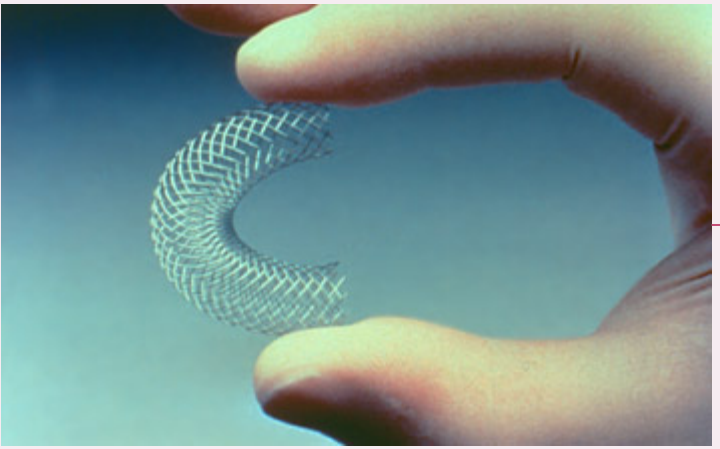
http://www.youtube.com/watch?v=iaZhJuxPNpA



http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3631569/

Bio-Medical Devices

A broad range of surgical devices and equipment used in cardiovascular, orthopedics, respiratory, ophtalmic, neurology, urinary, disposable and other applications.



http://virchicago.com/carotid-artery-blockage/

Bio-Signals

Hyperspectral Imaging

HANDHELD APPLICATIONS TARGETED BY IMEC HSI

Food quality grading (e.g. sugar content in fruits, monitoring calorie intake, etc...)

Cosmetic / Skin tone measurement
(e.g. make-up advice, etc...)

Anti counterfeiting spectral tag readers

Skin-care / personalized medicine (e.g. melanoma, diabetic ulcers, wound care...)

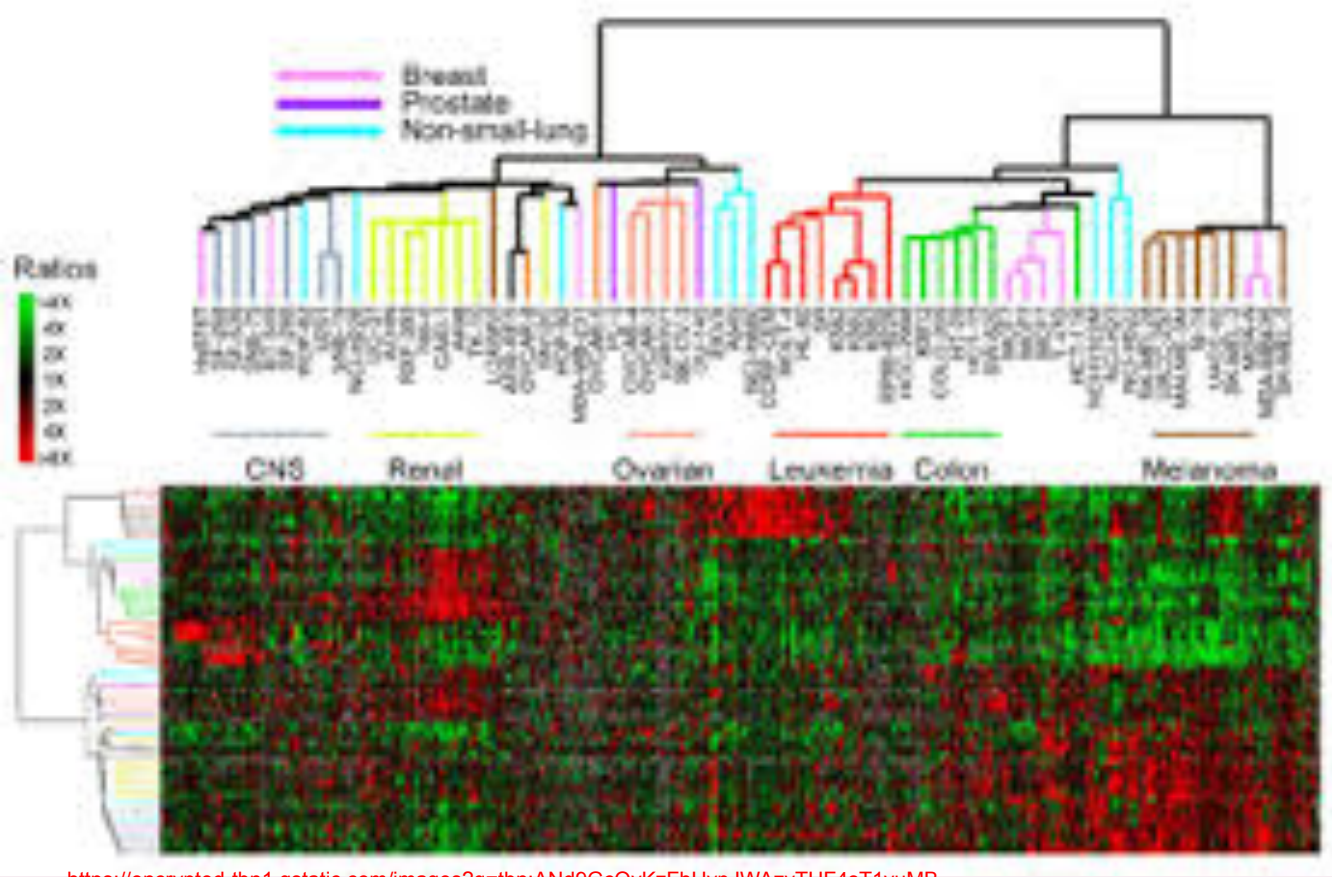
+ many new ideas / application to be generated when HSI handled platform ready!

http://sites.ieee.org/scv-mems/files/2014/01/TSensors-1-22-14_final.pdf

Genomics/Bio-Informatics

A major focus of the ***Human Genome Project*** is the development of sequencing schemes that are faster and more economical.

Bio-Informatics is the analysis of proteins, genes and genomes using computer algorithms and computer databases for ***data-mining***.



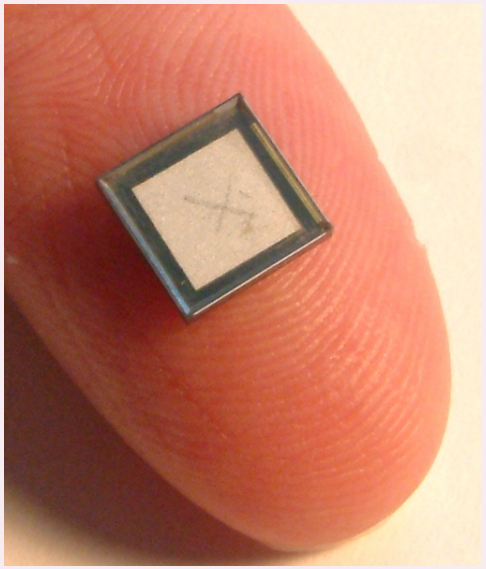
https://encrypted-tbn1.gstatic.com/images?q=tbn:ANd9GcQyKzFhUypJWAzyTUF4sT1yuMB-I87Is3bzF5orlSe72yDWWwtu

Bio-Diagnostics and Bio-MEMS

miniaturized total chemical analysis systems (μTAS)

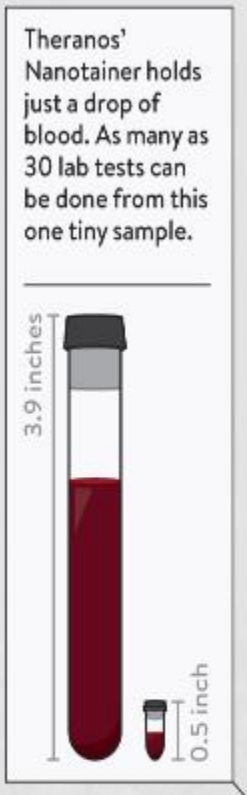
Bio-Chip and Micro Device Development

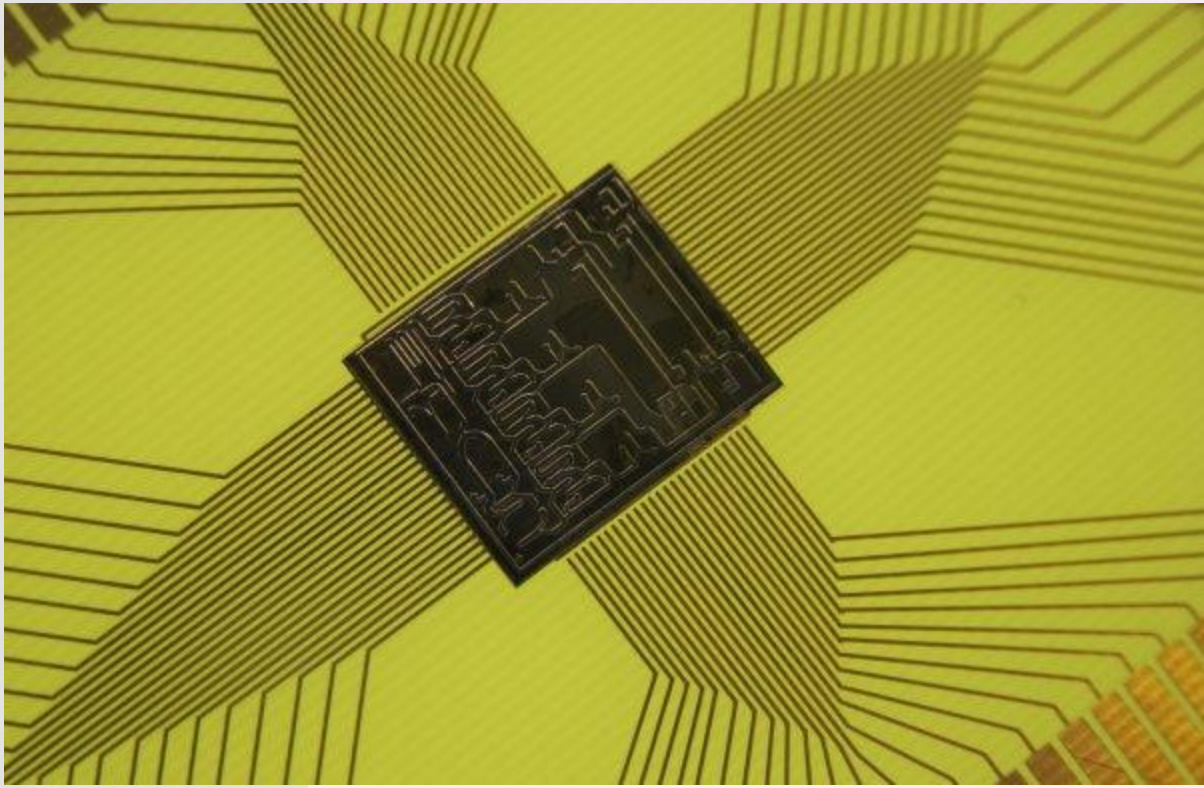
Miniaturized



http://djhurij4nde4r.cloudfront.net/images/images/000/121/043/fullsize/99058.Drug_Delivery_Infusion_Micropump.m.jpg?1390576193

http://www.wired.com/2014/02/elizabeth-holmes-theranos/





http://www.genome.gov/dmd/img.cfm?node=Photos/Technology/Genome%20analysis%20technology&id=79284

How Are We Bringing the 21st Century Bio-Engineering to SCU?

Department of Bioengineering at Santa Clara University

- BS degree program established in 2009
  - Medical device, Biomolecular engineering and Pre-med tracks
- Department of Bioengineering and MS degree program in 2012
- 14 core and affiliate faculty members
- Total enrollment: 186 UG and 35 Grad
- 12 IAB (Industry Advisory Board) members

Bioengineering Laboratories & Expanding

Biomolecular Engineering Laboratory
Facilitates processing of synthetic biomolecules towards biomedical and industrial applications.

Tissue Engineering Laboratory
Equipped to design & develop *in vitro* functional biological substitutes and toxicity screening models.

Micro/Nanosystems Laboratory
Develops innovative microfluidic platforms for applications in diagnostics and cellular engineering.

Biosignals Laboratory
Wide range of instrumentation and computational systems to analyze and interpretate various human biosignals.

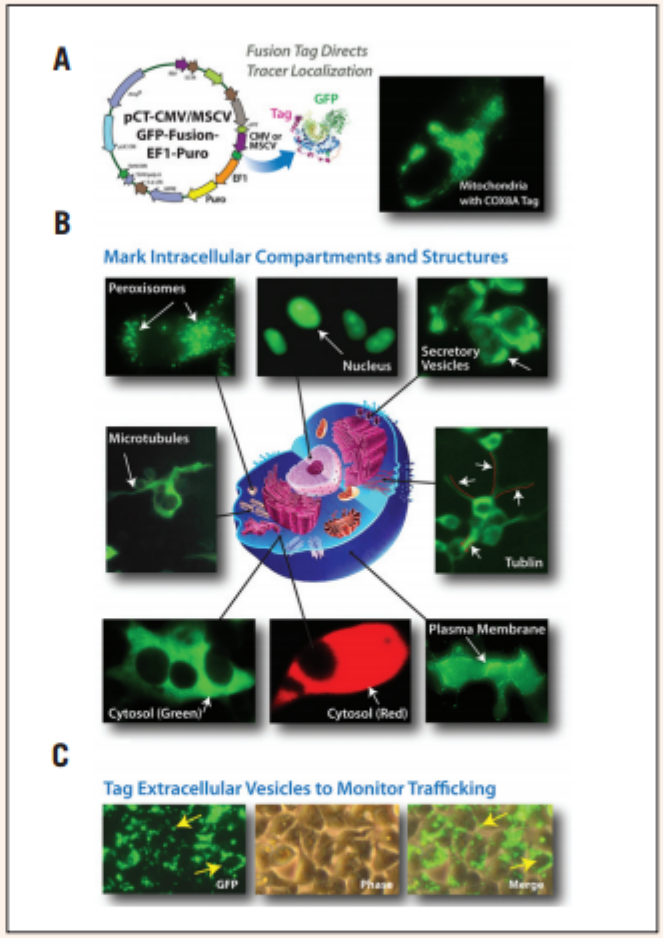
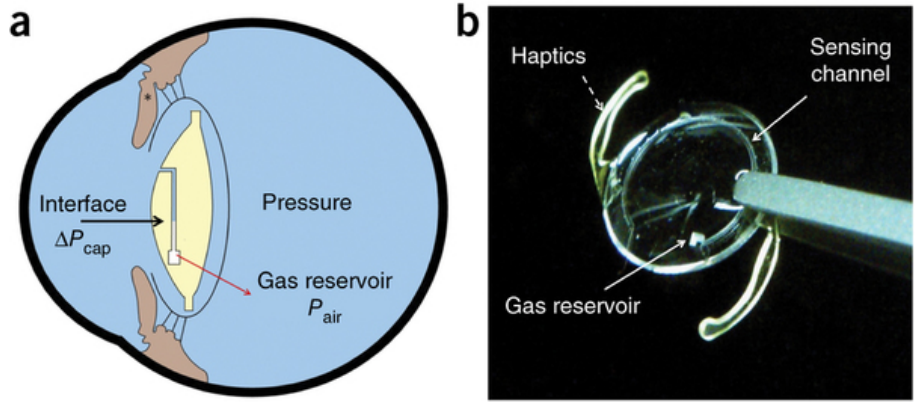


Figure 1. Construction and expression of Cyto-Tracers. Vector configuration and expression of fluorescent fusion proteins using Cyto-Tracers (A). Transient transfection of HEK293 cells shows the specific GFP lighting of various intracellular organelles or structures (A and B). Viral transduction of human fibroblastoma HT1080 cells with CD63-Cyto-Tracer GFP fusion construct shows the formation of intracellular vesicles and subsequent secretion of the exosomes (C).

http://www.biotechniques.com/multimedia/archive/00108/BTN_A_000113553_O_108677a.pdf

Figure 1: IOP measurement system embedded in an intraocular lens.



(**a**) The embedded IOP sensor can be implanted into the eye of a patient with glaucoma during a routine cataract surgery or as a stand-alone implant. Intraocular fluid (aqueous) enters the sensor channel and fills it until equilibrium between IOP and the air inside channels is achieved. The gas-liquid interface (solid black arrow) is captured by a camera or a smartphone equipped with optical and illumination adaptor. The gas-fluid interface is detected by image processing and the pressure (P) is calculated and recorded for follow up and can be optionally sent to the patient's eye care givers. ΔP_{cap}, capillary pressure within the channel; P_{air}, air pressure within the reservoir. *, iris. (**b**) Photograph of the microfluidic pressure sensor embedded within the intraocular lens. A 50-μm-wide channel is connected on one side to the eye aqueous and on the other side to a 500 × 500 × 300 μm^3 volume gas reservoir. Lens arms (haptics, dashed white arrow) are used for stabilizing the lens in place within the eye.

http://www.nature.com/nm/journal/v20/n9/full/nm.3621.html

SCU BIOE Student Presentations at World Class Conferences

- μTAS (Miniaturized Sys. for Chem. and Life Sci.)
- ACS, MRS , AIChE, BMES, IEEE EMBS
- ICBBE (Int. Conf. on Bioinformatics & Bioengineering)
- CMBE (Int. Conf. on Computational and Mathematical Biomedical Engineering)
- Annual PVSF (Pacific Voice & Speech Foundation) Conference

Department of Bioengineering at Santa Clara University

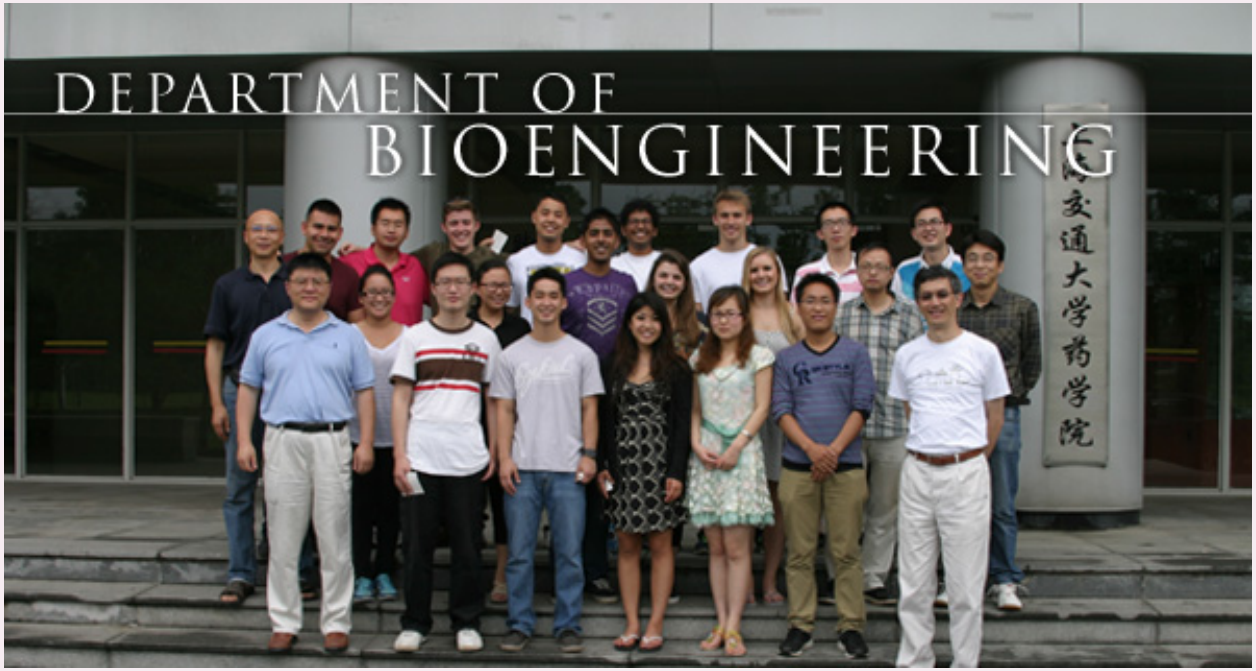
Past Senior Design Capstone projects

- Engineering mammalian cells as biosensors to detect diseases
- Detecting baby at home: detect fetal movement using ultrasound
- Probing mechanical properties of stem cells using AFM
- SAFire: Gas sensing mechanism to prevent surgical airway fires during electrosurgery *(In collaboration with Medtronics)*
- Pathogen detection using microfluidic electrochemical DNA sensors
- Improving mechanical strength of biological glues using nanotubes
- Recognition of blood vessel proximity using Doppler Ultrasound

Transcutaneous transfer of radio frequency energy as an alternative power source for implantable medical devices

- TheraPE - a minimally invasive pulmonary embolectomy device *(In collaboration with GVMED)*

International Summer Exchange Program



Jointly organized by Santa Clara University (SCU) Bioengineering and the Shanghai Jiao Tong University (SJTU) School of Pharmacy

- *International Summer Academy of Bioengineering (ISAB) was held on SCU campus in Summer 2014*
- *International Summer Academy of Pharmacy (ISAP) was held on SJTU campus in Summer 2013*

BIOE students - where are they now ?

BIOE students - where are they GOING ?

UC-Berkeley, UCSF, UCLA, USC

Johns Hopkins

Columbia University

Stanford University

Rensselaer Polytechnic Institute (RPI)

Univ. of Kentucky

Oregon State University

Bioengineering and Global Initiatives

- Biotechnology and Global Warming
- Bioengineering and Malaria Diagnosis
- Bioengineering and Cancer
- And Several Others….

Thank You

Any Questions?

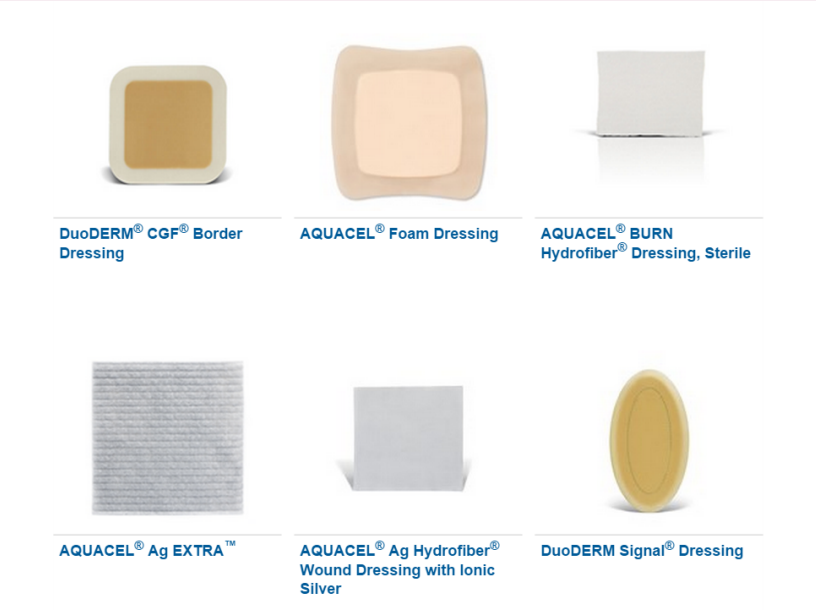
Biomaterials Characterization

Why?
When?
How?

PreClinical Testing has 3 main Stages

- Biomaterials Characterization
- Biocompatibility Testing
- Animal Trials

Classification of Devices

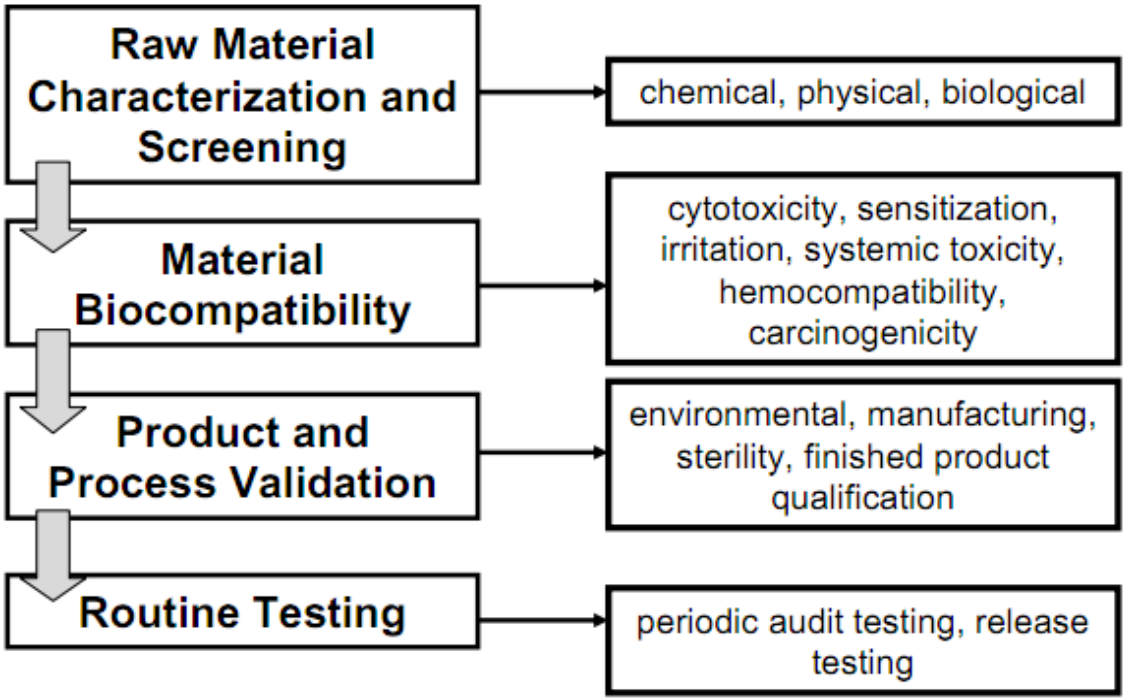


CCONVATEC WEBSITE

https://www.google.com/webhp?sourceid=chrome-instant&rlz=1C1CHFX_enUS592US592&ion=1&espv=2&ie=UTF-8#q=Glucometer+picture

https://www.youtube.com/watch?v=Bcfc73z_yqA

Testing Biomaterials: Four Phases



BIOCOMPATIBILITY TESTING MATRIX

Nelson Laboratories Tests for Consideration

[Based on ISO 10993-1:2003(E) and FDA G95-1 Guidelines]

Device Categories			Biological Effect									
			Initial								Other[4]	
Body Contact		Contact Duration A- Limited [≤ 24 hrs] B- Prolonged [>24 hrs to ≤30 days] C- Permanent [>30 days]	Cytotoxicity	Sensitization	Irritation	Systemic Toxicity	Subacute (Subchronic Toxicity	Genotoxicity	Implantation	Hemocompatibility	Chronic Toxicity	Carcinogenicity
Surface Devices	Skin	A	■	■	■							
		B	■	■	■							
		C	■	■	■							
	Mucosal Membranes	A	■	■	■							
		B	■	■	■	◊	◊		◊			
		C	■	■	■	◊	■	■	◊		◊	
	Breached or Compromised Surfaces	A	■	■	■	◊						
		B	■	■	■	◊	◊		◊			
		C	■	■	■	◊	■	■	◊		◊	
External Communicating Devices	Blood Path, Indirect[3]	A	■	■	■	■				■		
		B	■	■	■	■	◊			■		
		C	■	■	◊	■	■	■	◊	■	■	■
	Tissue[1] /Bone/Dentin Communicating	A	■	■	■	◊						
		B	■	■	■	■	■	■	■			
		C	■	■	■	■	■	■	■		■	■
	Circulating Blood[3]	A	■	■	■	■		◊[2]		■		
		B	■	■	■	■	■	■	■	■		
		C	■	■	■	■	■	■	■	■	■	■
Implant Devices	Tissue/Bone	A	■	■	■	◊						
		B	■	■	■	■	■	■	■			
		C	■	■	■	■	■	■	■		■	■
	Blood[3]	A	■	■	■	■	■		■	■		
		B	■	■	■	■	■	■	■	■		
		C	■	■	■	■	■	■	■	■	■	■

[1] "Tissue includes tissue fluids and subcutaneous spaces.

[2] For all devices used in extracorporial circuits.

[3] Pyrogenicity/Materials Mediated should be considered.

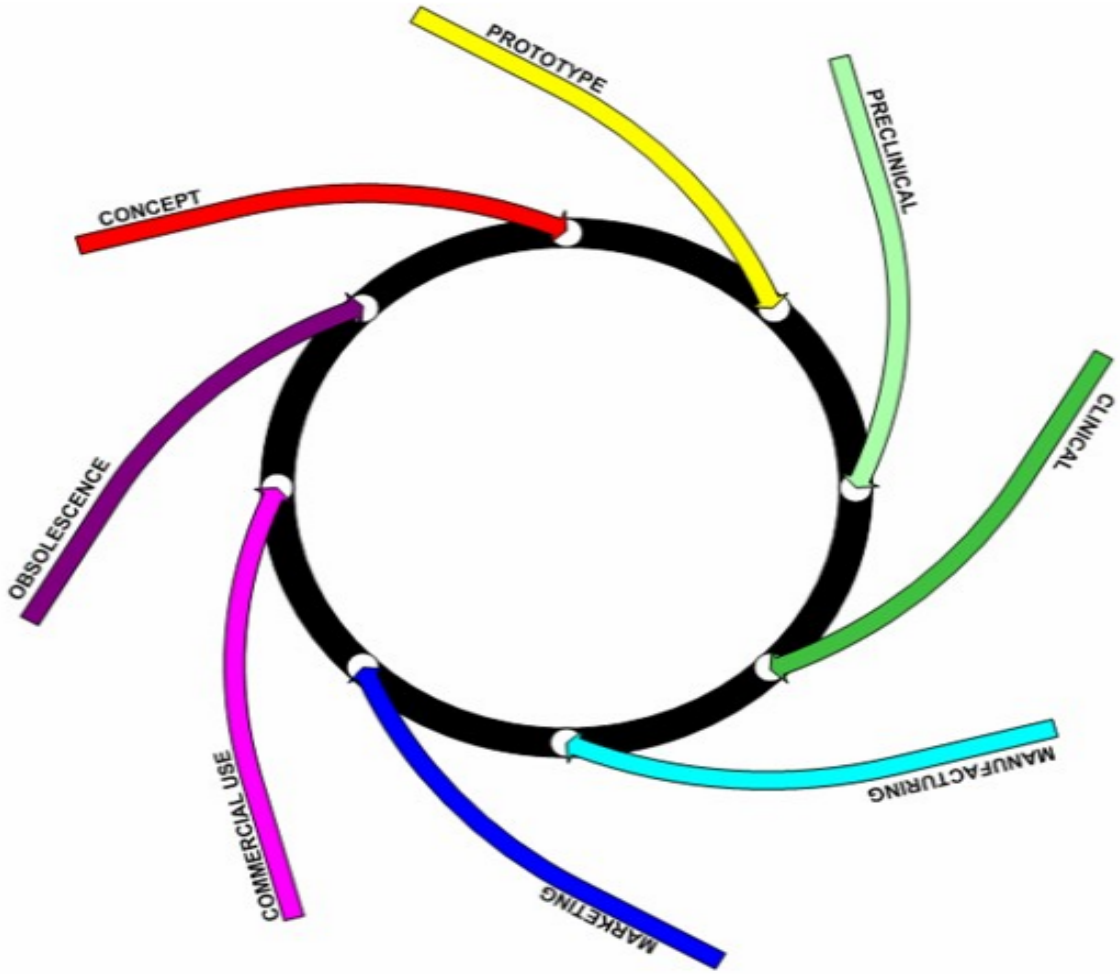
[4] Supplemental tests for consideration

■- ISO Evaluation Tests for Consideration

◊- Additional tests which the FDA considers may be applicable

For additional information or a price quote contact
sales@nelsonlabs.com

TIMING OF BIOCOMPATBILITY TESTING

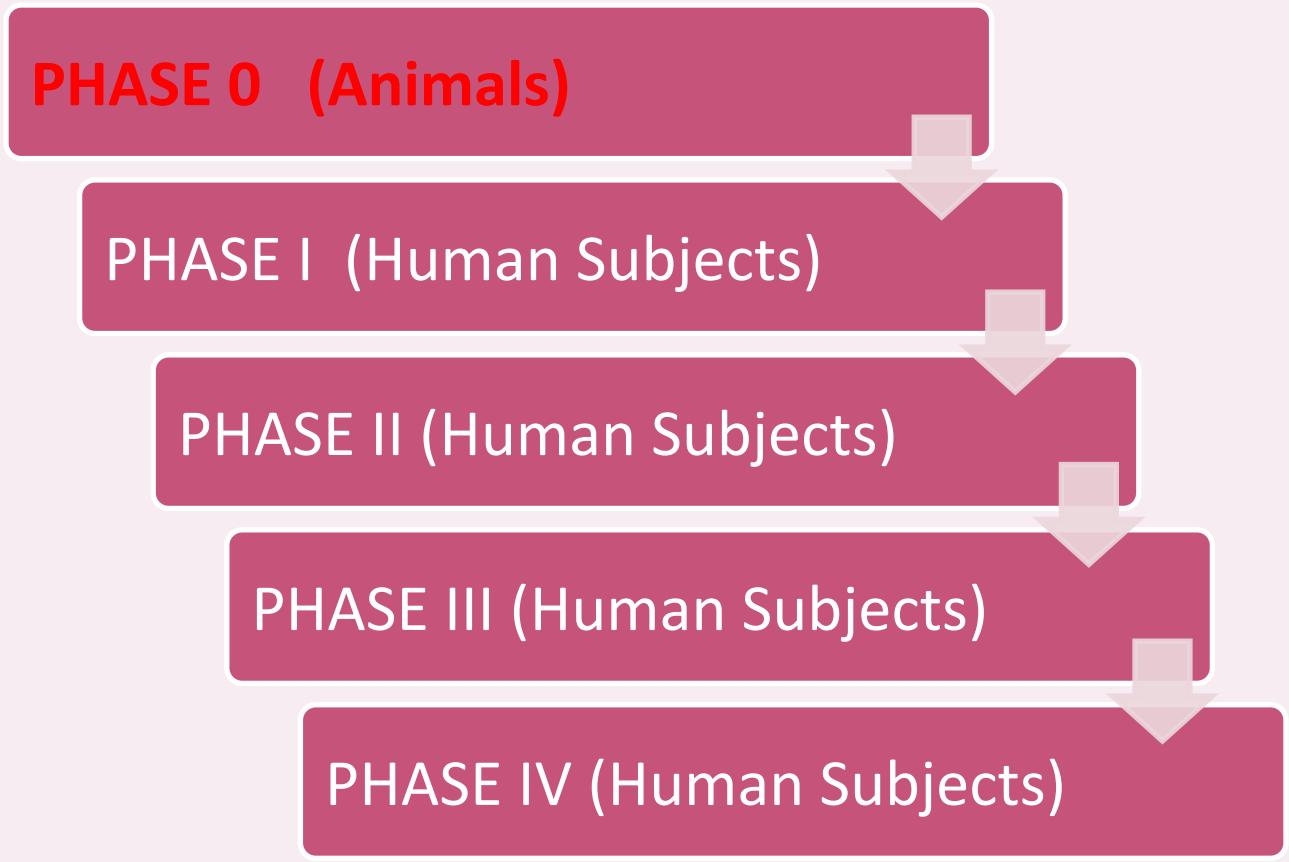


[+] Enlarge Image

Figure 1. This diagram shows the medical device design life cycle as defined by the FDA.[1]

Source: http://www.ni.com/white-paper/5711/en

- Biocompatibility testing begins in PHASE 0 of FDA Clinical Trials in small animals (i.e. rodents) . The extent of testing and carry-over to the other phases depend on the trial design. All trials are conducted according to **GCP and ISO standards**.
- Substituting animal trials by using **simulated biomaterial constructs** is a very active pursuit for **ethical and technical** reasons: Depending on the test, the behavior of the biomaterial in animals does not yield to the same outcome in humans.

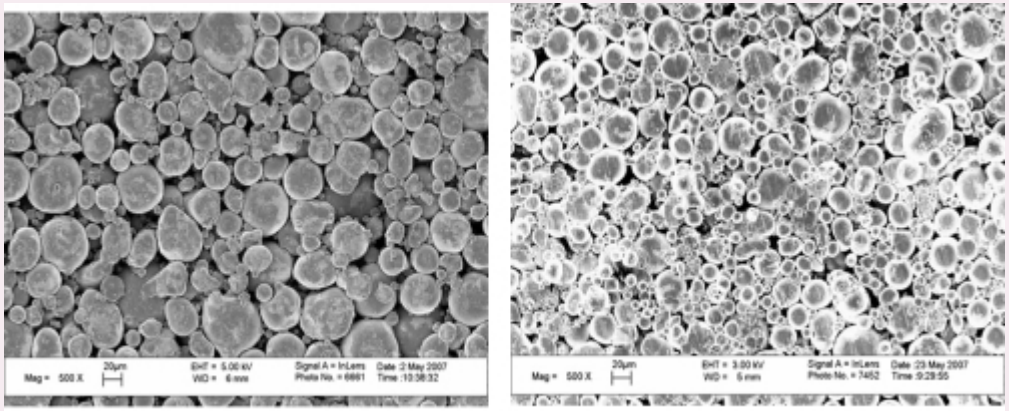


BULK vs SURFACE PROPERTIES

- For biomaterial surface properties rule adhesion and biocompatibility.
- Regardless of surface properties materials need perform mechanically to carry the imposed load, electrically, thermally, optically depending on the design criteria.

There are 2 types of material properties: Intrinsic and Ext

Grain Size is an **intrinsic** property of the material
Inherent to the chemical structure and independent of the amount of material present or direction of the material being stressed.



Coarse Grain NiTi (as purchased) Fine Grain NiTi (with mesh)

http://openi.nlm.nih.gov/detailedresult.php?img=2526362_ijn0301-75-02&req=4

Extrinsic properties such as **strength, stiffness** can be manipulated by intrinsic or other properties (number and distribution of crystal defects) at different length scales.

For the same stiffness, a finer grain size a material will exhibit a higher yield strength than coarser one.

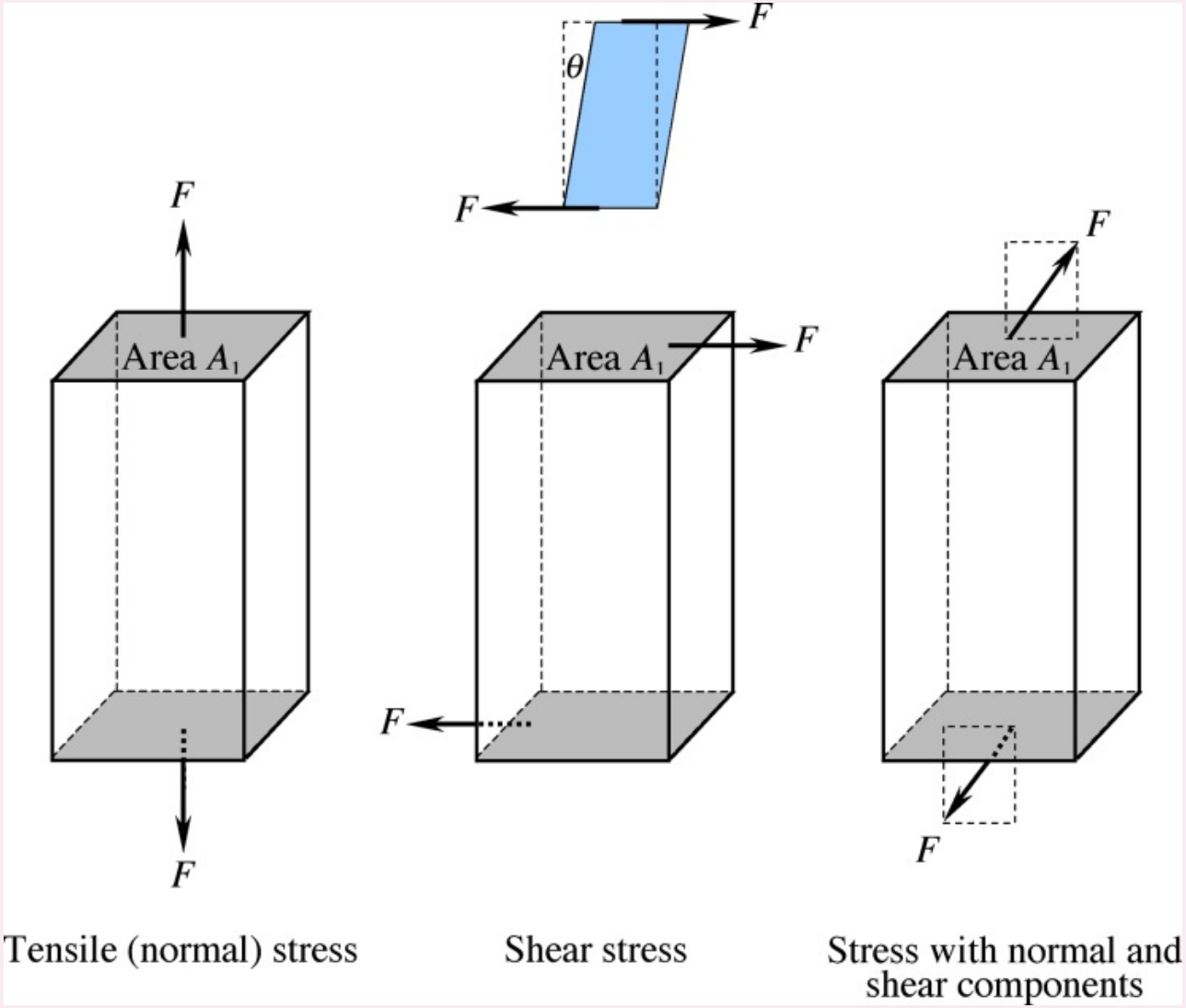

F
θ
F
F
Area A_1
F
Tensile (normal) stress
Area A_1
F
F
Shear stress
F
Area A_1
F
Stress with normal and shear components

Figure3.1

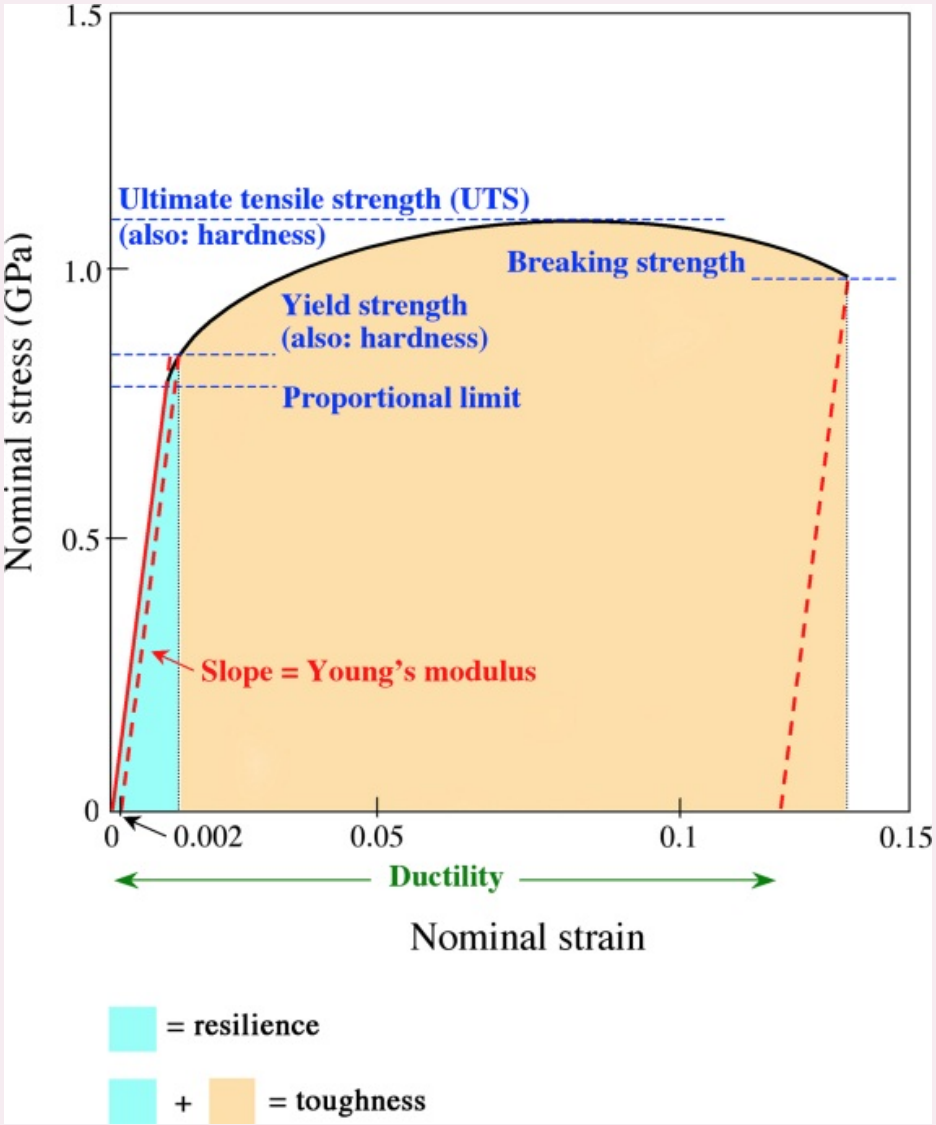

1.5
1.0
0.5
0
Nominal stress (GPa)
Ultimate tensile strength (UTS)
(also: hardness)
Breaking strength
Yield strength
(also: hardness)
Proportional limit
Slope = Young's modulus
0
0.002
0.05
0.1
0.15
Ductility
Nominal strain
= resilience
+
= toughness

Figure 3.3

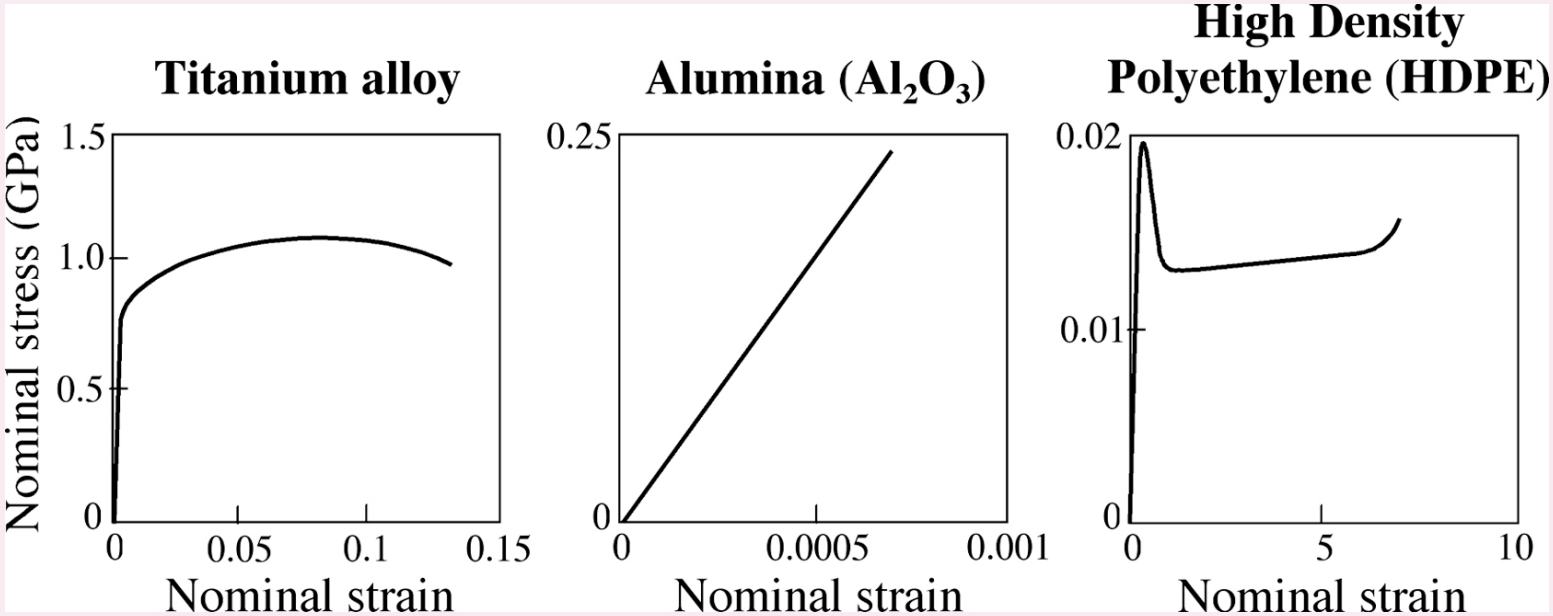
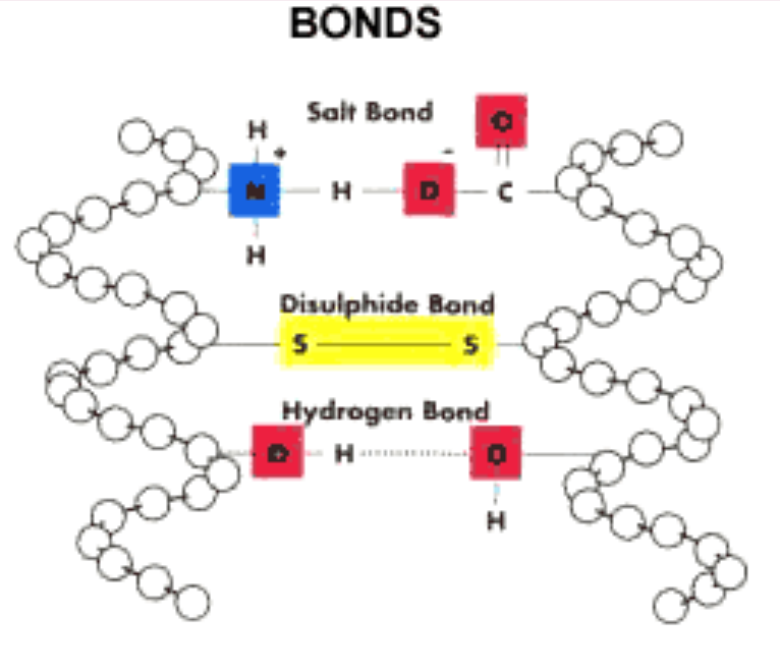
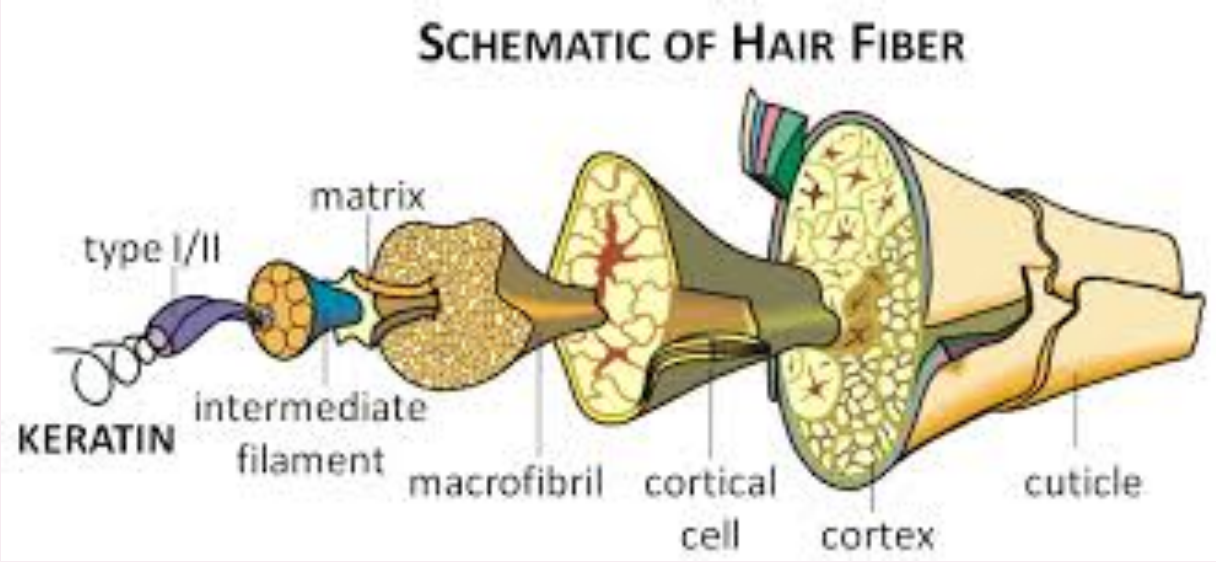

Titanium alloy
Alumina (Al_2O_3)
High Density Polyethylene (HDPE)
Nominal stress (GPa)
1.5
1.0
0.5
0
0
0.05
0.1
0.15
Nominal strain
0.25
0
0
0.0005
0.001
Nominal strain
0.02
0.01
0
0
5
10
Nominal strain

Figure 3.2

Today we are going to measure and compare the elasticity of a rubber band and that of humain hair by constructing a Stress/Strain Curve!



http://www.texascollaborative.org/hildasustaita/bonds.gif

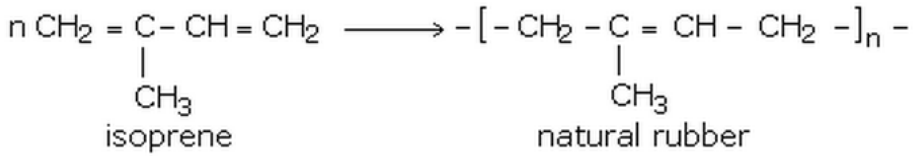


https://encrypted-tbn3.gstatic.com/images?q=tbn:ANd9GcQkVtuL5KT82Y7plYgihmo2QjgfuT5GKHh-l9hahSn8ich0Xcn1bQ

Structure of Natural Rubber

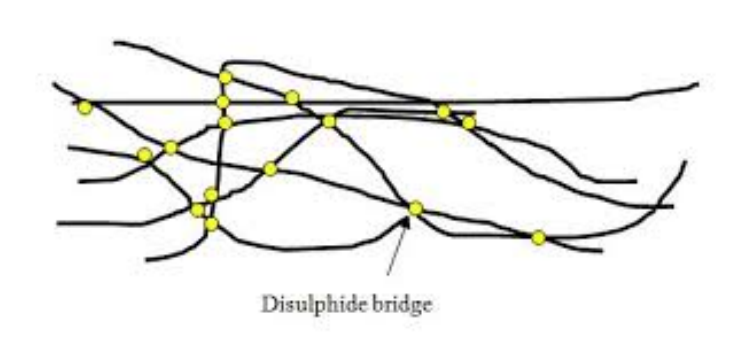
Back to Top

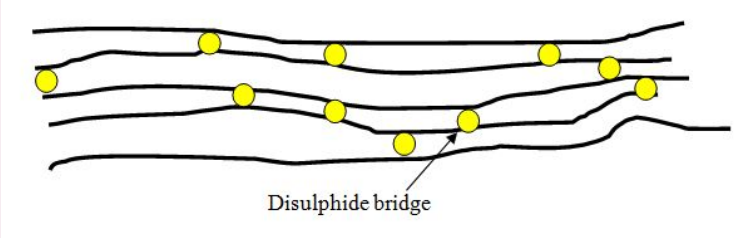
Natural rubber is a linear polymer of an unsaturated hydrocarbon called isoprene (2-methyl butadiene). There may be as many as 11,000 to 20,000 isoprene units in a polymer chain of natural rubber.



http://www.sciencedaily.com/releases/2013/02/130206141408.htm

WHETHER IS HAIR OR NATURAL RUBBER STRECHING UNTANGLES THE CHAINS HELD BY DISULFIDE BONDS.





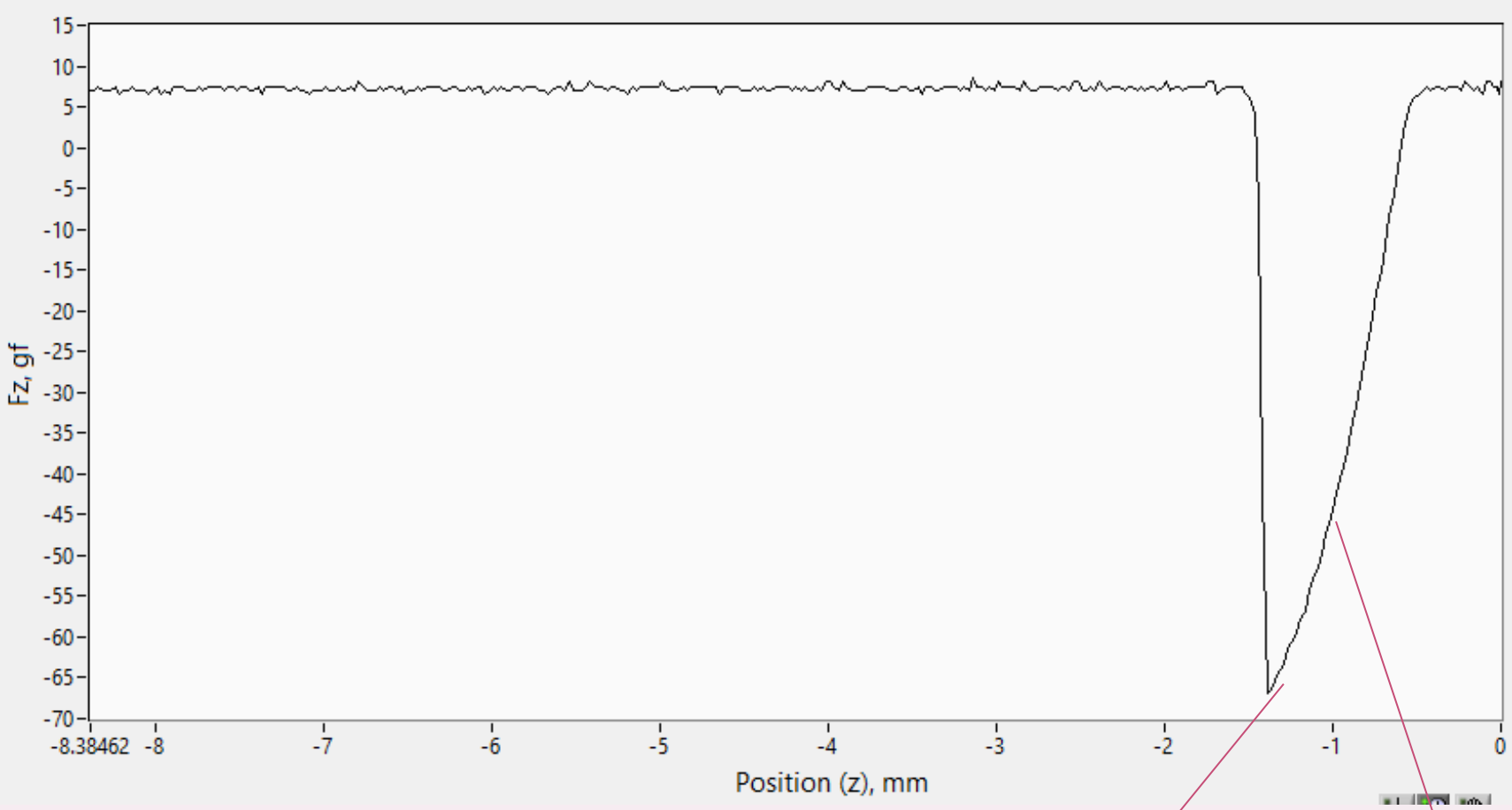
$$E = \frac{\sigma}{\varepsilon}$$

$$\sigma = \frac{F}{A_0}$$

$$\varepsilon = \frac{\Delta l}{l_o}$$

E Elastic modulus (Pa)
σ Stress (Pa)
ε Strain (no units)
A_0 Cross-sectional area (cm^2)

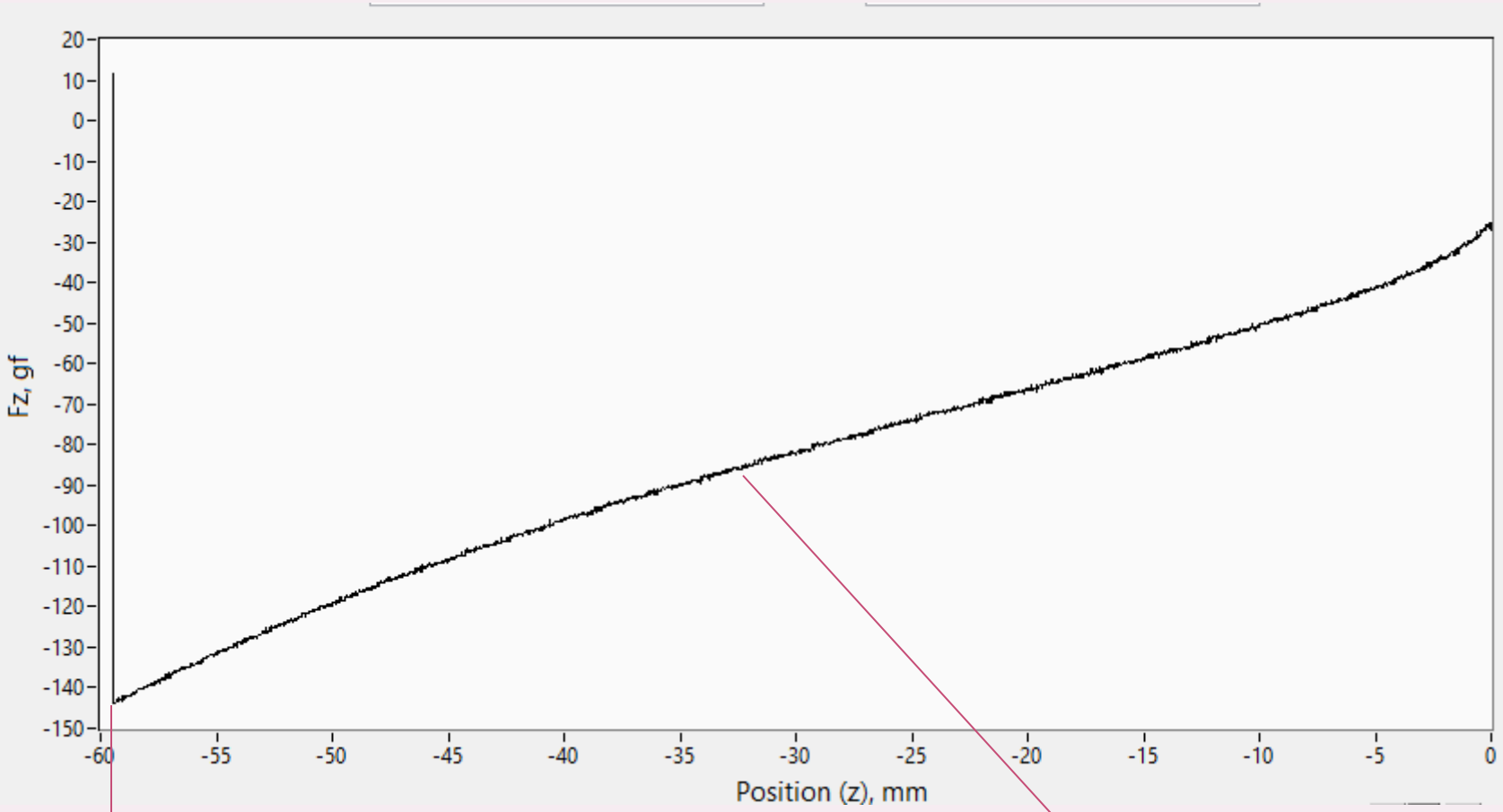
TENSILE TESTING OF HAIR (Lo = 2cm)



Snap

Elastic deformatio

TENSILE TESTING OF RUBBER Lo=2cm



snap

Elastic deformation

Now ½ of you stay here
and the other ½ go to the lab for
the tensile strength demo.

Prior to Experimentation by Student, Consent Form Required from Santa Clara IRB?

Research with Human Subjects

Forms

Human Subjects Application (eProtocol)
Modification Form (eProtocol)
Report Form (eProtocol)
Renewal Form (eProtocol)

Form Models

Basic Elements of Informed Consent (Appendix E)
Model Form for Verbal Script (Appendix F)
Model Form for Cover Letter (Appendix G)
Model Form for Letter of Consent for Adults (Appendix H)
Model Form for Parental Letter of Consent for Minors (Appendix I)
Model Form for Samples of Written Child Assent (Appendix J)
Model Form for Informed Consent Form for Adults (Appendix K)

MODEL FORM

PARENTAL LETTER OF CONSENT FOR MINORS

(Typically used for studies that would not exceed minimal risk)

Dear Parent:

I am a professor [a graduate student under the direction of Professor _____] in the Department of _____ at Santa Clara University. I am conducting a research study *to __ (state purpose of study)*_____.

I am requesting your child's participation, which will involve _____. (*Include the nature of the participation and the expected duration of the subject's participation*). Your child's participation in this study is voluntary. If you choose not to have your child participate or to withdraw your child from the study at any time, there will be no penalty, It will not affect your child's grade, treatment/care--***whichever applies***. Likewise, if your child chooses not to participate or to withdraw from the study at any time, there will be no penalty. The results of the research study may be published, but your child's name will not be used.

Although there may be no direct benefit to your child, the possible benefit of your child's participation is _____.

If you have any questions concerning the research study or your child's participation in this study, please call me at ( ) ___-_____ or Dr. ___ at ( ) ___ - _____.

Sincerely,

(Researcher's name)

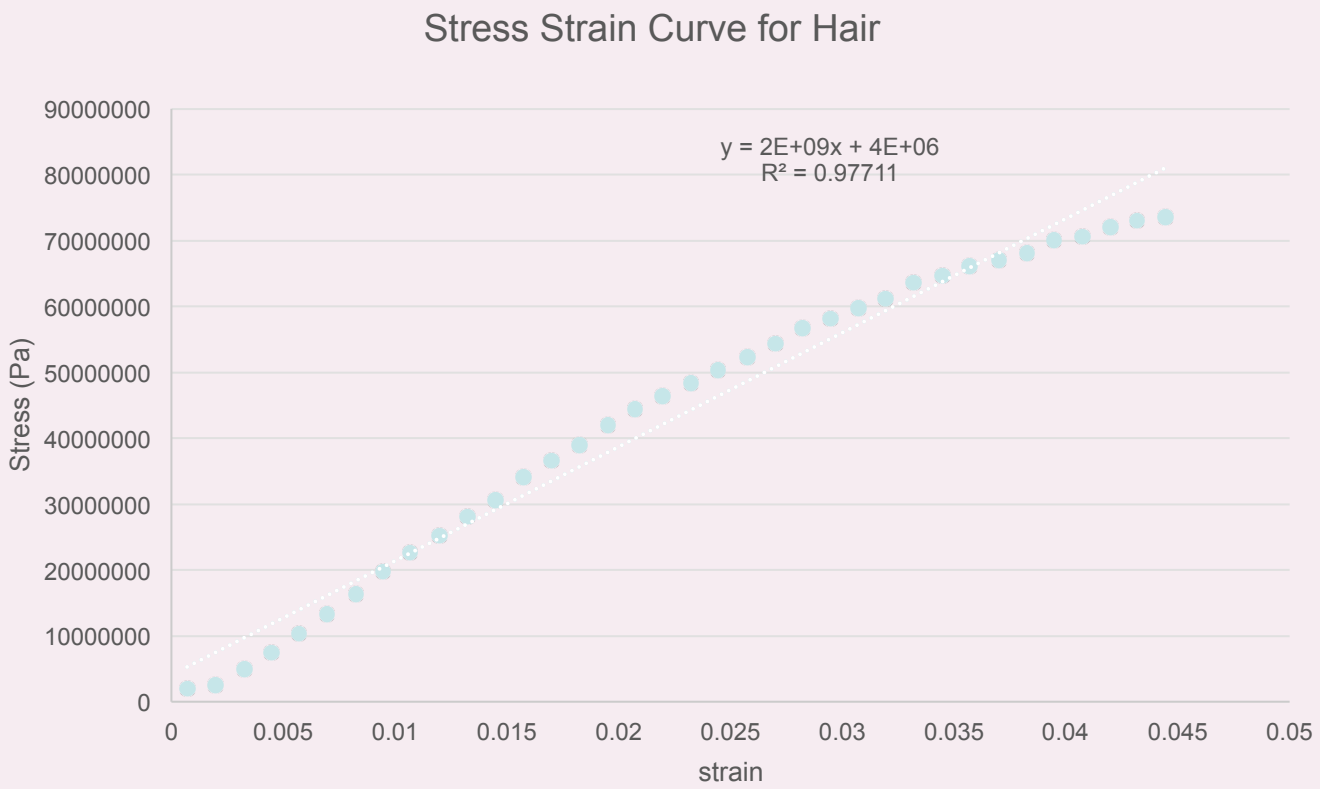
By signing below, you are giving consent for your child _____ to participate in the above study. *(Release statement for videotaping or relinquishing confidentiality must be inserted here if applicable.)*

_____	_____	_____
Signature	Printed Name	Date

If you have any questions about you or your child's rights as a subject/participant in this research, or if you feel you or your child have been placed at risk, you can contact the Chair of the Human Subjects Committee through Office of Research Compliance and Integrity at (408) 554-5591.

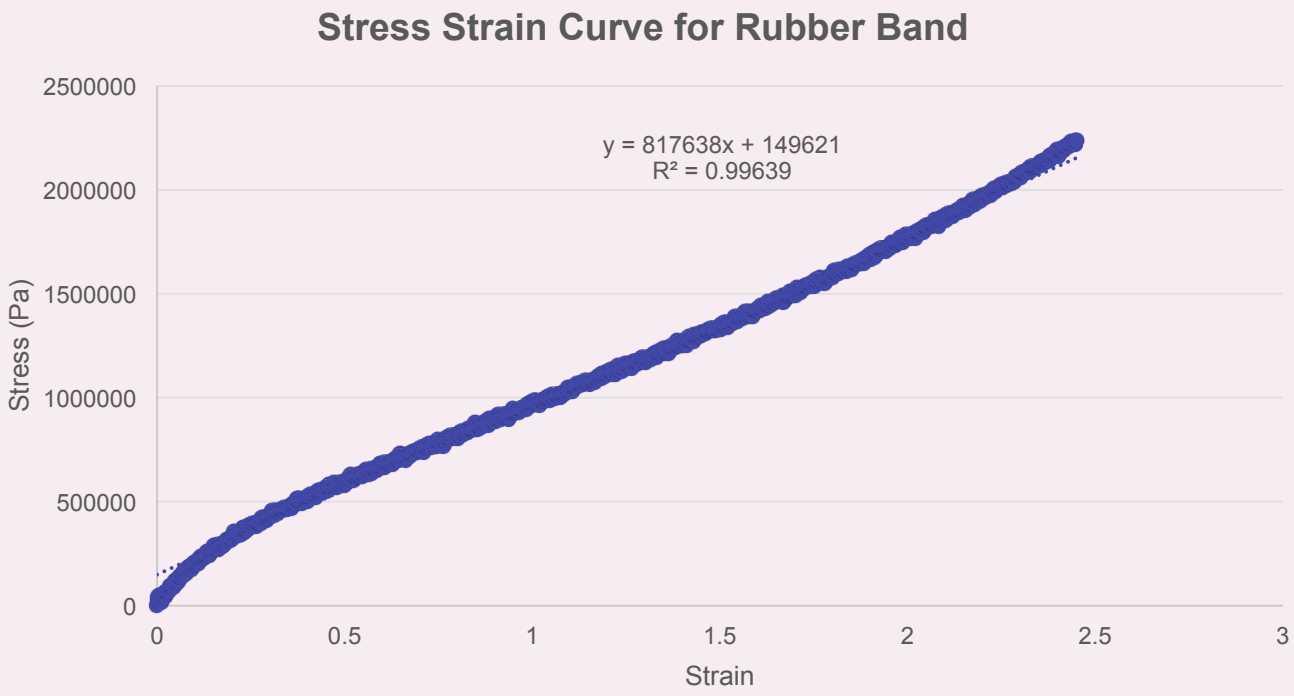
RESULTS

HAIR



E (Pa)	**2.00E+09E (Gpa)**	**2Published (GPa)**	**7**

RUBBER BAND



E (Pa)	**817638**	**E(GPa)**	**0.000818**	**Published (GPa)**	**0.01**

Sources of Error

CONCLUSION

HAIR IS STIFFER THAN THE RUBBER BAND!