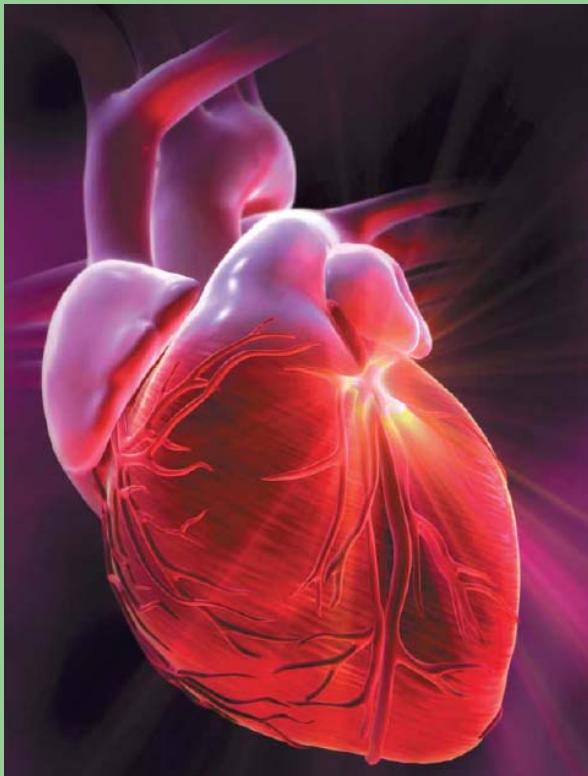


# Department of Biomedical Systems



Physicist  
Physician

# **Integration of macro-, micro- and nanotechnologies for biomedical engineering**

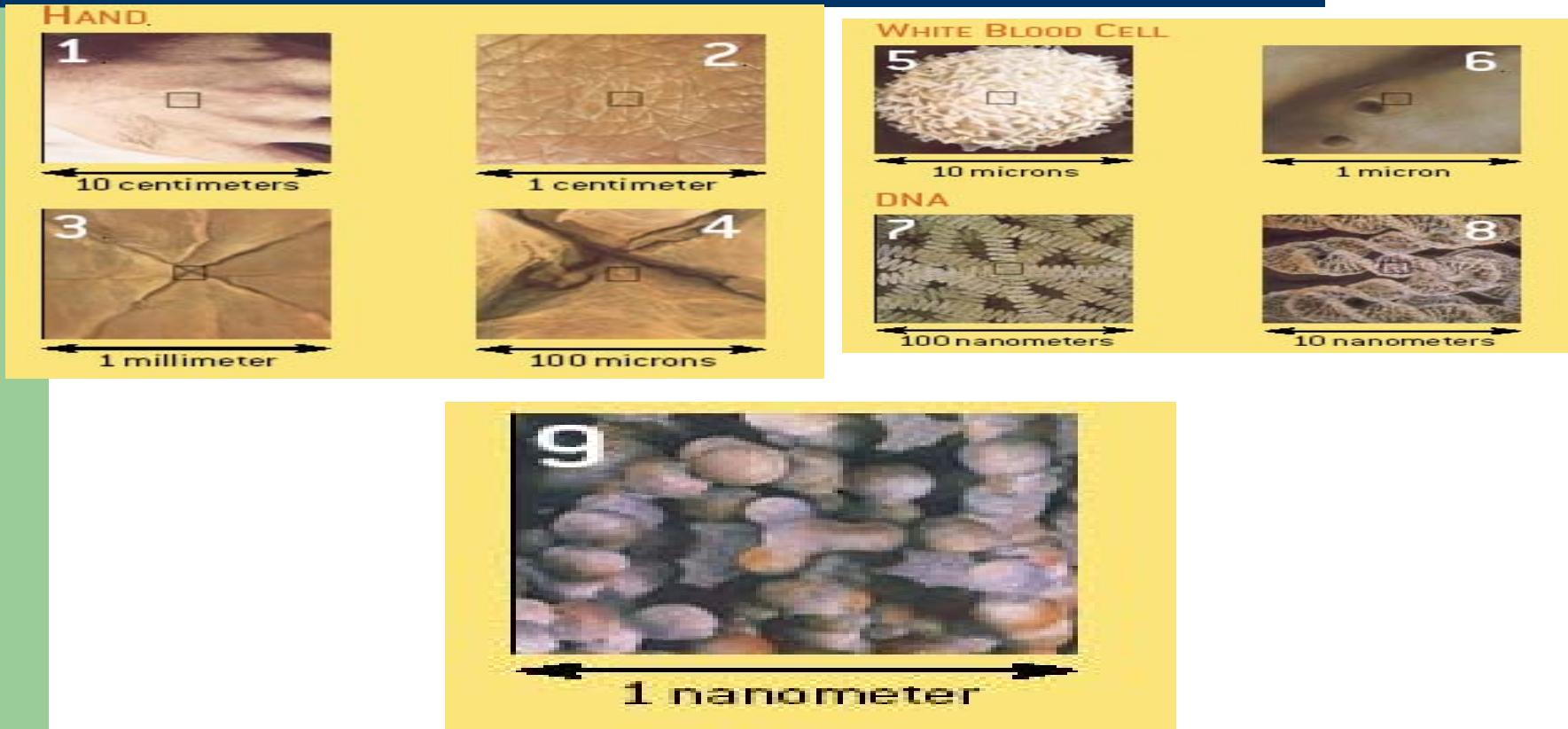


**Sergey Selishchev**

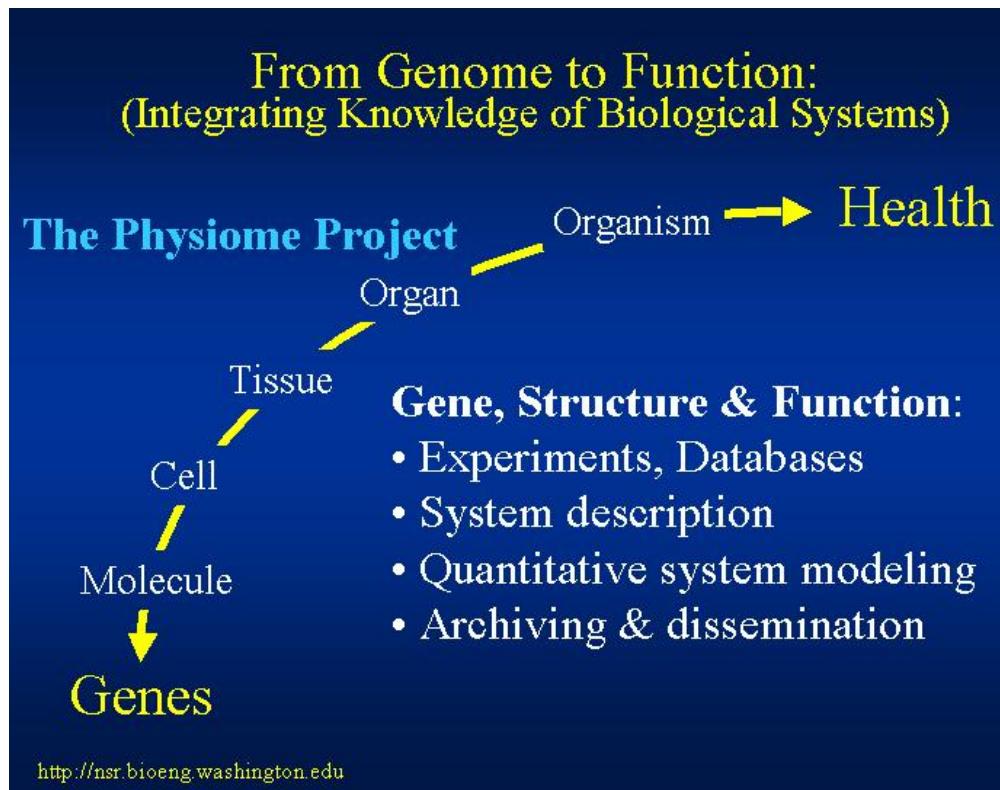
# Macro – micro – nano. “bottom-up” “top-down”



# Macro-micro-nano scales



# Physiome project



# Integration of macro-, micro and nanotechnologies for diagnostics and treatment of cardiovascular diseases



What challenge  
for physicists  
from physicians?

# Challenges

- Fibrillation – Defibrillation
- Atherosclerosis
- Artificial heart

# Macro scale of the heart

Heart of the adult	~ 100 mm	Length: 120 -130 mm Width: 70 – 80 mm
DNA	~ 10 mm	Length in unwrapped conditions
aorta	10 – 30 mm	Internal diameter
arteries	0,5 – 5 mm	Internal diameters

# Micro scale of the heart ( 1 )

arterioles	25 – 100 µm	Internal diameter
capillaries	3 – 10 µm	Internal diameter
bacteria	1 – 10 µm	
chromosome	9 µm	Human chromosome

## Micro scale of the heart ( 2 )

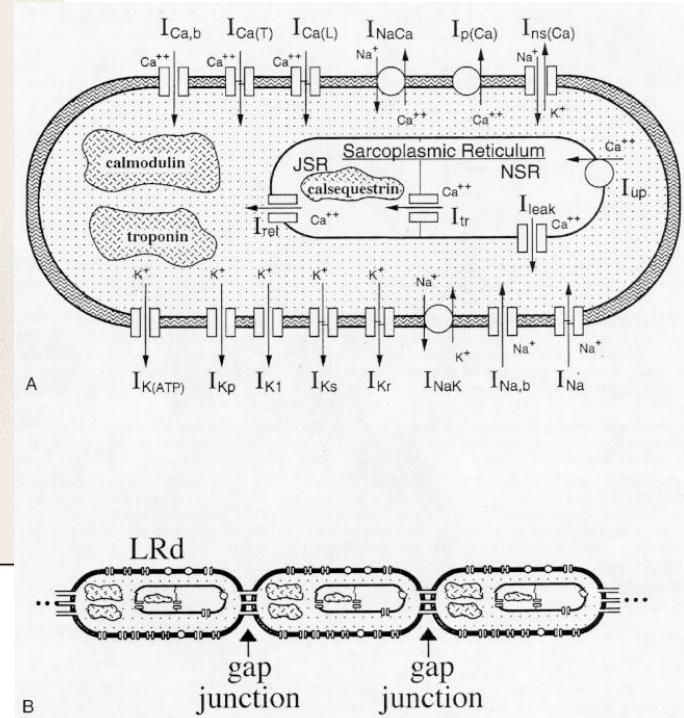
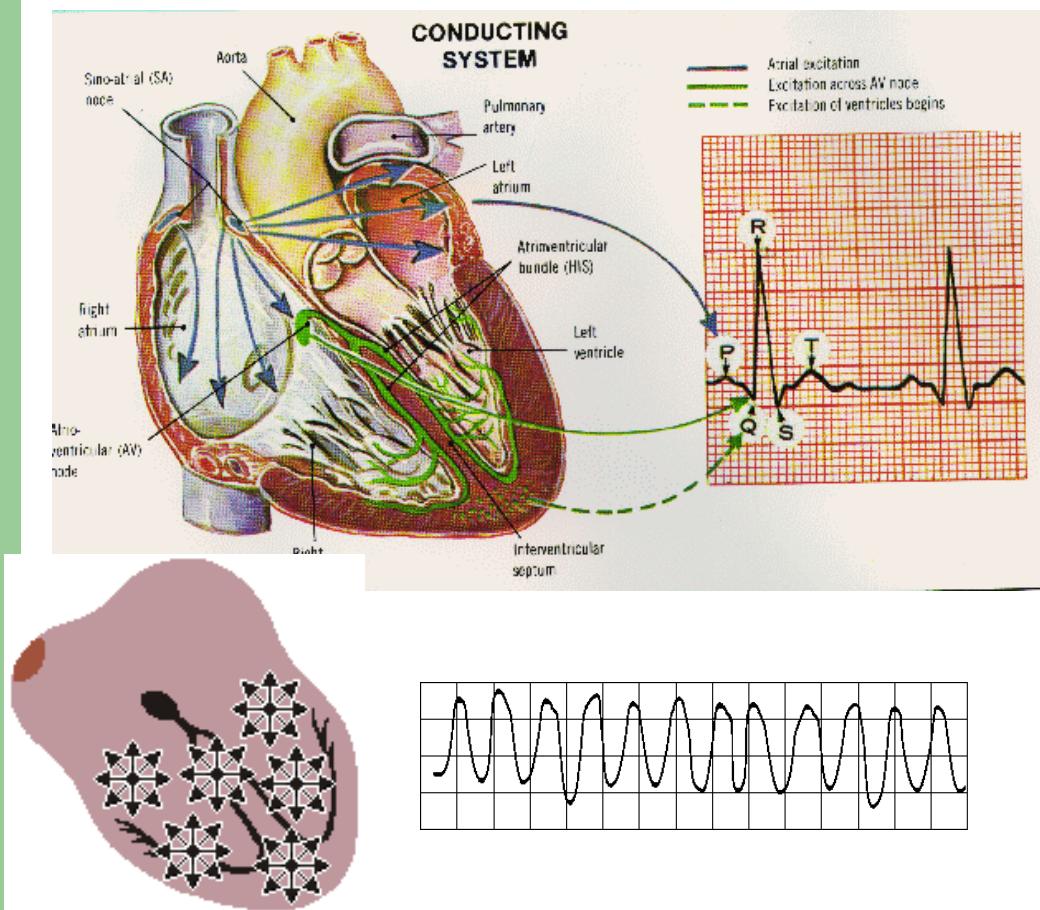
Myocyte	Cylindrical form	Length – 100 µm Diameter – 10 µm
White blood cell	Spherical form	8-15 µm
Red blood cell	Disk form	Diameter – 8 µm Thickness – 1,5 µm
Platelet	Spherical form	3 µm

# Nano scale of the heart

Virus	20 – 200 nm
Protein	7 – 50 nm
Membrane thickness	7 nm
DNA (The cross-section size)	2 nm
Molecular of water	0,3 nm
Atom of hydrogen	0,1 nm

$$U(t, \vec{r}) = \phi_i(t, \vec{r}) - \phi_e(t, \vec{r})$$

# Fibrillation



## External Defibrillators (20 A, 10 ms) up to 200 – 500 J

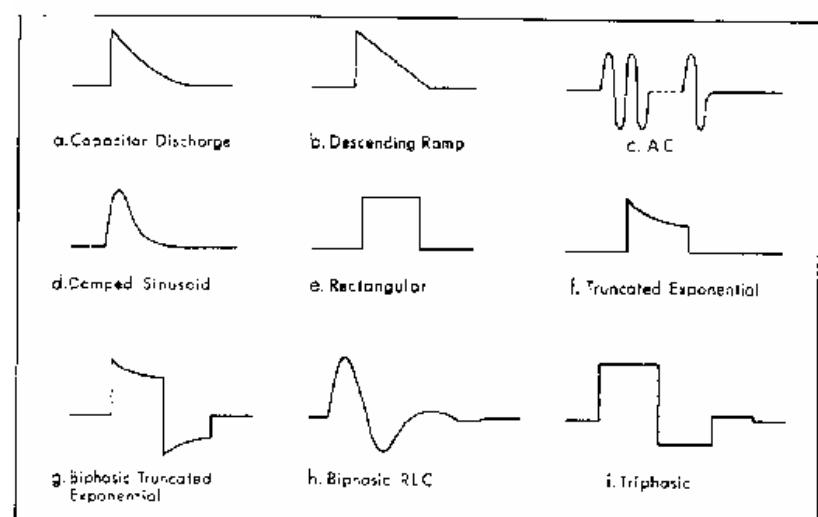
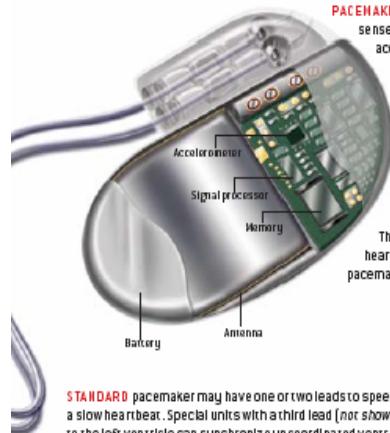
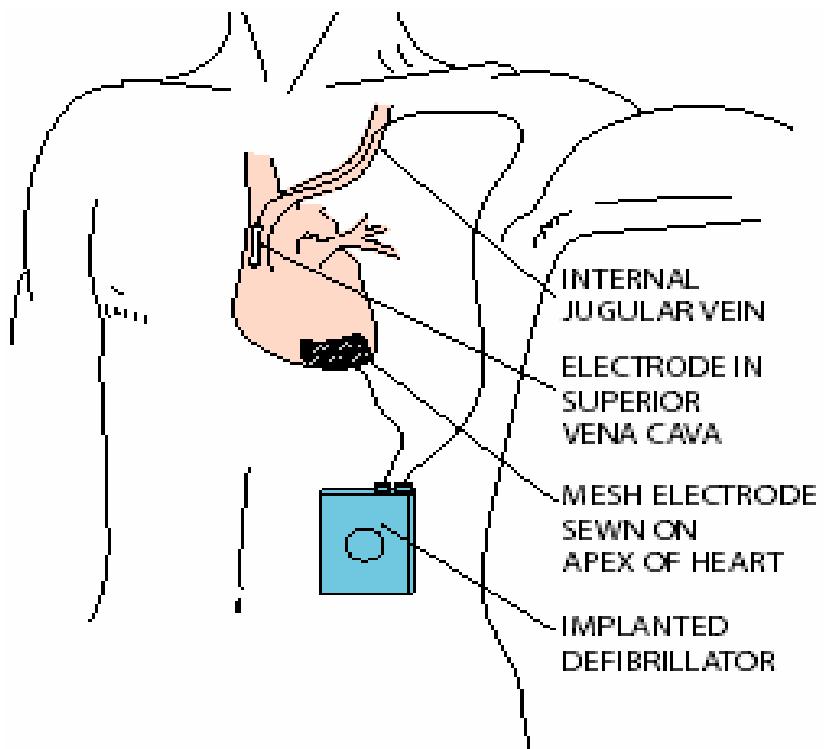


Figure 1. Waveforms that have been used for defibrillation research include decaying exponential (a); descending ramps (b); sinusoids (c); damped sinusoids (d); rectangular (e); truncated exponentials (f); biphasic truncated exponentials (g); biphasic from RLC networks (h); and triphasic (i).

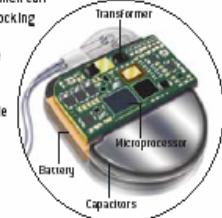
# Wearable cardioverter/defibrillator



# Implantable cardiostimulator-defibrillator



**PACEMAKER** circuitry emits a 1-to-5-volt impulse if the signal processor senses that the heart's pulse is too slow, stopped or uncoordinated. An accelerometer tells the unit to quicken the heartbeat if it senses physical activity. A technician can retrieve information from the memory using a magnetic wand that communicates through the skin via radio-frequency signals to an antenna. Implantable cardioverter defibrillators (inset) correct quivering (fibrillation) by the atria or ventricles, which can cause cardiac arrest, by shocking the heart with 30 joules or more of energy, resetting the heart's conduction system. The unit can also stop a racing heartbeat (tachycardia) and provide pacemaker functions.



**STANDARD** pacemaker may have one or two leads to speed up a slow heartbeat. Special units with a third lead (not shown) to the left ventricle can synchronize uncoordinated ventricle contractions, which plague some people who have weak or damaged hearts.

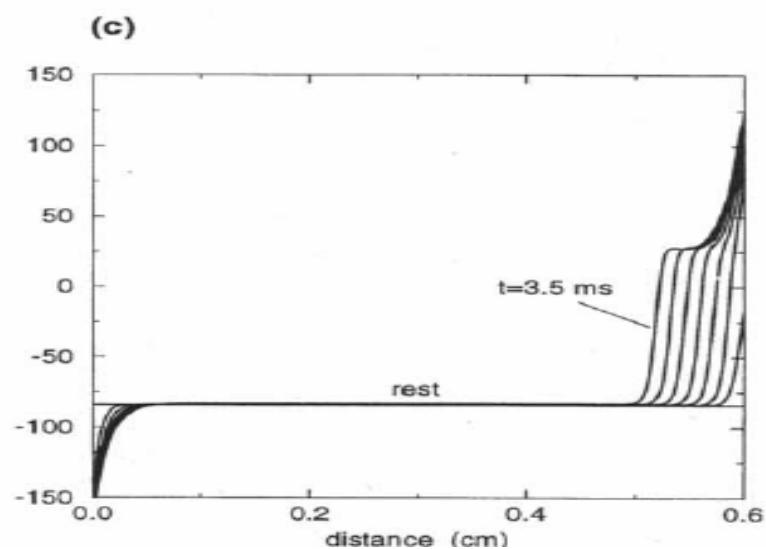
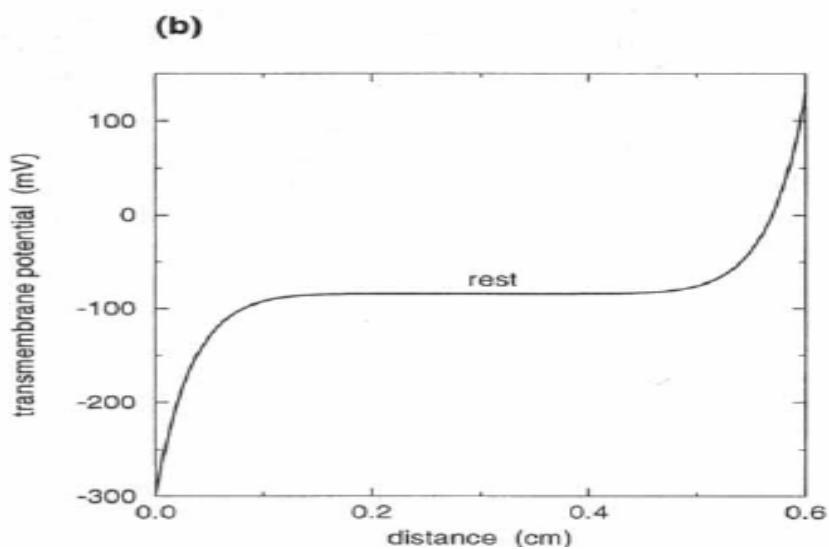
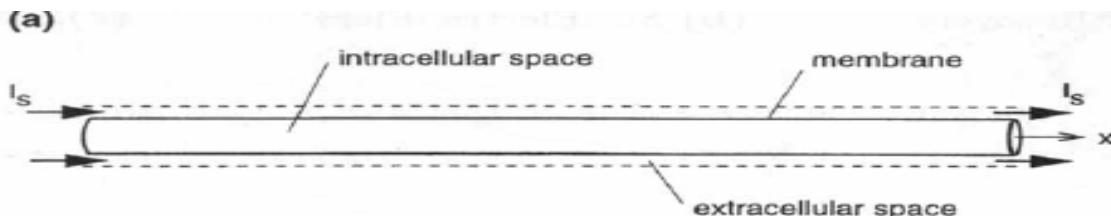


**TIP** of a wire lead is fixed into heart tissue and delivers a small electrical impulse that causes conduction cells to fire. The wire also senses heartbeat, tracked by the pacemaker. A reservoir of steroid is slowly released for several months after implantation, minimizing inflammation and the chance of rejection.

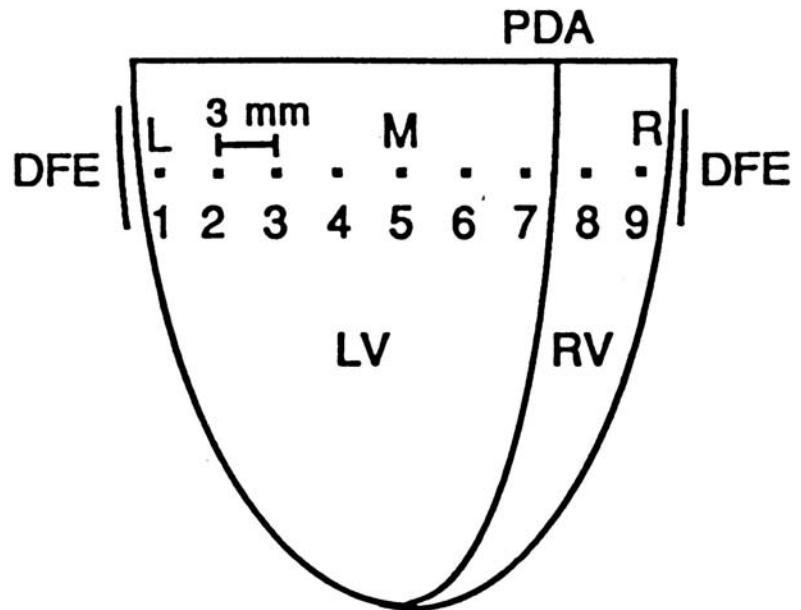


**HUMAN CASE** of a pacemaker or ICD is implanted in the chest, and leads are threaded through veins to the heart.

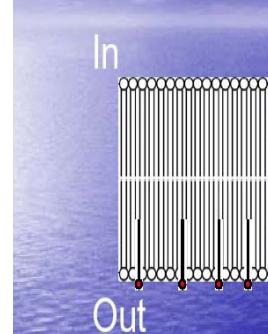
# TMP problem



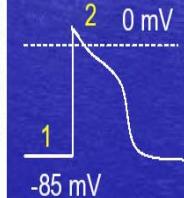
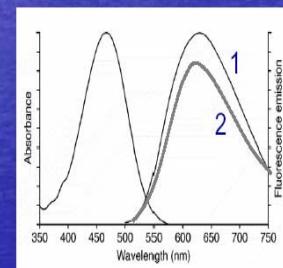
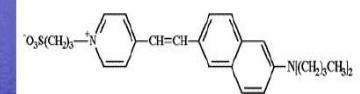
# TMP measurement



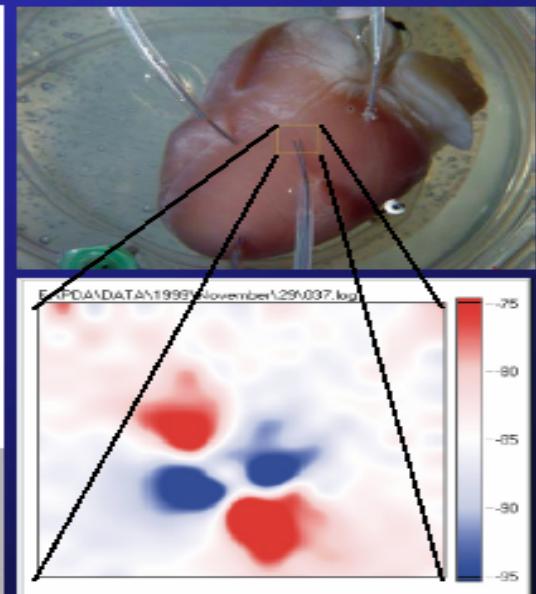
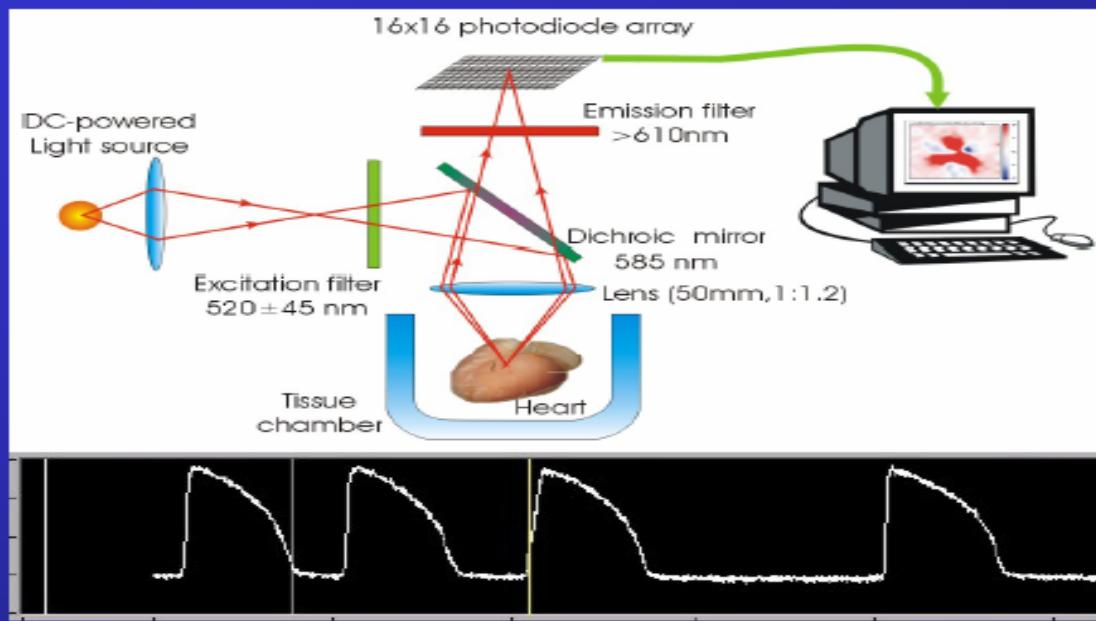
Recording action potential with voltage-sensitive dye di-4-ANEPPS



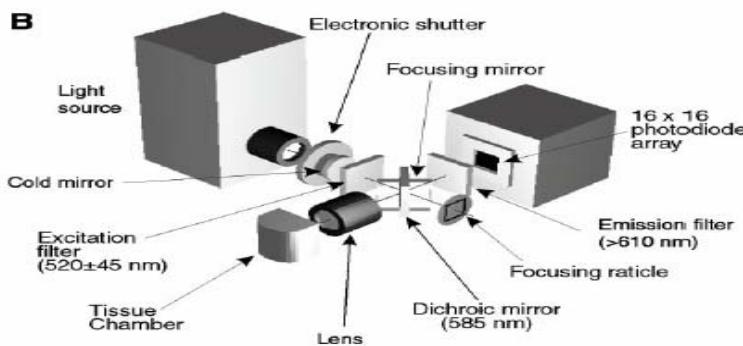
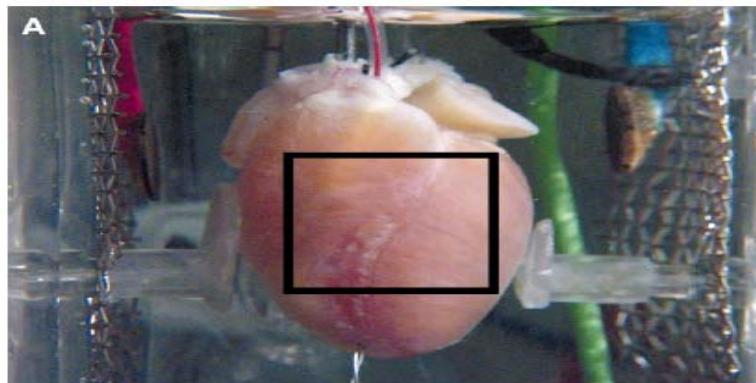
Di-4-ANEPPS



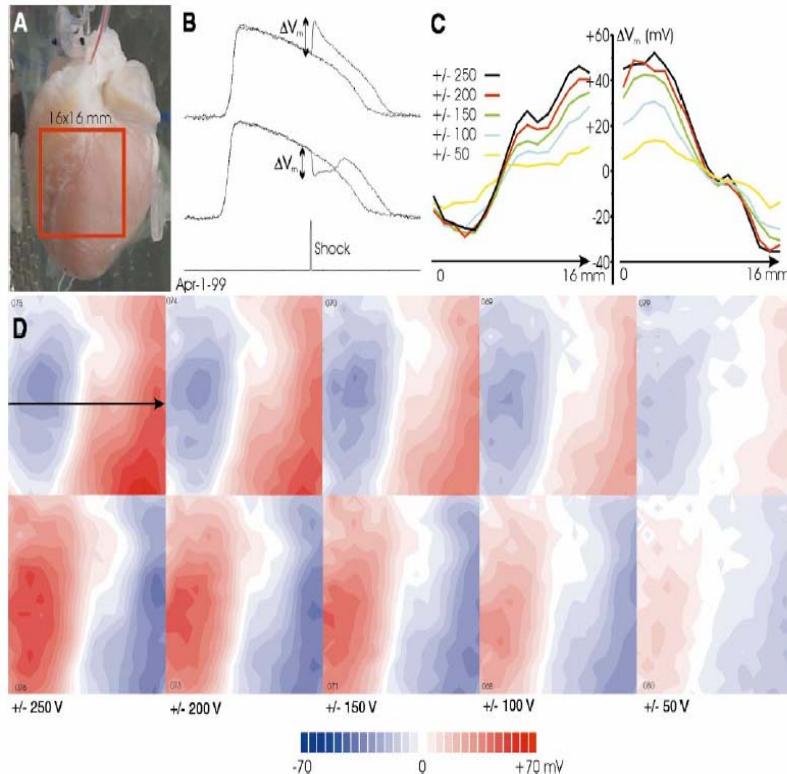
# Optical fluorescent imaging of transmembrane potential



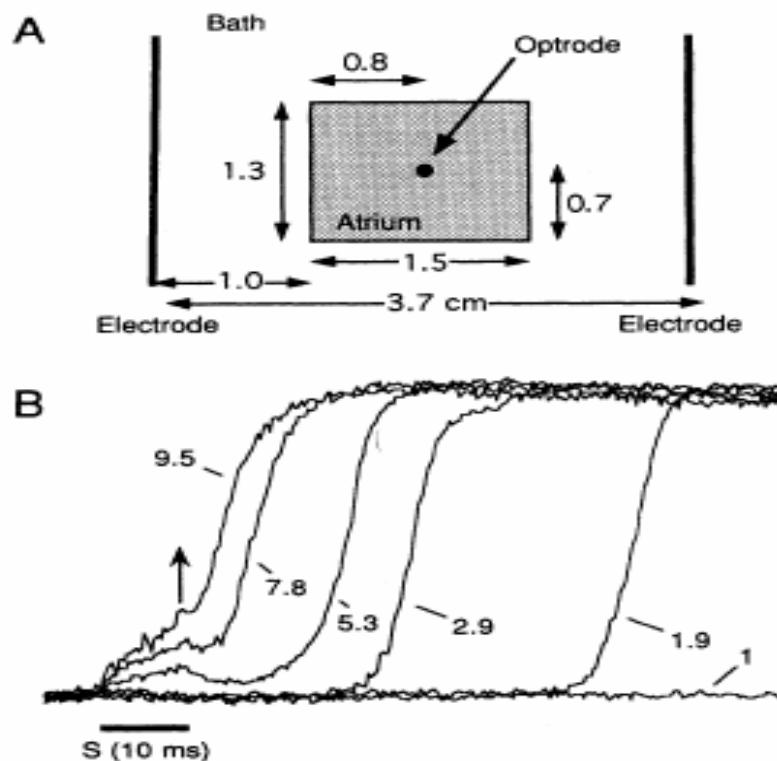
# TMP measurement at the electrical stimulation



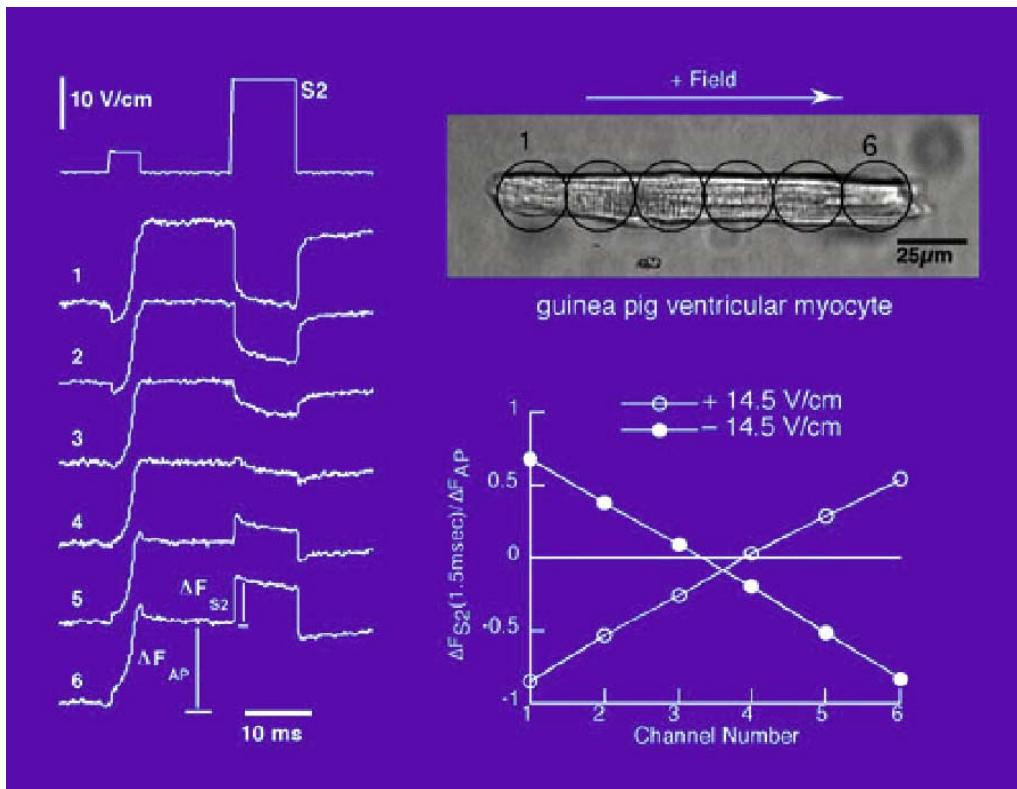
# Spatio-temporal distributions of the TMP

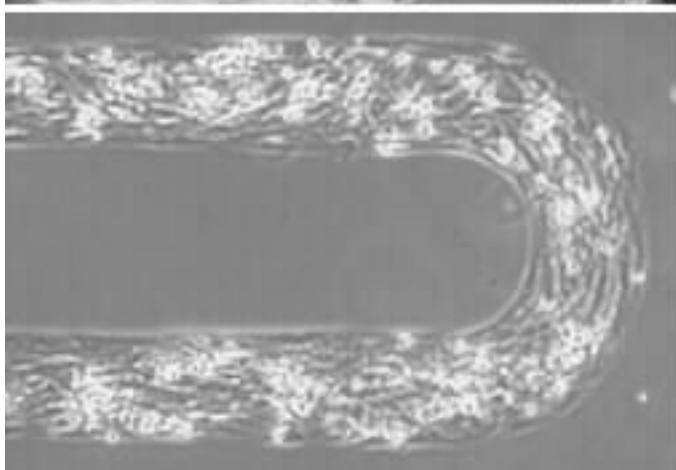
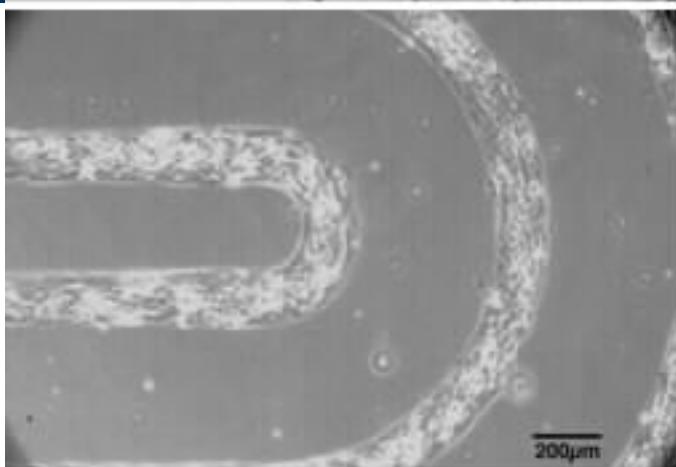


# TMP measurement in atrium

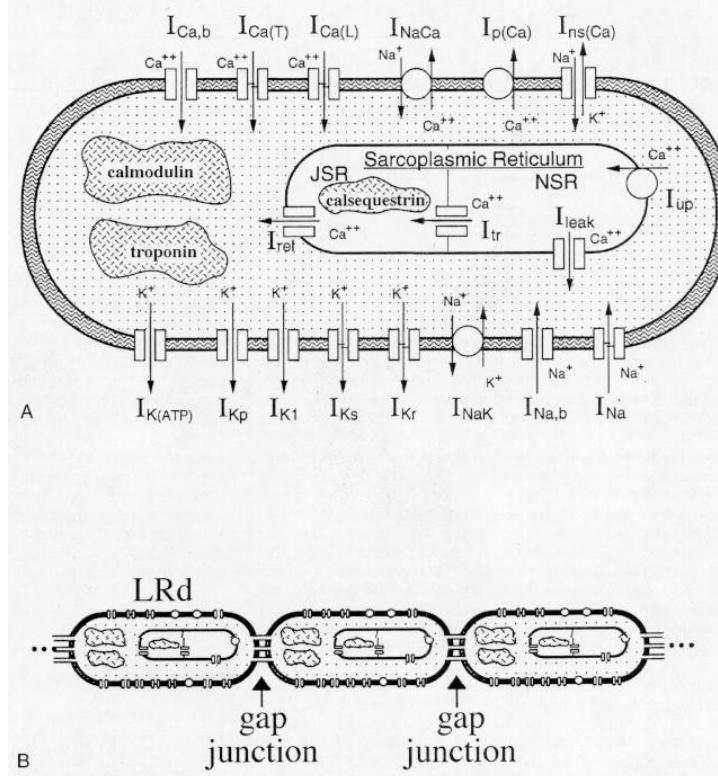


# TMP measurement in cells



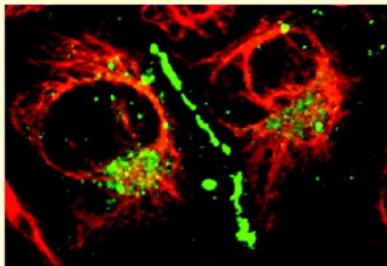


# Cell of heart



# Gap Junctions – From Cell To Molecule

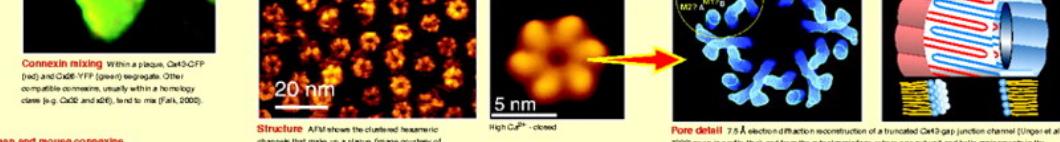
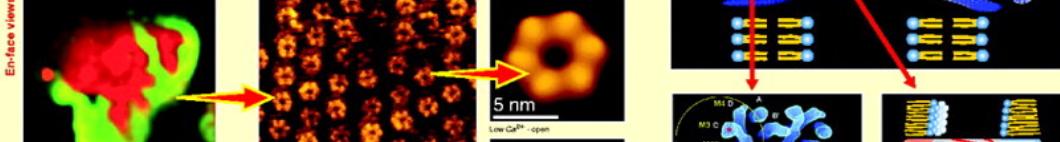
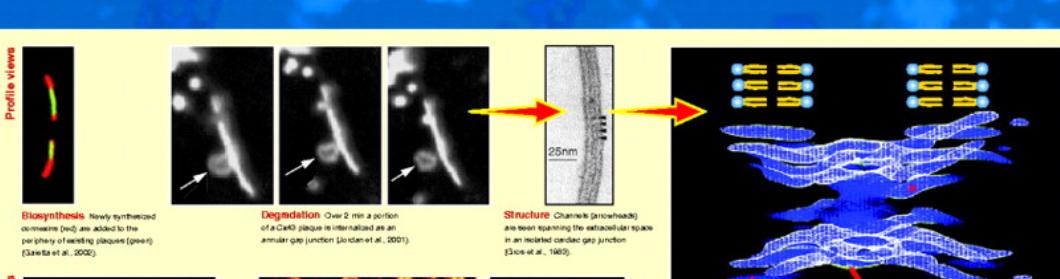
Bruce J. Nicholson



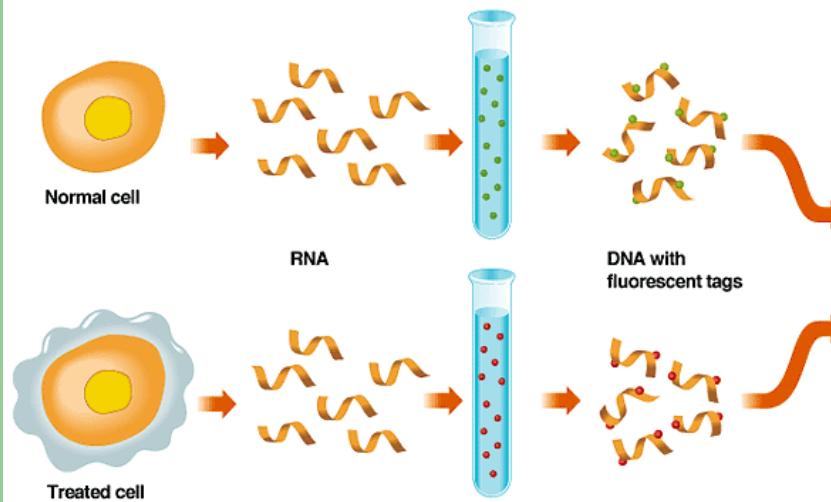
**Cell distribution** A connexin26 mutant associated with deafness (green) is found in punctate plaques at the interface between vimentin (red) filaments, and also happen in the ER and Golgi (image courtesy of T.T. Thomas and D.W. Laird, University of Western Ontario).

$\alpha$ -Group connexins	$\beta$ -Group connexins
mCx26.2	hCx1.0
mCx26.3	mCx26
mCx26.7	mCx26
mCx27	mCx26.3
mCx28	mCx26.3
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mCx425	mCx26.3
mCx426	mCx26.3
mCx427	mCx26.3
mCx428	mCx26.3
mCx429	mCx26.3
mCx430	mCx26.3
mCx431	mCx26.3
mCx432	mCx26.3
mCx433	mCx26.3
mCx434	mCx26.3
mCx435	mCx26.3
mCx436	mCx26.3
mCx437	mCx26.3
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mCx491	mCx26.3
mCx492	mCx26.3
mCx493	mCx26.3
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mCx495	mCx26.3
mCx496	mCx26.3
mCx497	mCx26.3
mCx498	mCx26.3
mCx499	mCx26.3
mCx500	mCx26.3

**Functional consequences of connexin loss** These are particularly diverse [PK = palmoplantar keratoderma; HED = Clouston's hereditary ectodermal dysplasia; EKV = erythrokeratoderma variabilis].

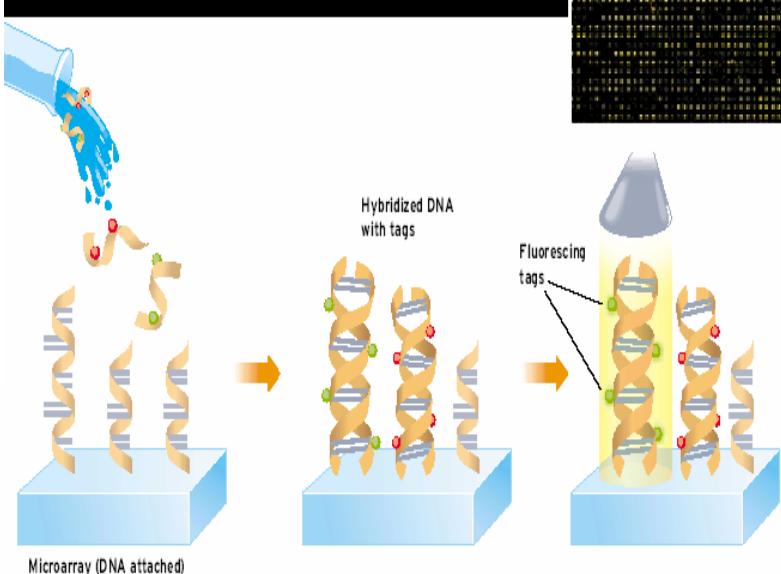


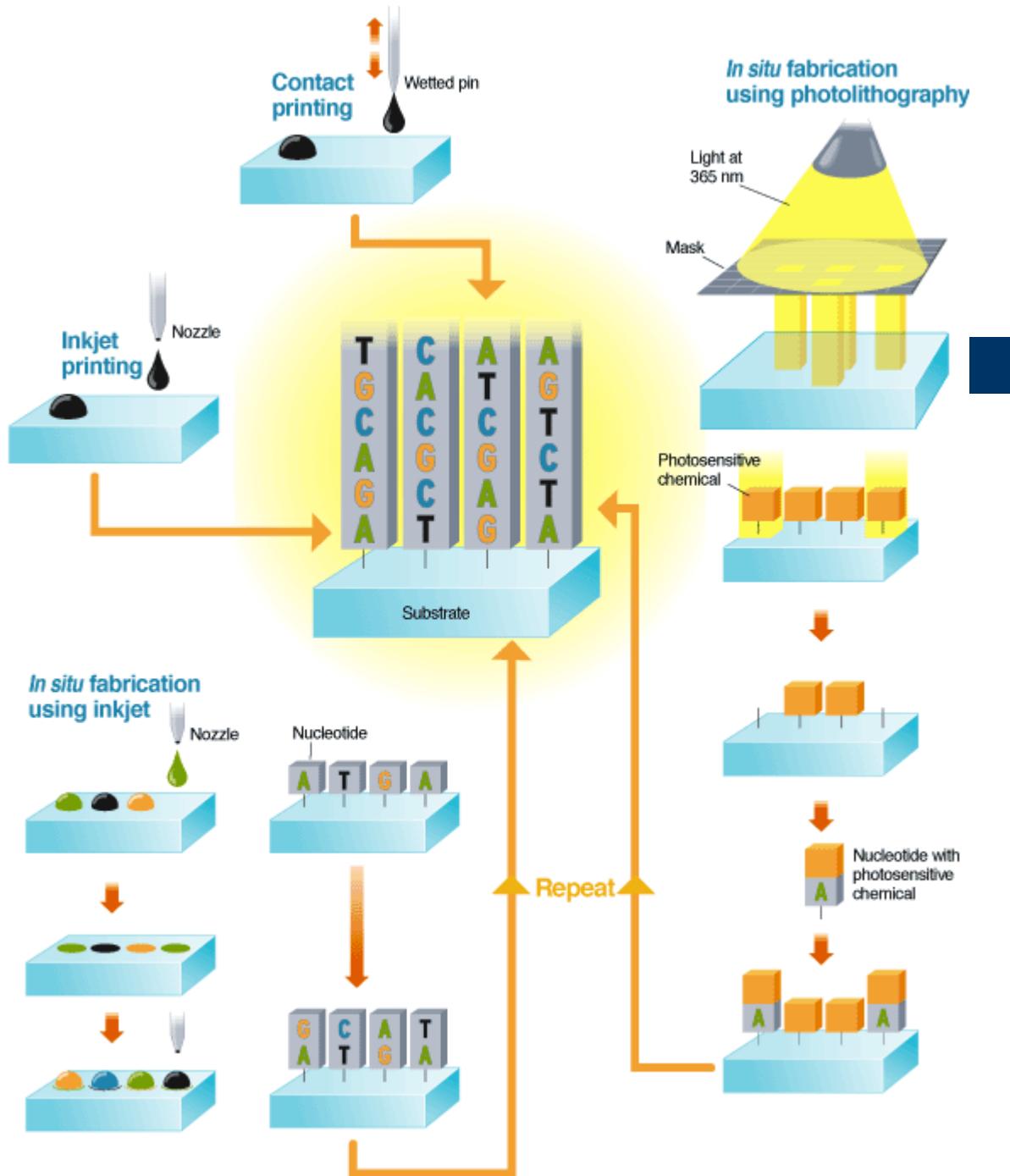
# Biochip



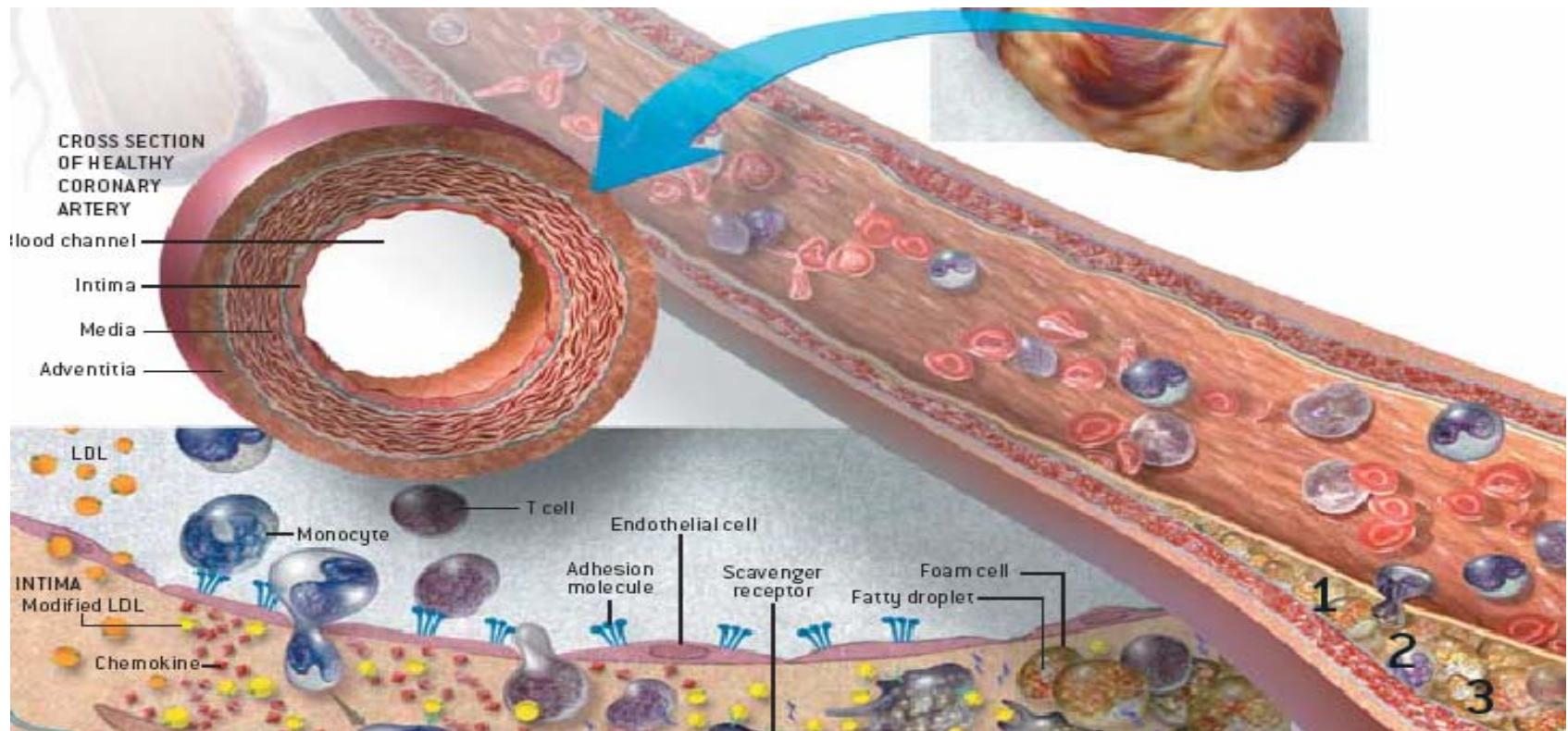
The tagged DNA is washed over a microarray that has single-stranded DNA fixed to its surface in known locations. This DNA represents important genes or parts of genes. If a gene has been expressed in a cell, it will bind to a copy of itself on the array; those with no complementarity on the array will wash off.

A light source scans the array, causing the dyes to fluoresce. The glow is picked up by a sensor, and a computer interprets the pattern of spots, indicating for each cell which genes are active and the relative abundance of the RNA.

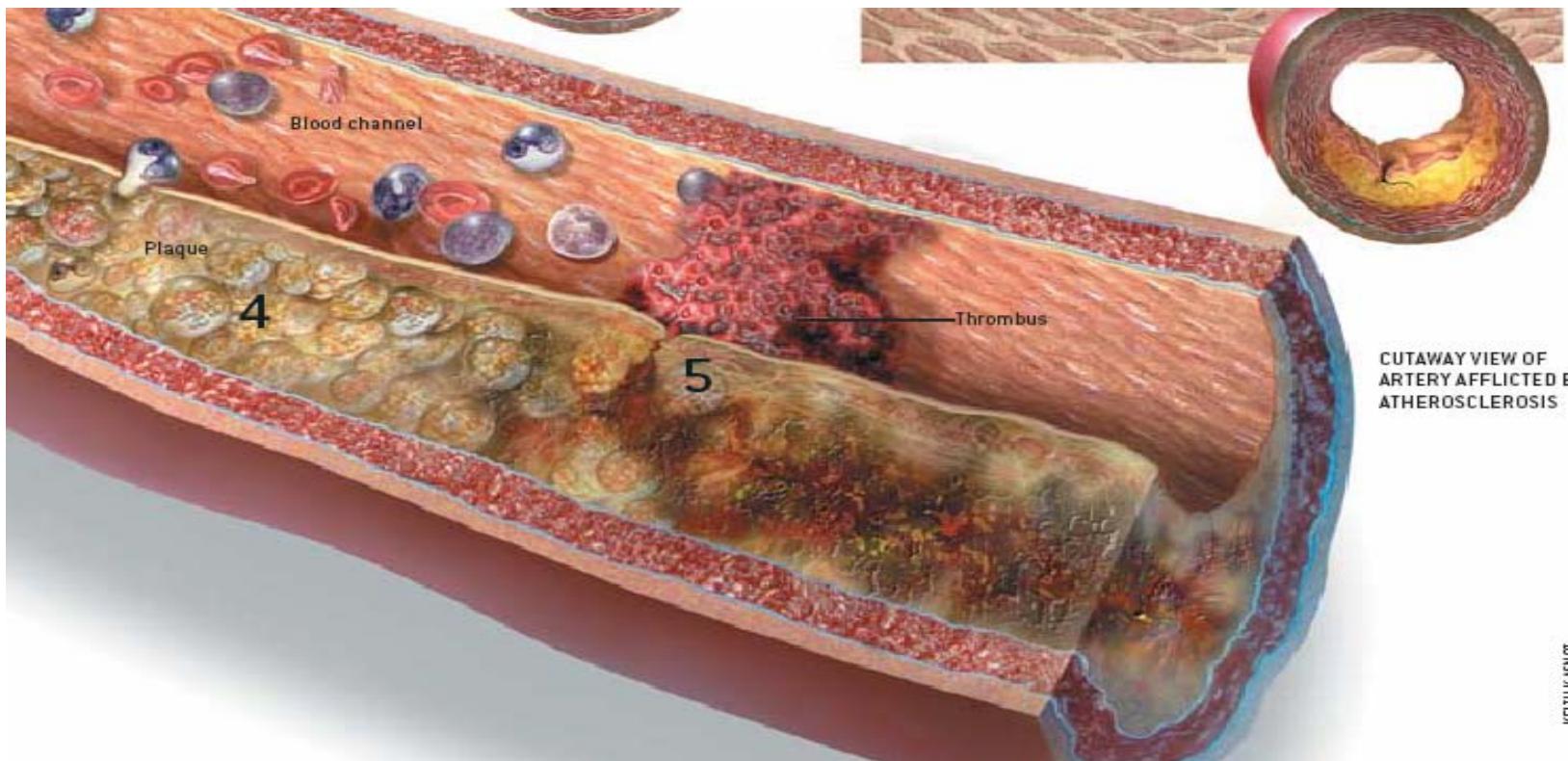




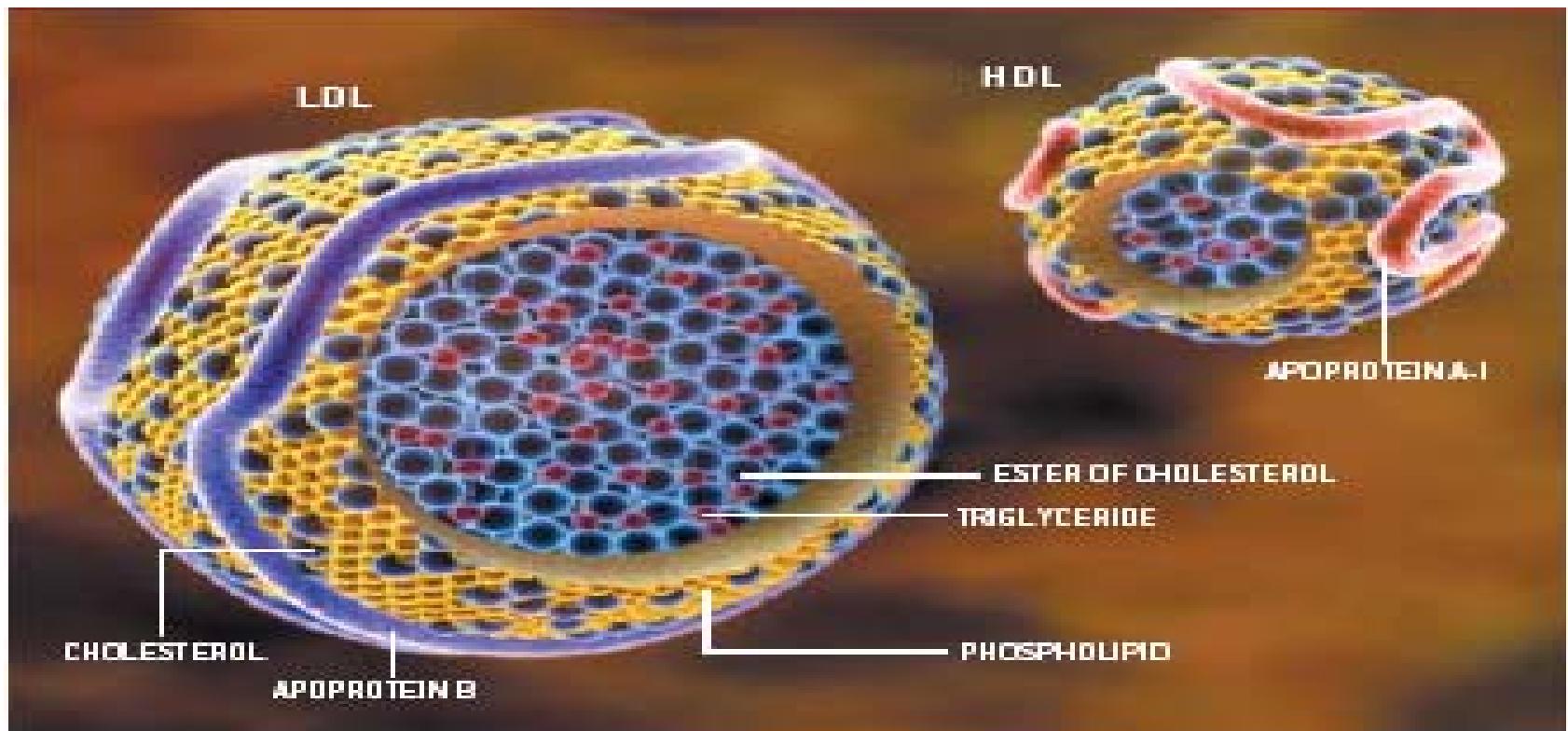
# Atherosclerosis (1-3 stages )



# Atherosclerosis (4-5 stages)



# LDL, HDL



# Detection of Biomolecules Using $\text{In}_2\text{O}_3$ Nanowires

Chao Li, Daihua Zhang, Bo Lei, and Chongwu Zhou  
Dept. of Electrical Engineering - Electrophysics  
University of Southern California

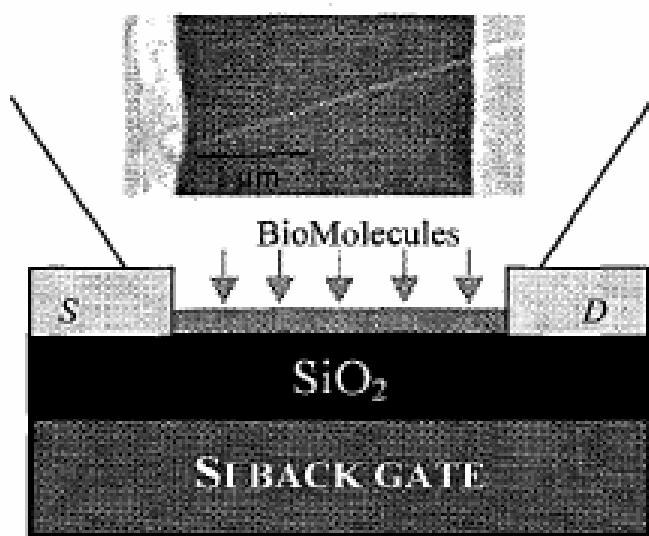


Figure 1. Scheme for molecular absorption on an  $\text{In}_2\text{O}_3$  nanowire device and a SEM image of the device, which clearly showed a nanowire bridging drain and source electrode.

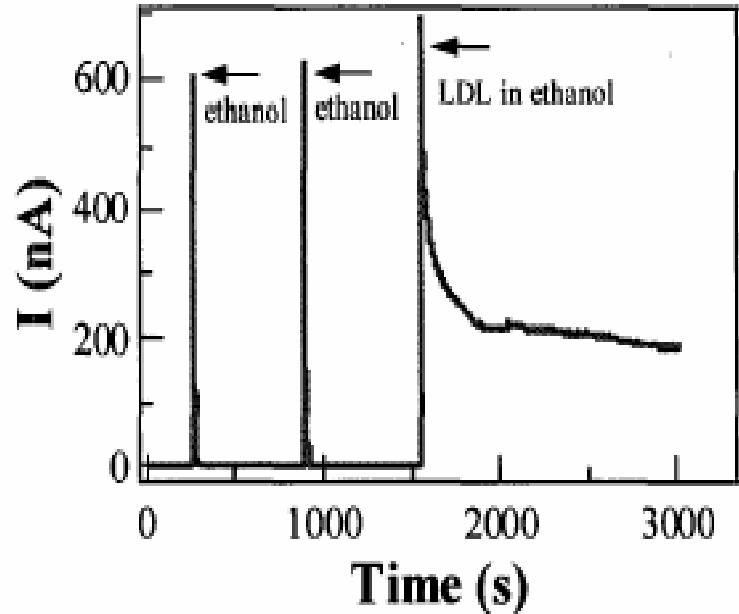
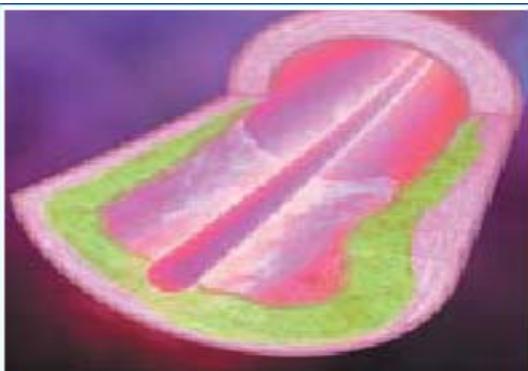


Figure 2. Time domain measurement for the device after exposure to pure ethanol twice and then LDL in ethanol.

# Photodynamic therapy

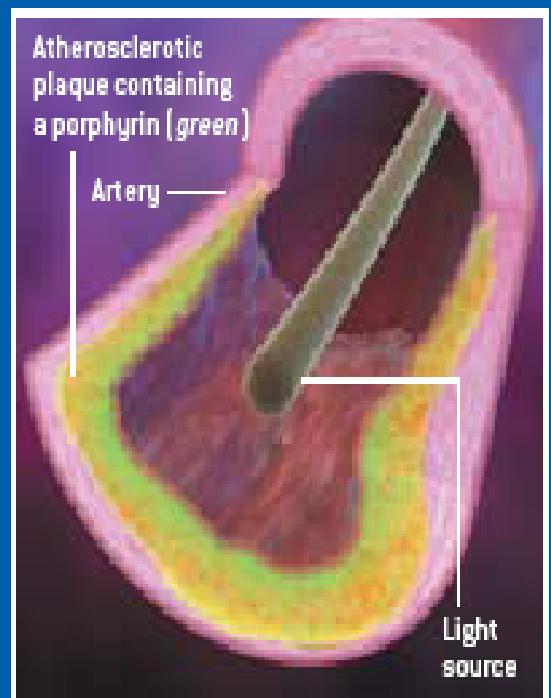
**2** The fiber produces red light, activating the porphyrin.



**3** Over the course of a few days, the porphyrin destroys unwanted plaques.

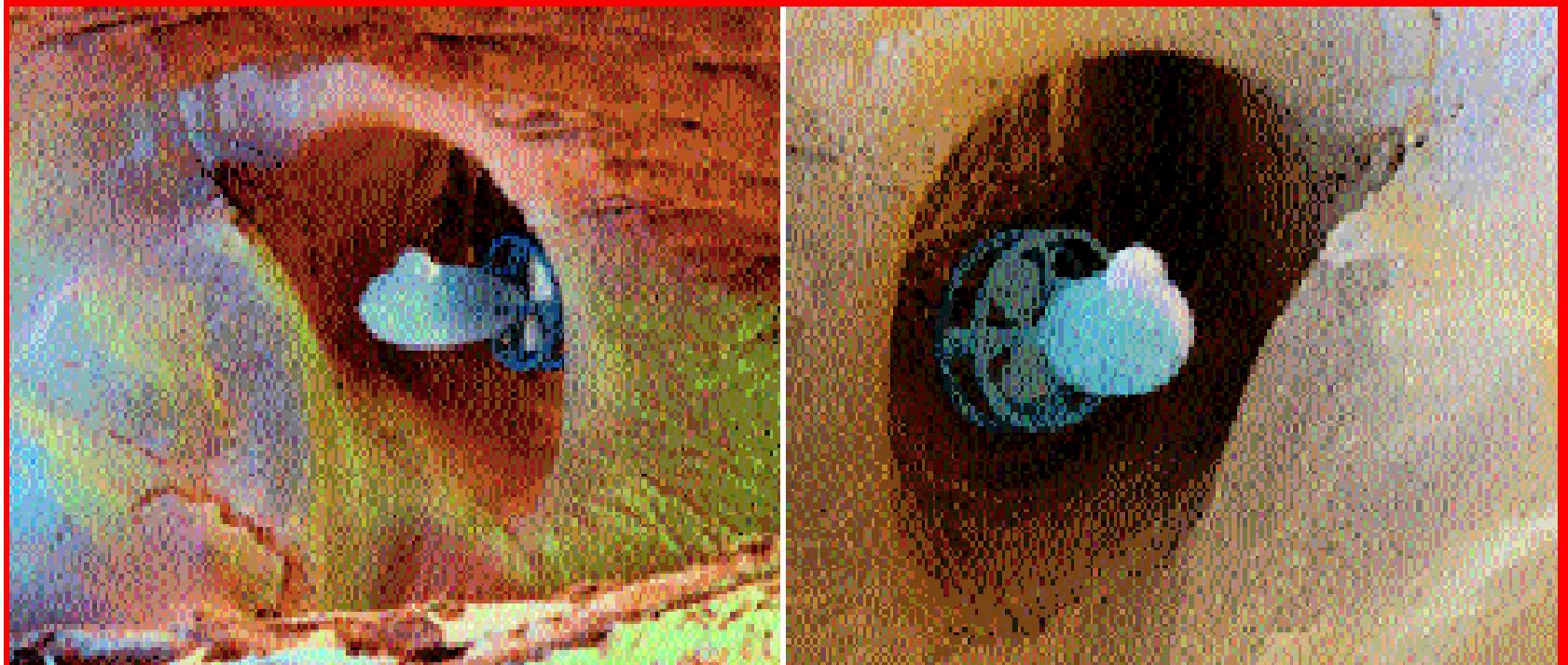


**1** Here, in an experimental therapy, an optical fiber has been threaded into an artery in which a porphyrin has accumulated in atherosclerotic plaques.



# Self-sufficient micro-robot

**Figure 1:** Microsubmarine built by Microtec.



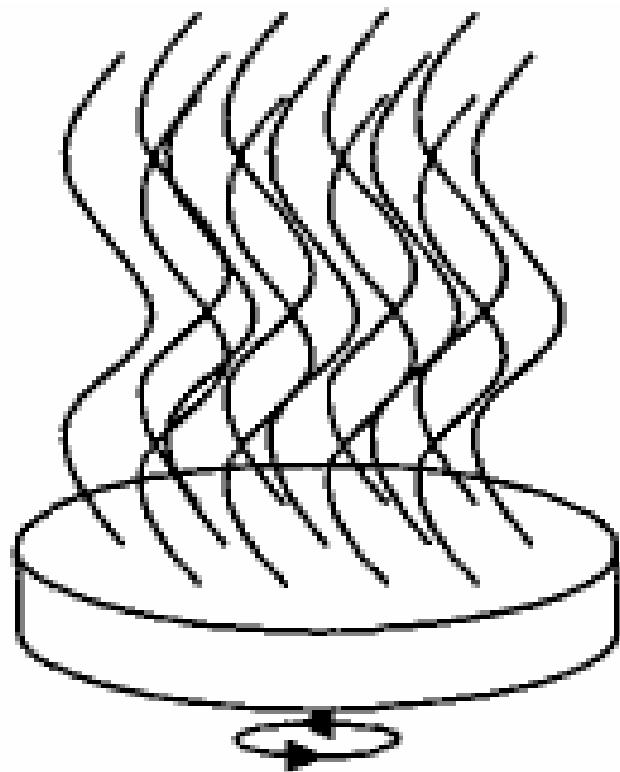
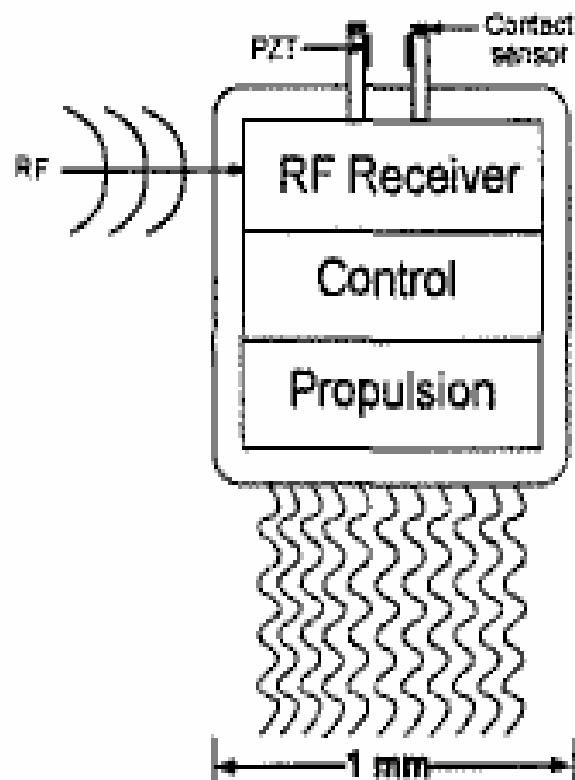
# Swimming Surgical Micro-Robot

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<sup>2</sup>Department of Urology, University of California, San Francisco, CA 94143

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## NANOROBOTICS CONTROL DESIGN: A PRACTICAL APPROACH TUTORIAL

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adrianocavalcanti@ieee.org, rfreitas@rfreitas.com, kretly@dmo.fee.unicamp.br

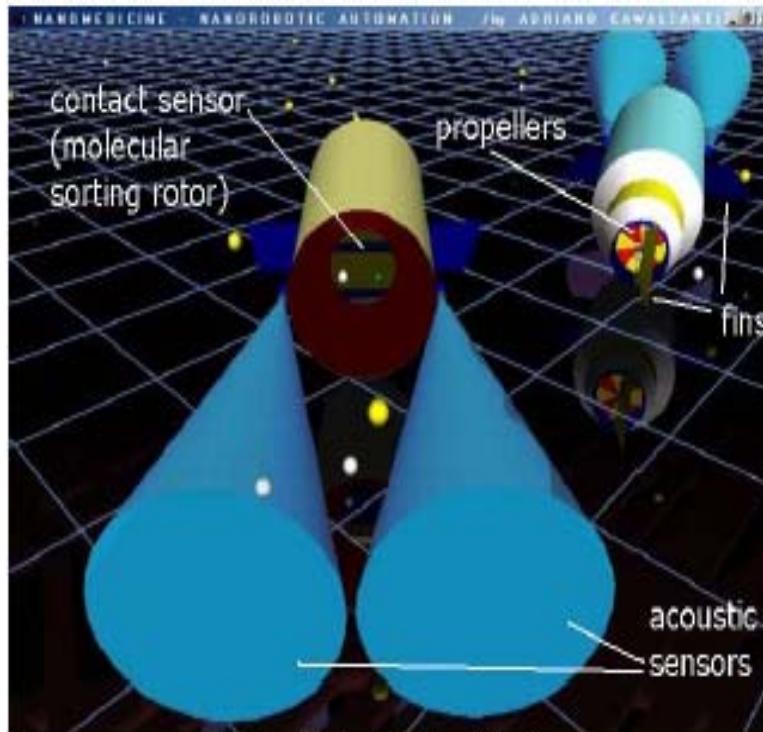


Fig. 2. Molecular identification.

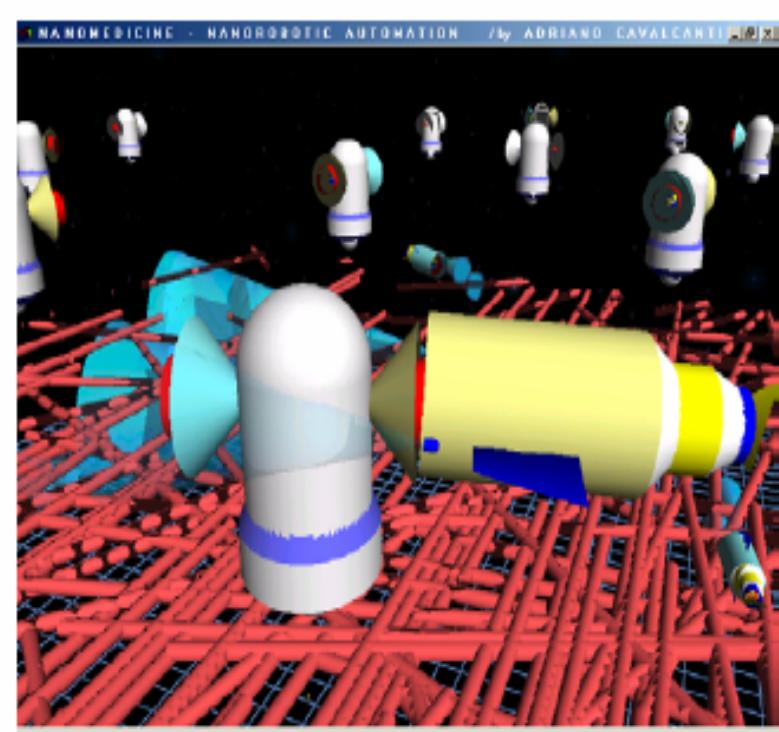
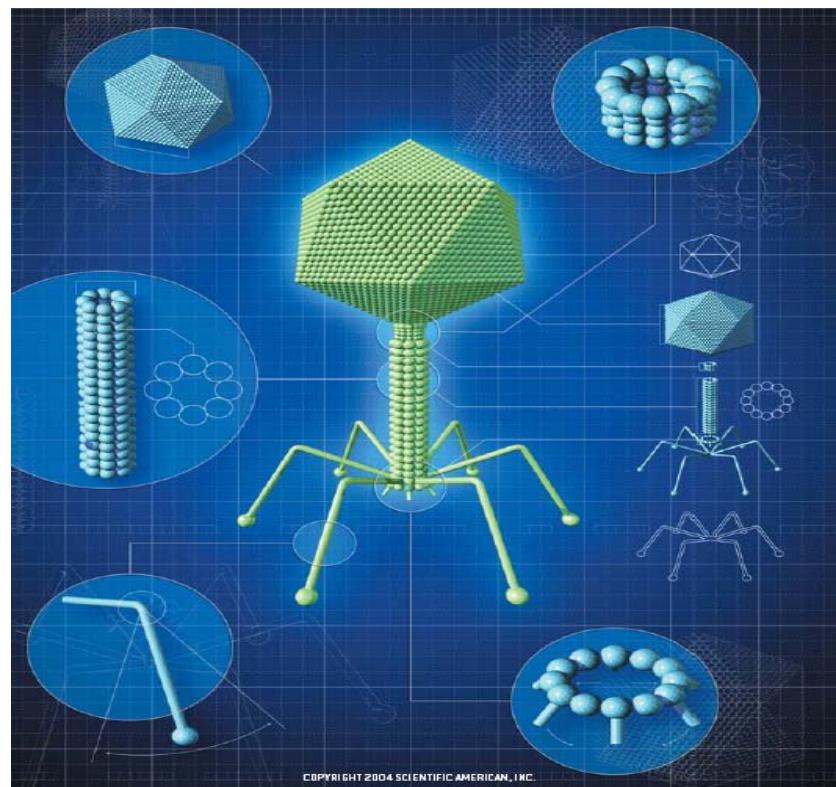
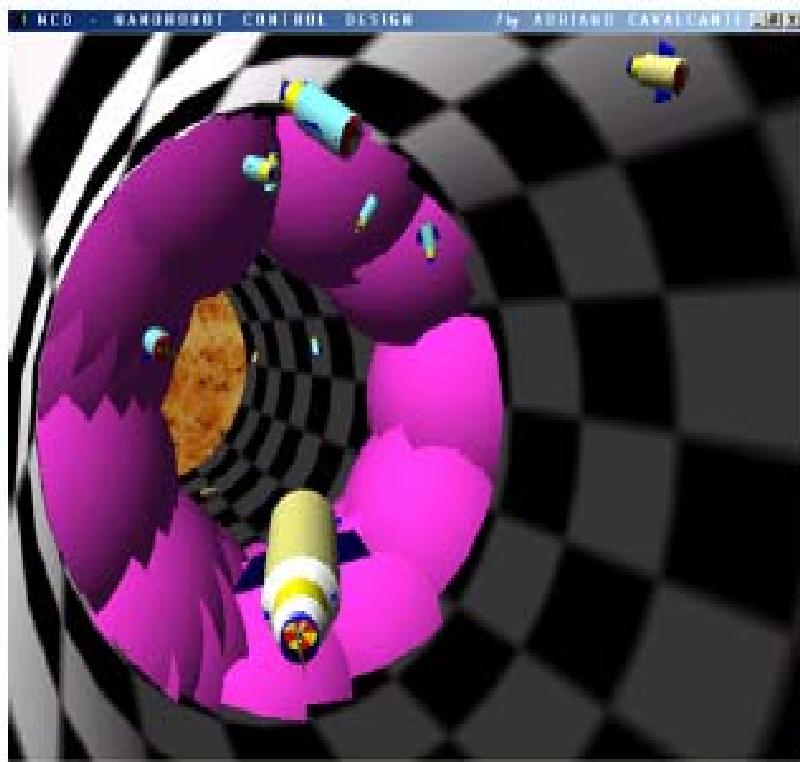


Fig. 3. Nanorobot molecule delivery.

# Nanorobots



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# Artificial heart



# Future

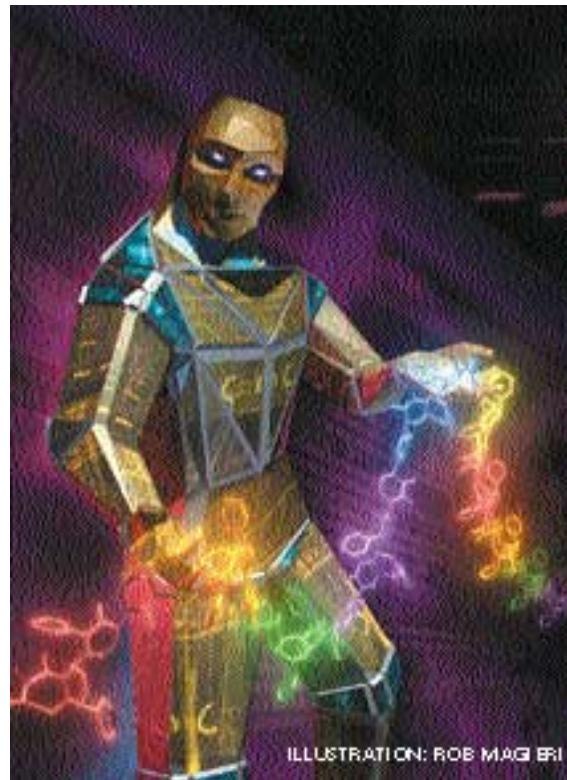


ILLUSTRATION: ROB MAG BRI