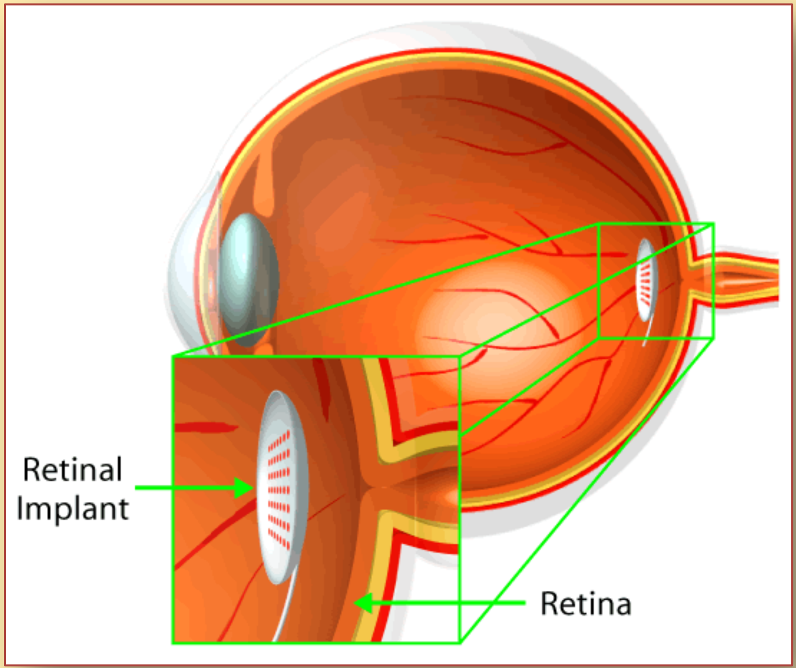
THERAPEUTIC BIOMEMS OVERVIEW



Unit Overview

In medicine, therapeutics is the process of caring for the patient in a comprehensive manner, preventing disease, as well as managing disease or disease specific problems.

BioMEMS are being designed and commercially distributed that are revolutionizing therapeutic medicine.

This unit provides an overview of bioMEMS therapeutic applications.

Objectives

- Explain why microtechnology could be advantageous for therapeutics.
- Briefly describe a therapeutic bioMEMS device and explain how it works.
- List and define the areas of medicine that would benefit from bioMEMS technology.

Introduction

Therapeutic bioMEMS manage disease using three methods:

- In vitro (external) devices gather and process information.
- In vivo (internal) devices detect changes in a disease.
- A combination system detect, monitor and manage disease.

Prototype of a Retina Implant [Photo by Randy Montoya. Courtesy of Sandia National Laboratories]

The retina implant in the picture is an in vivo device that works with external components enabling the blind to see.

Therapeutic MEMS

There are several therapeutic devices already on the market and others at the human testing stage.

Examples include

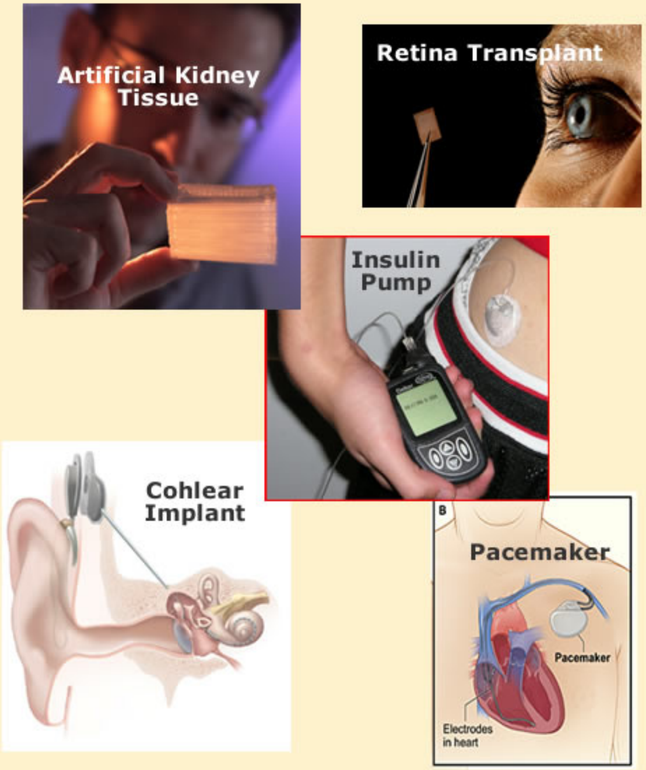
- drug delivery systems,
- devices for invasive surgeries, and
- artificial retinal prostheses.

The Possibilities

The possibilities for bioMEMS therapeutic applications for healthcare are numerous:

- minimal invasive surgery
- drug delivery
- treatment of cardiovascular diseases, diabetes and cancers
- applications in neurology, ophthalmology, audiology
- applications in dermabrasion and tissue engineering

Therapeutic bioMEMS devices already exist for many of these applications.



BioMEMS Therapeutic Applications

Diabetes

One of the most successful applications has been for disease control in diabetes, both Type 1 and Type 2.

Type 1 is an autoimmune disease resulting in the destruction of the beta cells in the pancreas, preventing the production of insulin or enough insulin.

Type 2 is a chronic condition affecting the way the body metabolizes sugar (glucose). The pancreas many not be producing enough insulin or the body does not know what to do with the insulin produced.

Diabetes

About 28 percent of all diabetics in the United States use insulin to control their disease.

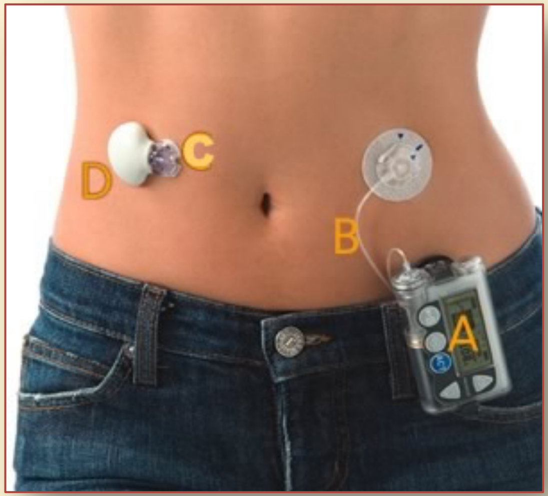
The therapeutics for treating diabetes has been a twice daily prick to determine glucose concentration, and twice daily shot to administer insulin.

Compliance to this regimen is a major problem, especially for juvenile diabetics.

A lack of compliance causes hypoglycemic events (a drop in blood glucose) to go undetected.

Undetected hypoglycemic events can lead to seizures, loss of consciousness, or increase in the risk of diabetic eye disease, and kidney and nerve damage.

Therapeutics for Diabetics



MiniMed Paradigm[R] 522 insulin pump, with MiniLinkTM] transmitter and infusion set.
[Printed with permission from Medtronic Diabetes]

The MiniMed Paradigm[R] 522 insulin pump, with MiniLinkTM] transmitter and infusion set monitors and manages glucose levels. Its components are
(A) an external pump and computer
(B) a soft cannula that delivers the insulin
(C) an interstitial glucose sensor
(D) a wireless radio device that communicates with the computer.

MiniMed Paradigm® 522

A biosensor (C) is placed under the skin.

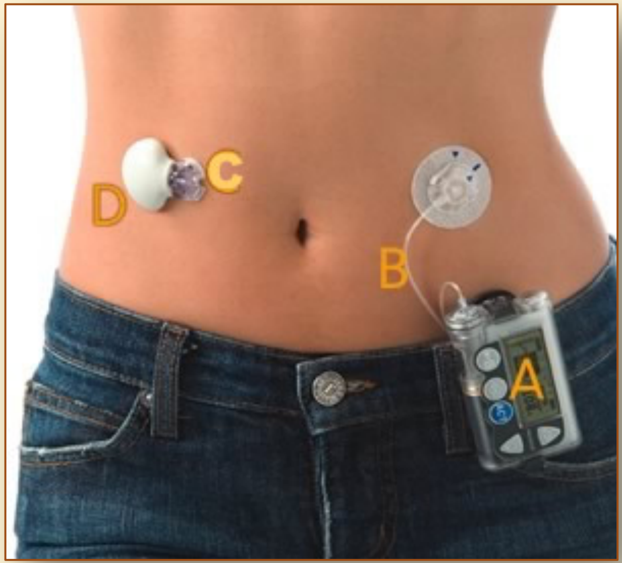
The sensor continuously measures glucose levels in the interstitial fluid (the fluid between body tissues).

The measurements from the sensor are transmitted in real time to the wireless radio device (D).

This device sends the readings to the computer (A) which determines the amount of insulin needed.

The pump (A) administers that amount into the patient via the cannula (B).

The Mini-Med Paradigm ® also stores all the data.



MiniMed Paradigm[R] 522 insulin pump, with MiniLinkTM] transmitter and infusion set. [Printed with permission from Medtronic Diabetes]

Drug Delivery

Medications are currently administered using several different methods.

BioMEMS devices that use biomolecules as drug delivery components decrease the necessity for many of these methods.

BioMEMS also allow for controlled drug delivery directly to the targeted tissue or organ, bypassing metabolic processing by the liver and other organs.

An example of such a bioMEMS device is the liposome vesicle (cavity) discussed in the next slide.

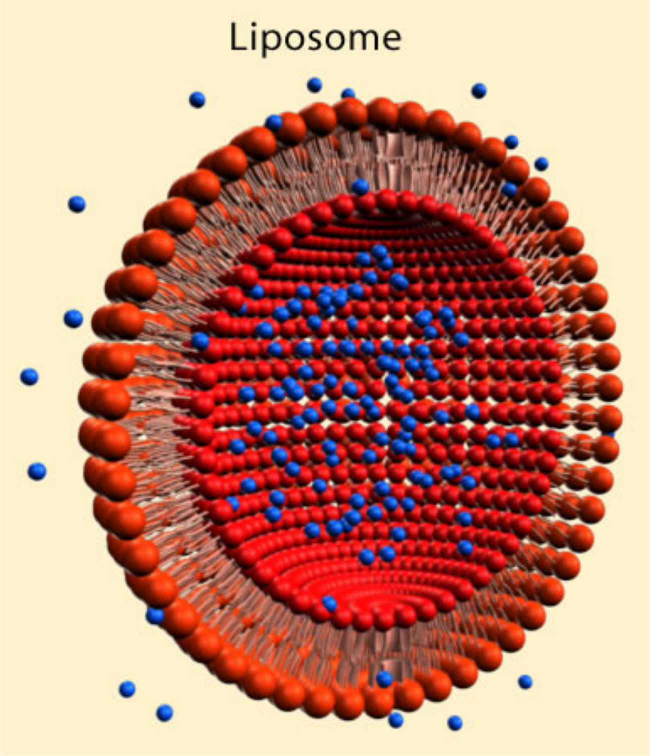
Liposome Vesicle

This liposome has a nano-sized cavity formed by a phospholipid bi-layer.

The cavity is filled with a drug (blue).

Several of these drug filled vesicles can be injected into the bloodstream and "guided" to the target tissue where they are either absorbed or adsorbed by the tissue.

Once there, the drug migrates through the membrane, destroying or neutralizing the diseased tissue.



Liposome vesicle filled with drugs (blue)

Advantages

Advantages of bioMEMS devices for drug delivery include

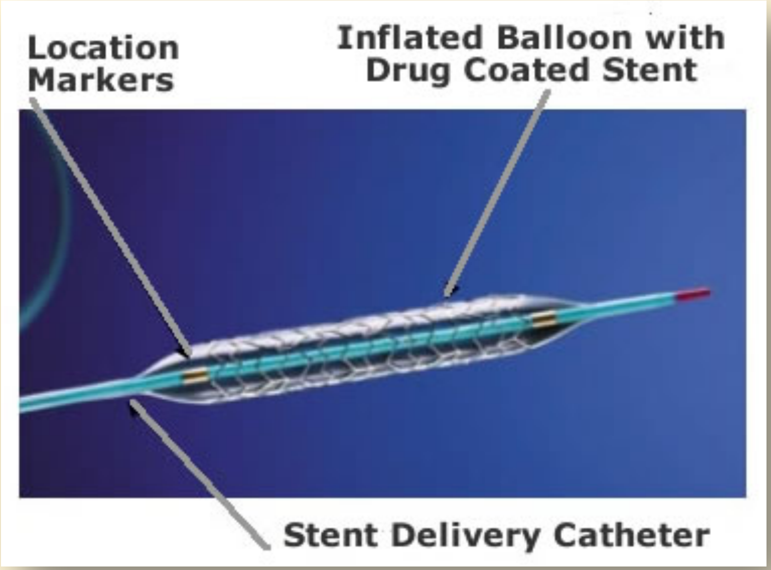
- controlled release,
- reliable dosing,
- targeted therapy,
- precise delivery, and
- automated or semi automated feedback control.

Designing Drug Delivery Devices

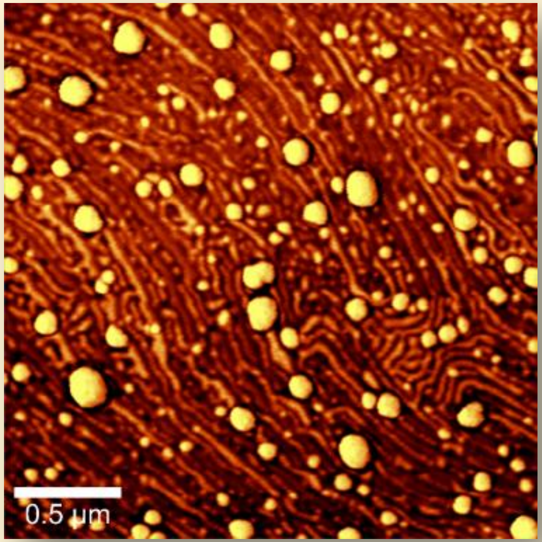
Parameters to be considered:

- Dose
- Frequency
- Duration
- Toxicity
- Drug interaction
- Allergies
- Oscillatory behavior of the drug in the body
- Therapy may change over time as the disease state of the patient changes or as new therapies become available.

Nanopore Coated Stents



TAXUS Express2 Paclitaxel-Eluting Coronary Stent System [Image source: FDA]



High-resolution AFM phase image of a drug eluting stent surface showing the polymer substrate structure (red) with the embedded drug particle (yellow). Image courtesy of [WITec, Focus Innovation]()

Drug eluting stents are used for blocked arteries.

The stent coating is a medication that is slowly released (eluted) to decrease restenosis (tissue growth in the artery lining that decreases the diameter of the opening in the stent).

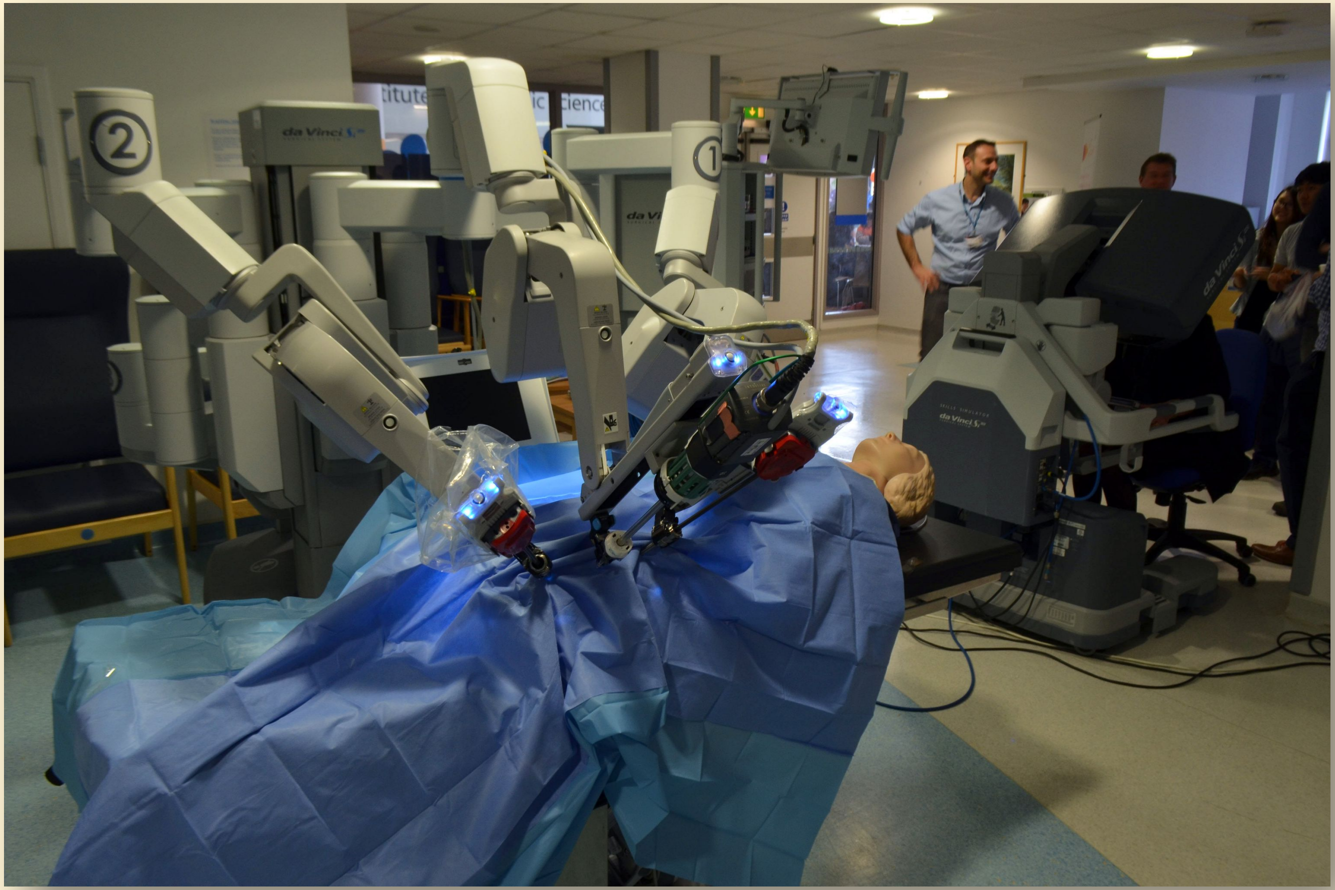
Minimal Invasive Surgery (MIS)

Minimal Invasive Surgery (MIS) is the process of accomplishing a surgical task with the least amount of intrusion and harm to the patient.

Typically with MIS, there is

- less postoperative pain,
- shorter hospital stays,
- quicker recoveries, and
- less scaring.

The di Vinci S Robot



The di Vinci minimally invasive surgery (MIS) robot-assisted system.
Patient-side component (left) Surgeons console (right)

A da Vinci Surgical System at Addenbrooke's Treatment Centre during the 2015 Cambridge Science Festival

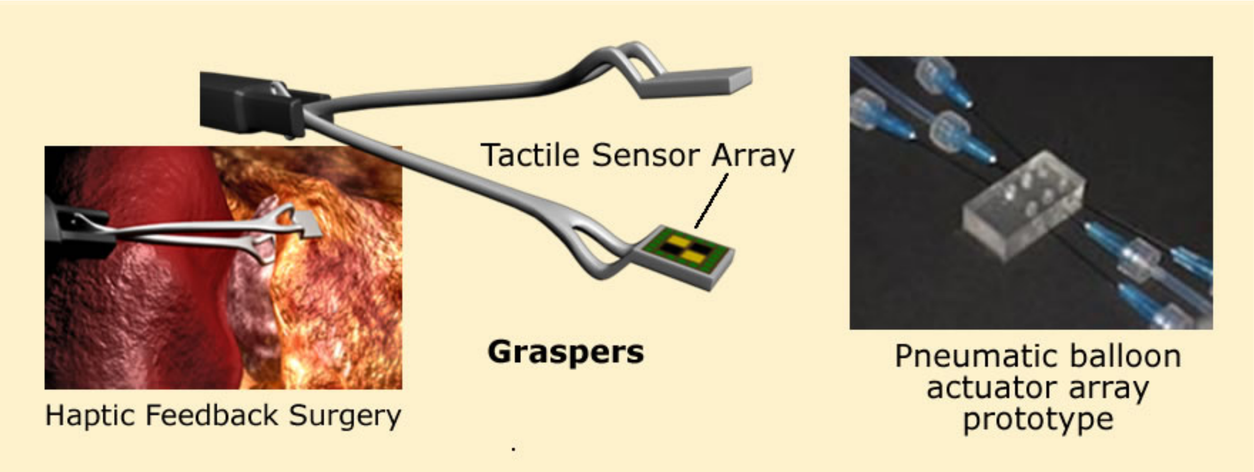
Disadvantage

Unfortunately, most MIS robots are characterized by a total loss of haptic (sense of touch) feedback, requiring surgeons to rely solely on visual clues.

Visual information is sufficient for many procedures, however, it is often challenging to characterize tissues and apply appropriate force to sutures without tactile information.

MEMS devices with haptic feedback could enable expansion of robotic surgery to procedures that are difficult to perform without a sense of touch.

Haptic Feedback



Haptic Feedback Graspers with tactile sensor array (left images)

Pneumatic Balloon Actuator Array Prototype (right image - Printed with permission of UCLA)

The Center for Advanced Surgical and Interventional Technology (CASIT) at UCLA is developing a pneumatic balloon-based haptic feedback system.

Mounted on the end of the surgical tool (grasper) is a force sensor array with several sensing points (*see graphics*).

Each point (transducer) of the sensor array detects the force applied to the patient's tissue by the grasper.

This force is translated to proportional pressures that are sent to a joystick in the surgeon's hand. The surgeon "feels" the change in pressure and adjusts as needed.

Artificial Retinal Prosthesis

The Argus™ Retinal Stimulation System.

This retinal prosthesis consists of an artificial retina implanted onto the retina of a human eye *(see picture).*

In the initial testing phase, six patients received the retina prosthesis. Each of these previously blind patients have been able to distinguish and identify objects and motion. *(D.M. Deupree, The Macula Center)*

Prototype of a Retina Implant [Photo by Randy Montoya. Courtesy of Sandia National Laboratories]

How Does it Work?

As with any bioMEMS device, it is important to fully understand how the biological device works.

Let's take a quick look at how the human eye works before discussing how an artificial retina works.

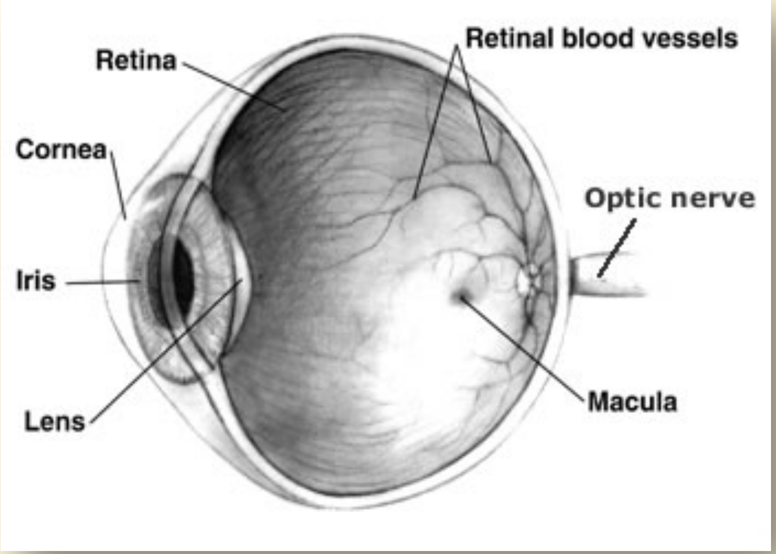
The Human Eye

Normal vision occurs when light enters the eye through the cornea then the lens.

The lens focuses the light on the retina, the inner-most lining of the eyeball.

The retina contains photoreceptors cells which convert the light to electric impulses.

These impulses travel into the optic nerve then to the brain where the information is processed.

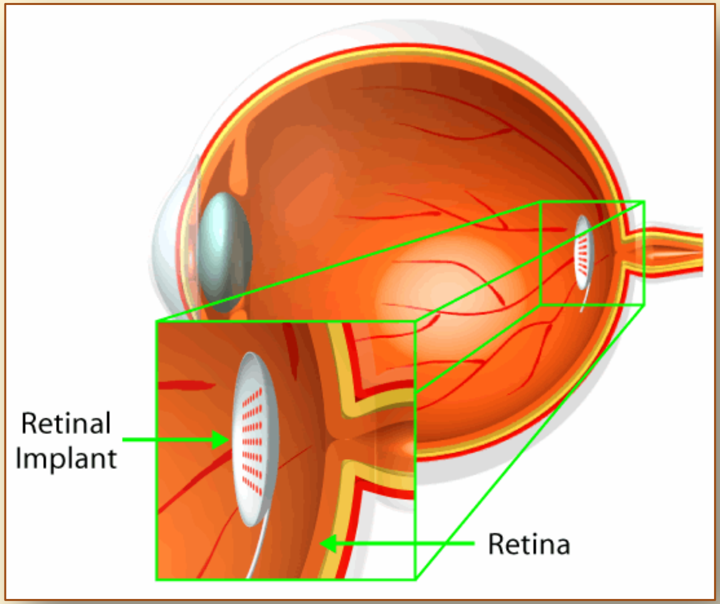


The Human Eye
[Public Domain: National Eye Institute]

MEMS Artificial Retina

In retinal diseases, such as age-related macular degeneration and retinitis pigmentosa, the photoreceptor cells in the retina are destroyed.

- ❖ An artificial retina (graphic) bypasses these cells and transmits signals directly to the optic nerve.
- ❖ The artificial retina is an electrode studded array placed on or beneath the surface of the retina.
- ❖ Light hitting the array is converted to electric impulses.
- ❖ These electric impulses stimulate the retinal neurons which transmit to the optic nerve then to the brain.

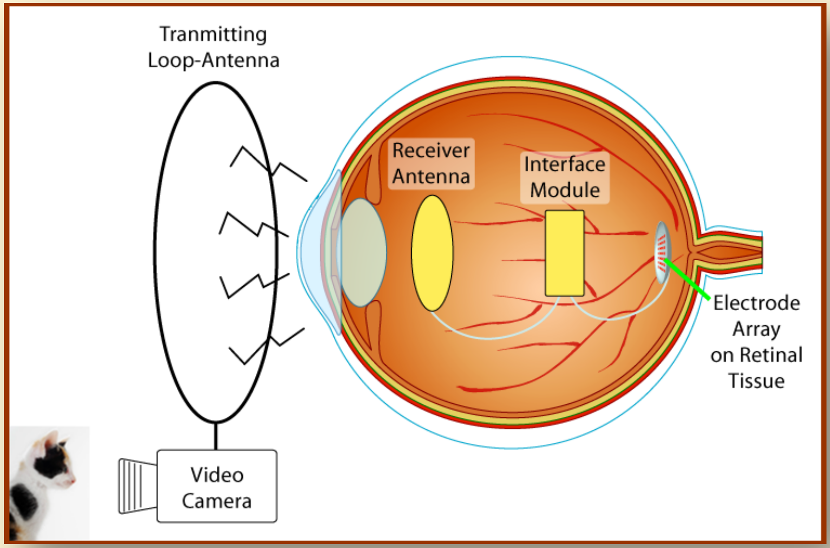


MEMS Artificial Retinal Implant

Restoring Sight In Vivo

The Artificial Retina MEMS consists of a camera, microprocessor, transmitter, receiver, interface module and the artificial retina.

- Camera captures an image and sends the information to the microprocessor (in the glasses frame or on the belt).
- Microprocessor converts the data and transmits it via the transmitter to the receiver antenna on the eye.
- Antenna transmits the optical signal to the array.
- Signal stimulates the array to emit electronic pulses in the retinal nerves.
- Pulses travel through the optic nerve to the brain.



Artificial Retina MEMS - image to brain

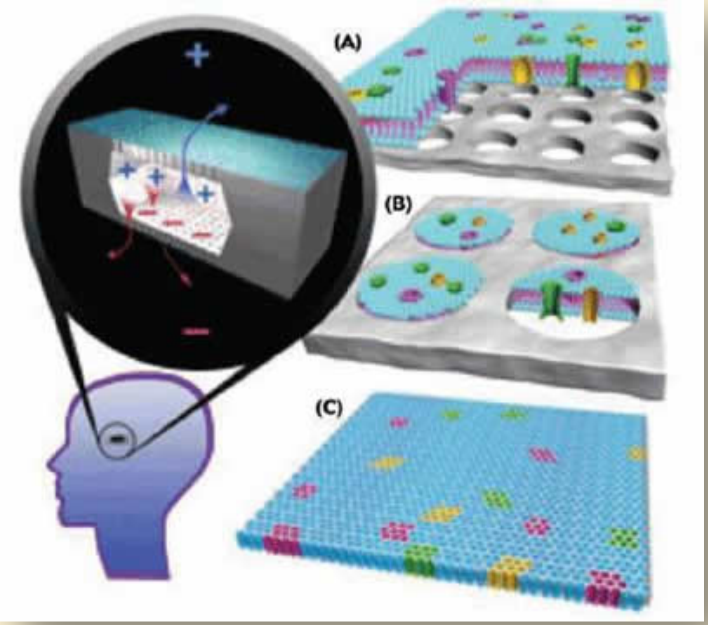
To see more on how this works, view this YouTube Video develop by a manufacturer of the artificial retina – Second Sight Europe

Second Sight EN 2012 Argus II Retinal Prosthesis System Artificial Retina Bionic Eye

Powering the Artificial Retina

Artificial retina MEMS are powered by a wireless battery pack worn on the person's belt.

Sandia National Laboratories is working on a battery that can be implanted in the person’s head (*as shown in the graphic*).



Battery Pack for Artificial Retina system [Courtesy of Sandia National Laboratories]

What Does a Patient See?

(Images generated by the Artificial Retinal Implant Vision Simulator devised and developed by Wolfgang Fink at the Visual and Autonomous Exploration Systems Research Laboratory, California Institute of Technology.)

Images produced by the artificial retina prosthesis [Images generated by the Artificial Retinal Implant Vision Simulator]

These images show what a patient with retinal devices should see.

Increasing the number of electrodes in the retina array results in more visual perceptions and higher resolution vision.

In 2007 six patients were successfully implanted with the first prototype Model 1 device or Argus I™. Argus I™ contained 16 electrodes (16 pixels - left picture). The Argus II™ (256 pixels-middle picture) is currently being tested in phase two of clinical trials. The third model (1000+ pixels – right picture) is under development.

UPDATE: In February 2011 the FDA granted market approval of the Argus II™

Tissue Engineering

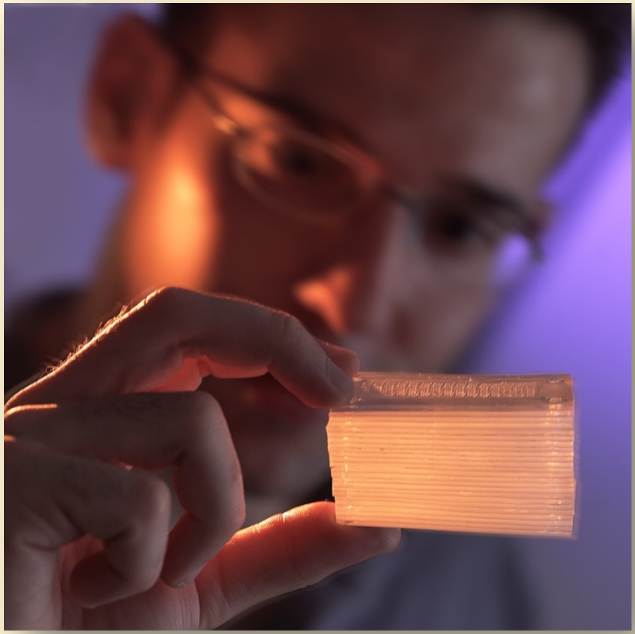
- Almost ninety-thousand Americans are waiting for a new organ.
- On average, there are only three thousand livers for thirty thousand patients annually.
- For patients waiting for a kidney, dialysis offers some mechanical support; however, a quarter of them will not survive the wait.
- BioMEMS innovation is addressing this problem.

CIMIT Tissue Engineering

The CIMIT (Center for Integration of Medicine and Innovative Technology) tissue engineering program is working to develop a kidney dialysis unit that can be worn around the waist.

CIMIT is also working on MEMS that can build complex organs such as kidneys, livers, and replacement tissue. This is possible because microtechnology enables the replication of the internal network of capillaries and vessels that bring blood and oxygen to living growing tissue.

The picture shows a prototype of an artificial kidney based on microtechnology.



Artificial Kidney
[The Charles Stark Draper Laboratory, Inc.

What are the possibilities?

Let's brainstorm on the possibilities for future MEMS and bioMEMS Therapeutic Devices.

The possibilities are endless!

Advantages

What are the advantages of MEMS and bioMEMS therapeutic devices compared to the current macro-equivalents?

Summary

The therapeutic bioMEMS presented in this unit are the tip of the iceberg. Presently, the majority of therapeutic bioMEMS are a combination of external and internal components. In many cases they are still larger than micro or nano-sized MEMS, however, this is quickly changing.

BioMEMS are getting smaller and smaller. There are many devices small enough to be totally in vivo, providing more mobility and independence to the patients.

Disclaimer

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