BME 2200: Biostatistics and Research Methods

Lecture 2: Papers, Reports, Patents, Talks

Lucas C. Parra
Biomedical Engineering Department
City College of New York

CCNY

parra@ccny.cuny.edu

Content, Schedule

1. Scientific literature:
- Literature search
- Structure biomedical papers, engineering papers, technical reports

2. Presentation skills:
- Report – Written report on literature search (individual)
- Talk – Oral presentation on biomedical implant (individual and group)

3. Graphical representation of data:
- Introduction to MATLAB
- Plot formats: line, scatter, polar, surface, contour, bar-graph, error bars. etc.
- Labeling: title, label, grid, legend, etc.
- Statistics: histogram, percentile, mean, variance, standard error, box plot

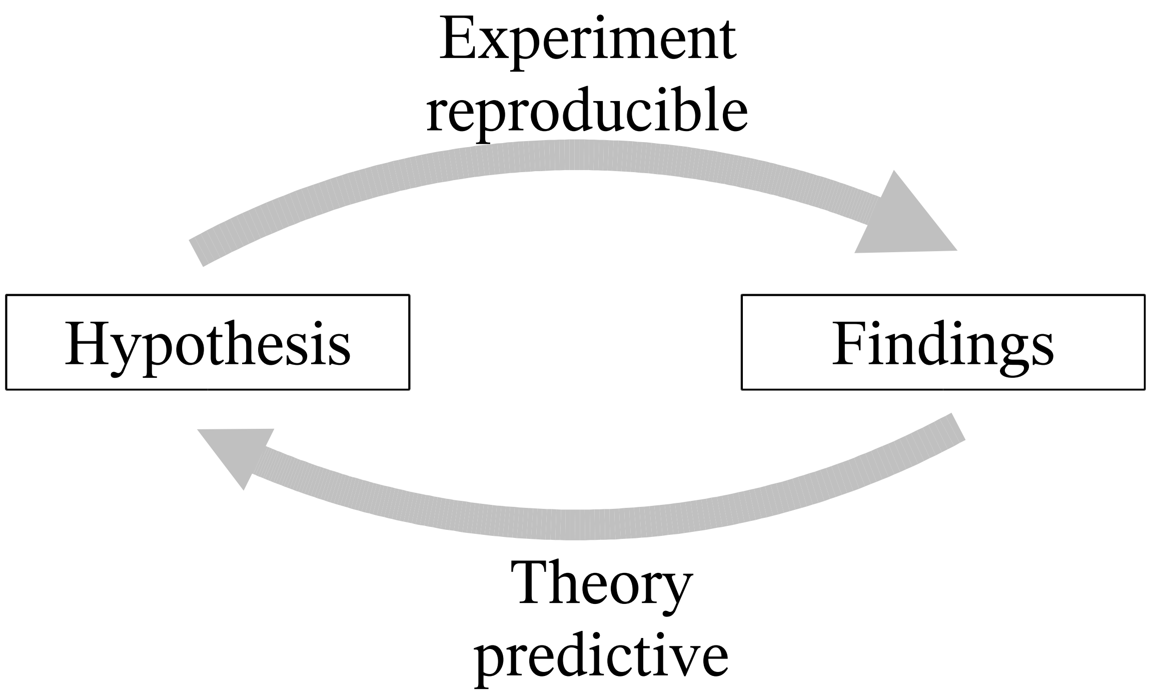
4. Biostatistics:
- Basics of probability
- Hypothesis testing, correlation, causality, significance
- t-Test, ANOVA
- Linear regression, cross-validation
- Error analysis
- Test power, sensitivity, specificity, ROC analysis

Evaluate Assignment #1

In groups of two students:

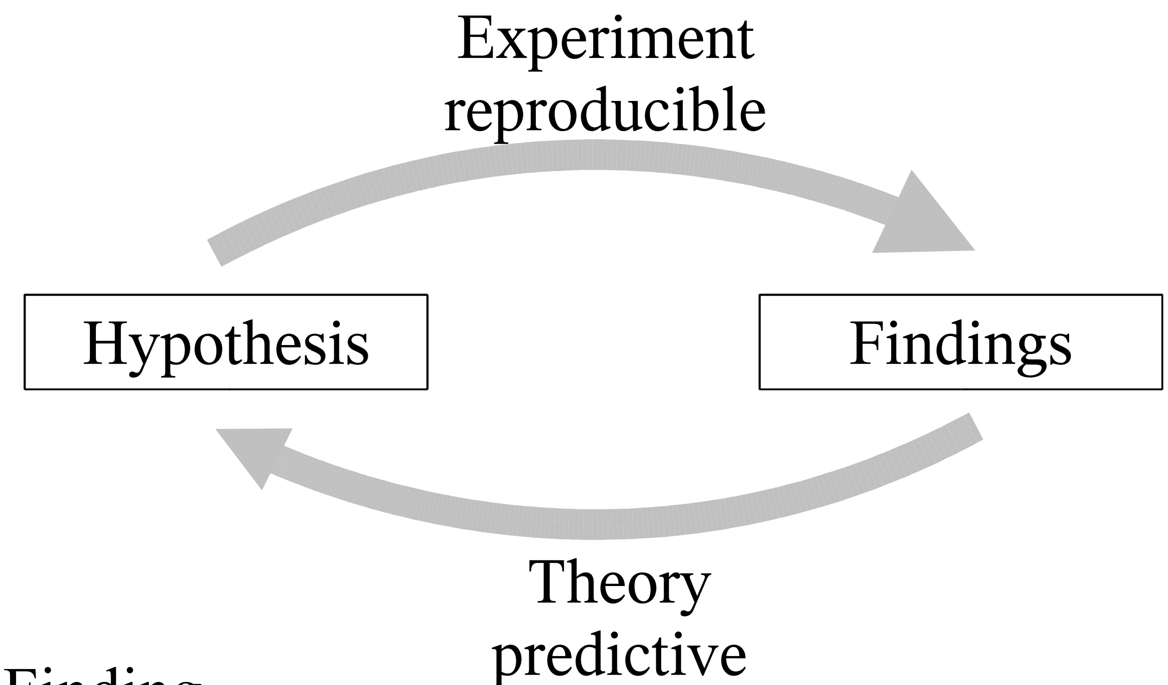
- Exchange your 1 page Assignment #1 and read the other students assignment (5 minutes).
- Discuss and make suggestions for improvement (5 minutes).
- Give short evaluation in writing of each others work (2 minutes).

The Scientific Method

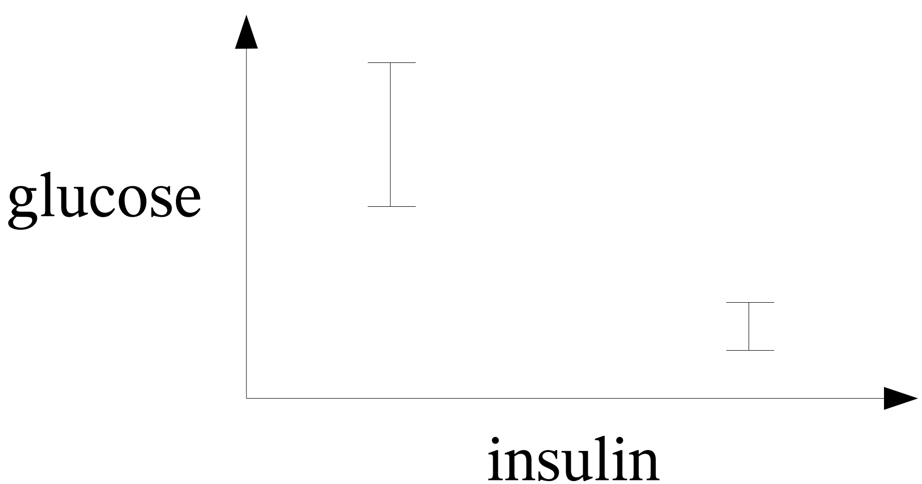


Theory – must predictive
Hypothesis – must be testable
Methods – must be reproducible
Results – must be significant

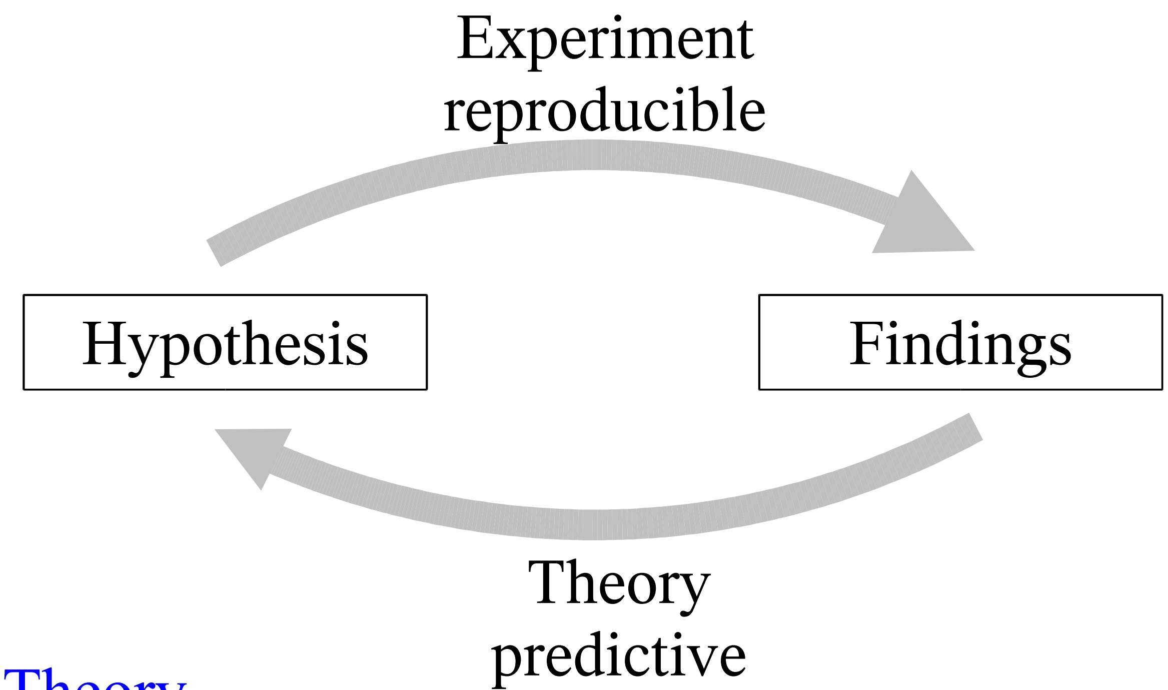
The Scientific Method



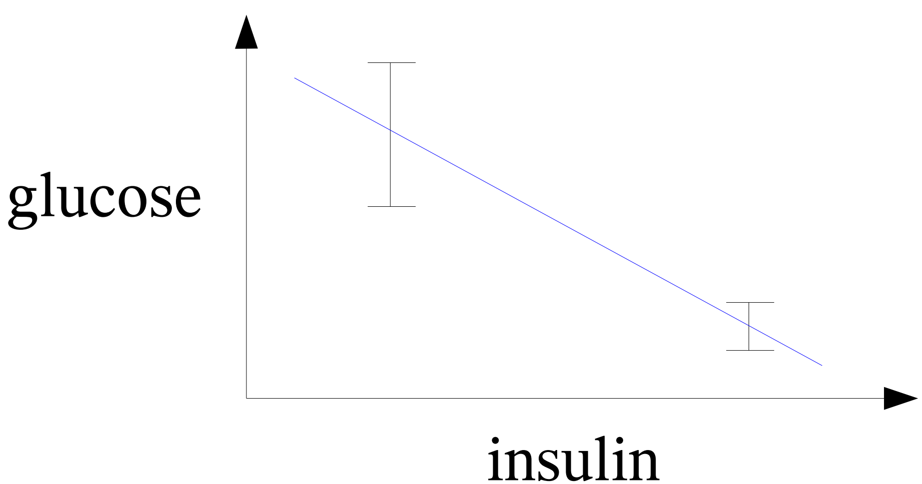
Example: Finding



The Scientific Method



Example: Theory



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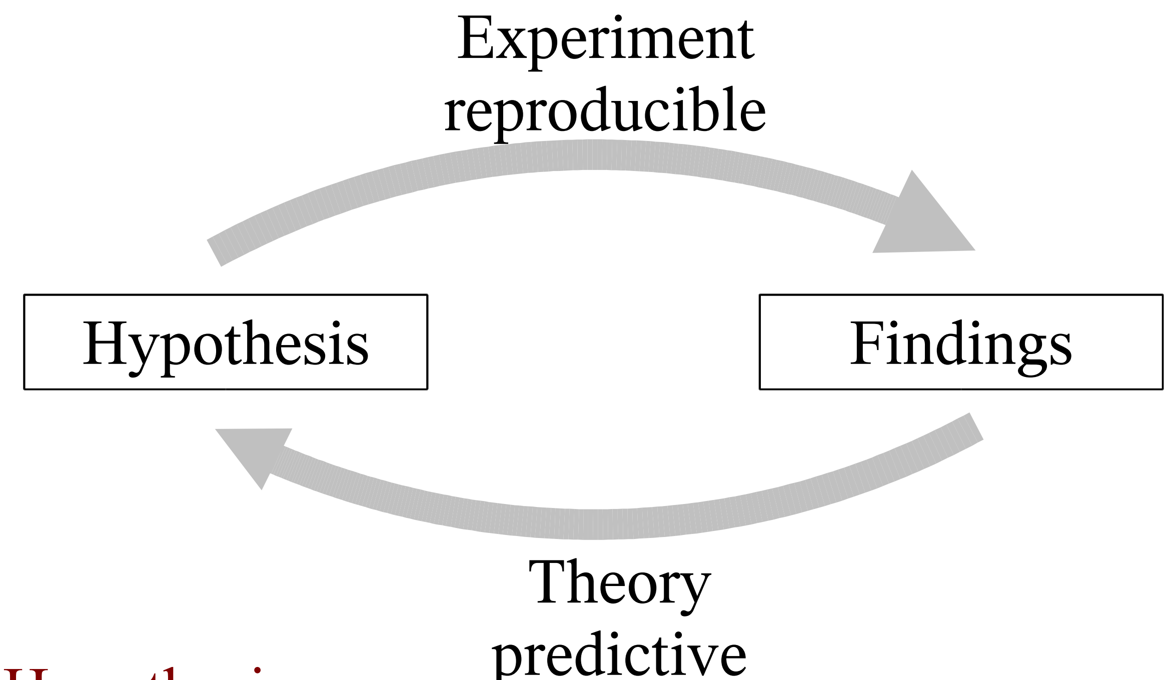
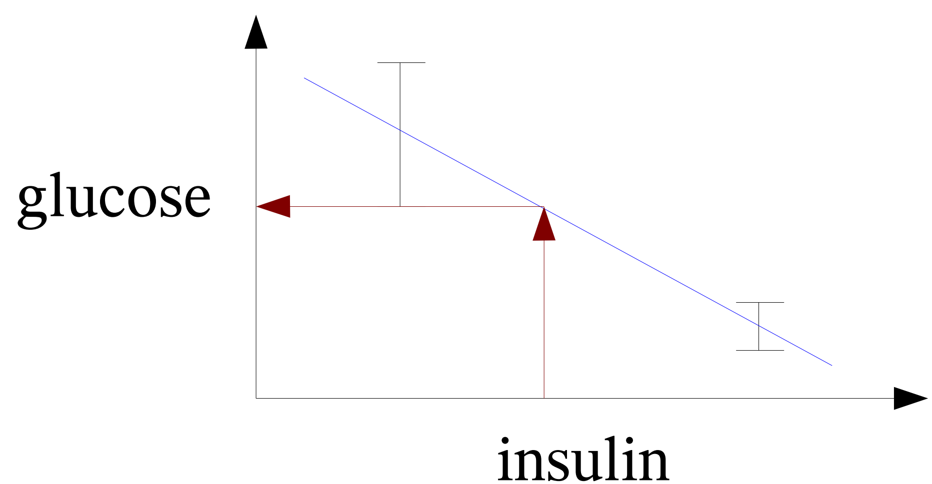
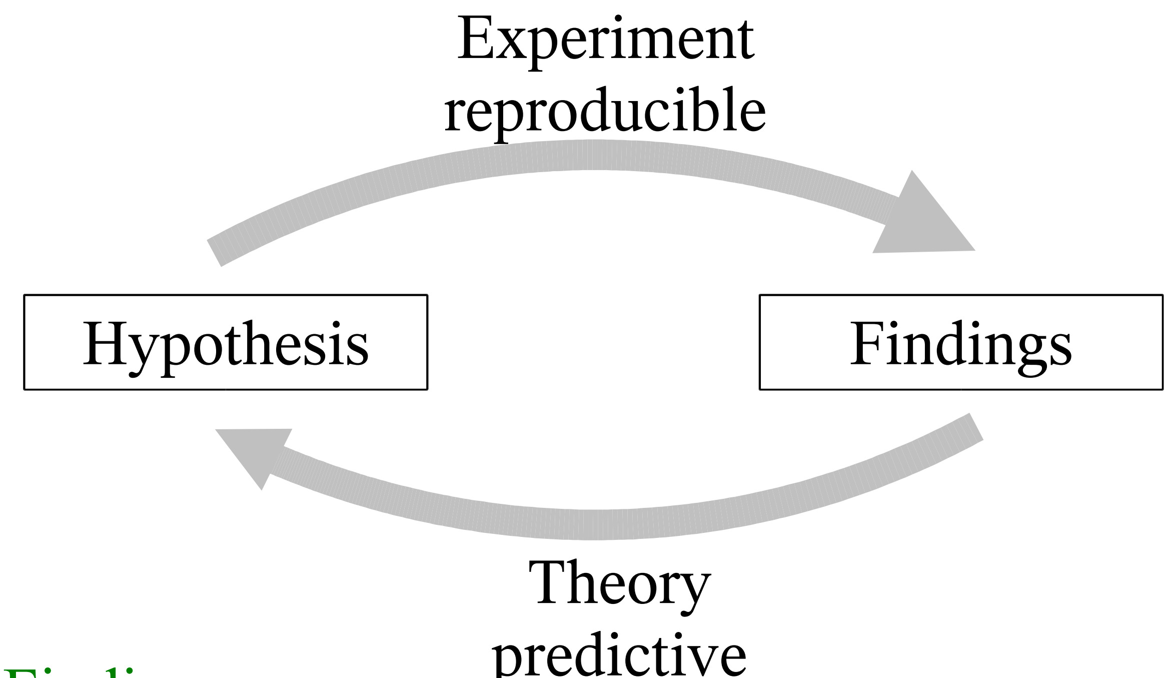


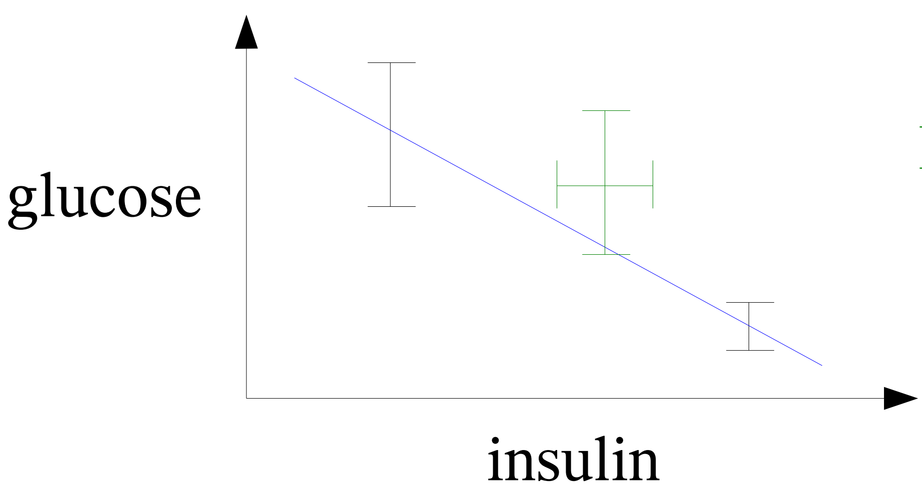
Example: Hypothesis



The Scientific Method

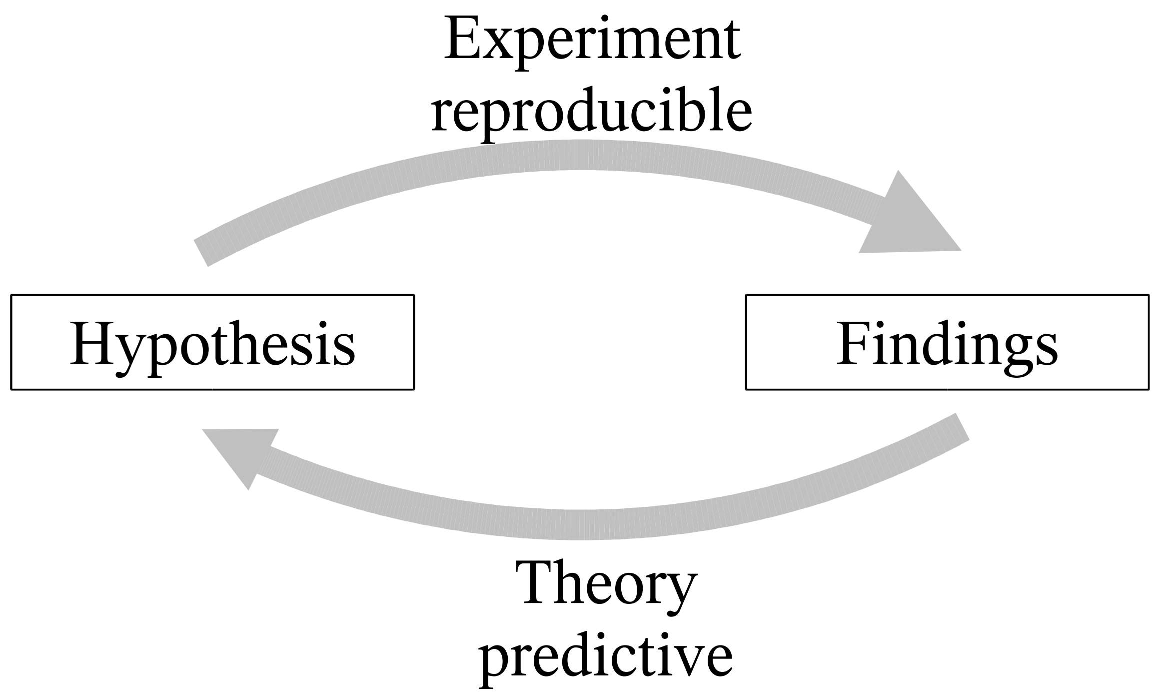


Example: Finding



Is this significant?

The Scientific Method



Papers are then **peer reviewed** and published to:

- keep records of the findings
- generate agreement on the conclusions of findings
- give credit to the researcher
- and keep everybody honest!

Structure of most BioMed research papers

Paper typically contains:
Title, Abstract, Background, Methods, Results, Discussion, References

Interindividual Variation in Posture Allocation: Possible Role in Human Obesity

James A. Levine,* Lorraine M. Lanningham-Foster, Shelly K. McCrady, Alisa C. Krizan, Leslie R. Olson, Paul H. Kane, Michael D. Jensen, Matthew M. Clark

Obesity occurs when energy intake exceeds energy expenditure. Humans expend energy through purposeful exercise and through changes in posture and movement that are associated with the routines of daily life [called non-exercise activity thermogenesis (NEAT)]. To examine NEAT's role in obesity, we recruited 10 lean and 10 mildly obese sedentary volunteers and measured their body postures and movements every half-second for 10 days. Obese individuals were seated, on average, 2 hours longer per day than lean individuals. Posture allocation did not change when the obese individuals lost weight or when lean individuals gained weight, suggesting that it is biologically determined. If obese individuals adopted the NEAT-enhanced behaviors of their lean counterparts, they might expend an additional 350 calories (kcal) per day.

Obesity is epidemic in high-income countries. In the United States alone poor diet and physical inactivity are associated with 400,000 deaths per year (*1*) and obesity-related medical expenditures in 2003 approximated $75 billion (*2*). Obesity is also an emerging problem in middle- and low-income countries, where the health and fiscal costs are likely to be devastating (*3*).

As the impact of obesity on health escalates, so too does the need to understand its pathogenesis. Weight gain and obesity occur when energy intake exceeds energy expenditure. We are interested in a specific component of energy expenditure called NEAT and the role it might play in human obesity. NEAT is distinct from purposeful exercise and includes the energy expenditure of daily activities such as sitting, standing, walking, and talking.

We have previously shown that when humans overeat, activation of NEAT helps to prevent weight gain (*4*). To better understand NEAT and its role in obesity, we separated NEAT into the thermogenesis associated with posture (standing, sitting, and lying) and that associated with movement (ambulation).

To investigate whether the obese state has an effect on NEAT, we first developed and validated a sensitive and reliable technology for measuring the postural allocation of NEAT in human volunteers (*5*, *6*). This physical activity monitoring system uses inclinometers and triaxial accelerometers to capture data on body position and motion 120 times each minute. By combining these measurements with laboratory measures of energy expenditure, we can summate NEAT and define its components (*7*).

To compare body posture and body motion in lean and obese people, we recruited 20 healthy volunteers who were self-proclaimed "couch potatoes." Ten participants (five females and five males) were lean [body mass index (BMI) 23 ± 2 kg/m^2] and 10 participants (five females and five males) were mildly obese (BMI 33 ± 2 kg/m^2) (*8*) (table S1). We deliberately selected mildly obese subjects who were not incapacitated by their obesity and who had no joint problems or other medical complications of obesity. The volunteers agreed to have all of their movements measured for 10 days and to have their total NEAT measured with the use of a stable isotope technique (*9*). They were instructed to continue their usual daily activities and occupations and not to adopt new exercise practices. Over the 10-day period, we collected ~25 million data points on posture and movement for each volunteer.

Our analysis revealed that obese participants were seated for 164 min longer per day than were lean participants (Fig. 1A). Correspondingly, lean participants were upright for 152 min longer per day than obese participants. Sleep times (lying) were almost identical between the groups. Total

Endocrine Research Unit, Mayo Clinic, Rochester, MN 55905, USA.

*To whom correspondence should be addressed. E-mail: Jim@Mayo.edu

Structure of most BioMed research papers

Abstract

Gives a summary including the main question, its relevance, the specific hypothesis, the method of testing the validity of the hypothesis, and an outlook.

Introduction/Background

Explains the main objectives and rationale for the study. It should cover relevance, existing knowledge leading to the main hypothesis, and how the hypothesis will be tested. Except for the hypothesis everything that is stated here must be supported by previous published research.

Methods

Presents the methods that are used to confirming or falsifying the hypothesis. Should be detailed enough for others to repeat the experiment if they wished to replicate the outcomes.

Structure of most BioMed research papers

Results

Gives (only!) the factual findings of the experiments that have been performed. All quantitative results should be analyzed for their statistical relevance.

Discussion

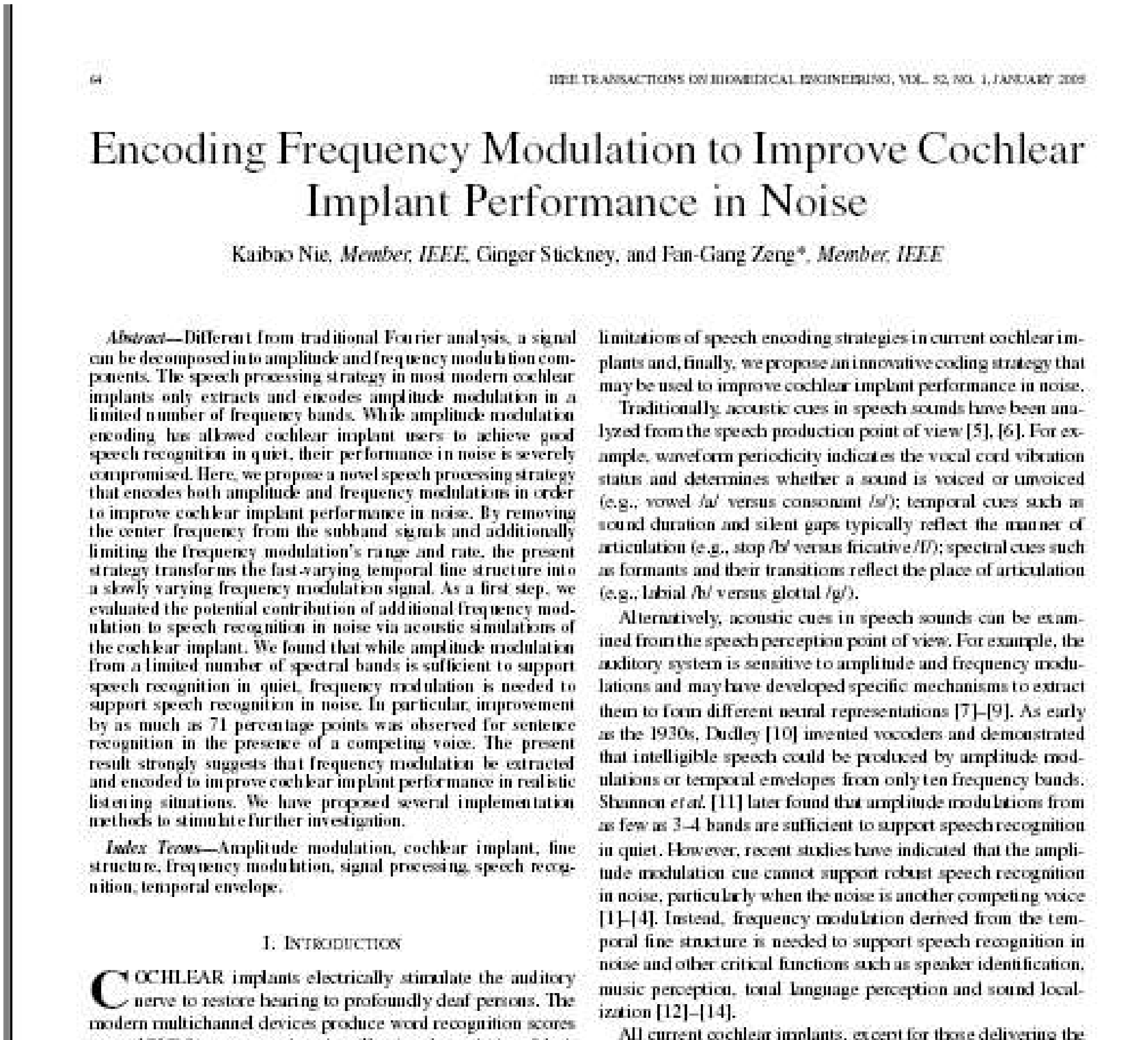
Discusses how the results confirm or contradict the hypothesis and discusses alternative explanations. Puts the results in perspective comparing them to previous work.

References

Complete list of scholarly publications of relevant prior work that have been cited in the paper (and nothing else).

Structure of most engineering papers

Similar: Title, abstract, references .... but



64 IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, VOL. 52, NO. 1, JANUARY 2005

Encoding Frequency Modulation to Improve Cochlear Implant Performance in Noise

Kaibao Nie, *Member, IEEE*, Ginger Stickney, and Fan-Gang Zeng*, *Member, IEEE*

Abstract—Different from traditional Fourier analysis, a signal can be decomposed into amplitude and frequency modulation components. The speech processing strategy in most modern cochlear implants only extracts and encodes amplitude modulation in a limited number of frequency bands. While amplitude modulation encoding has allowed cochlear implant users to achieve good speech recognition in quiet, their performance in noise is severely compromised. Here, we propose a novel speech processing strategy that encodes both amplitude and frequency modulations in order to improve cochlear implant performance in noise. By removing the center frequency from the subband signals and additionally limiting the frequency modulation's range and rate, the present strategy transforms the fast-varying temporal fine structure into a slowly varying frequency modulation signal. As a first step, we evaluated the potential contribution of additional frequency modulation to speech recognition in noise via acoustic simulations of the cochlear implant. We found that while amplitude modulation from a limited number of spectral bands is sufficient to support speech recognition in quiet, frequency modulation is needed to support speech recognition in noise. In particular, improvement by as much as 71 percentage points was observed for sentence recognition in the presence of a competing voice. The present result strongly suggests that frequency modulation be extracted and encoded to improve cochlear implant performance in realistic listening situations. We have proposed several implementation methods to stimulate further investigation.

Index Terms—Amplitude modulation, cochlear implant, fine structure, frequency modulation, signal processing, speech recognition, temporal envelope.

I. Introduction

COCHLEAR implants electrically stimulate the auditory nerve to restore hearing to profoundly deaf persons. The modern multichannel devices produce word recognition scores

limitations of speech encoding strategies in current cochlear implants and, finally, we propose an innovative coding strategy that may be used to improve cochlear implant performance in noise.

Traditionally, acoustic cues in speech sounds have been analyzed from the speech production point of view [5], [6]. For example, waveform periodicity indicates the vocal cord vibration status and determines whether a sound is voiced or unvoiced (e.g., vowel /a/ versus consonant /s/); temporal cues such as sound duration and silent gaps typically reflect the manner of articulation (e.g., stop /b/ versus fricative /f/); spectral cues such as formants and their transitions reflect the place of articulation (e.g., labial /b/ versus glottal /g/).

Alternatively, acoustic cues in speech sounds can be examined from the speech perception point of view. For example, the auditory system is sensitive to amplitude and frequency modulations and may have developed specific mechanisms to extract them to form different neural representations [7]–[9]. As early as the 1930s, Dudley [10] invented vocoders and demonstrated that intelligible speech could be produced by amplitude modulations or temporal envelopes from only ten frequency bands. Shannon *et al.* [11] later found that amplitude modulations from as few as 3–4 bands are sufficient to support speech recognition in quiet. However, recent studies have indicated that the amplitude modulation cue cannot support robust speech recognition in noise, particularly when the noise is another competing voice [1]–[4]. Instead, frequency modulation derived from the temporal fine structure is needed to support speech recognition in noise and other critical functions such as speaker identification, music perception, tonal language perception and sound localization [12]–[14].

All current cochlear implants, except for those delivering the

Structure of most engineering papers

Different: Does not contain any hypothesis!

Background

Engineering papers often start with a practical need detailing the limitations of current solutions and the novelty of the proposed solutions.

Methods

Discusses technical design challenges. Presents proposed solutions. Shows how to implement the solutions.

Results

Shows performance evaluation and should include benchmark with alternative approaches.

Discussion/Conclusion

Gives a discussion of the benefits and limitations and sometimes suggest future work.

Class work

In groups of 3 pick one of two papers and answer the following questions (be ready to read your answers aloud):

BioMed/Engr: Is this a science or engineering paper?

BioMed: What is the main hypothesis?

BioMed: Describe the main results.

BioMed: How do the results support the hypothesis?

Engr: What is the main need?

Engr: What is the main technical challenge?

Engr: What is the novelty?

BioMed/Engr: Is the result significant? Why or why not?

BioMed/Engr: What would you consider to be the most relevant reference on prior work, and why?

BioMed/Engr: What are the wider implications of this work on health/science/technology/society if any?

Technical report

Structure is similar to an engineering paper except for:

Executive summary:

- One page max!
- Contains one sentence summary of each topic the reader should know.
- This is the most important part of the document and the only thing that is typically read (the rest is a bonus "just in case").
- Must therefore be self contained including background and conclusions if any.

The rest of the document typically contains more detail than an engineering paper. It should allow anyone to reproduce the work exactly.

It is **not peer reviewed!**

Literature search and writing assignment

Assignment 4:

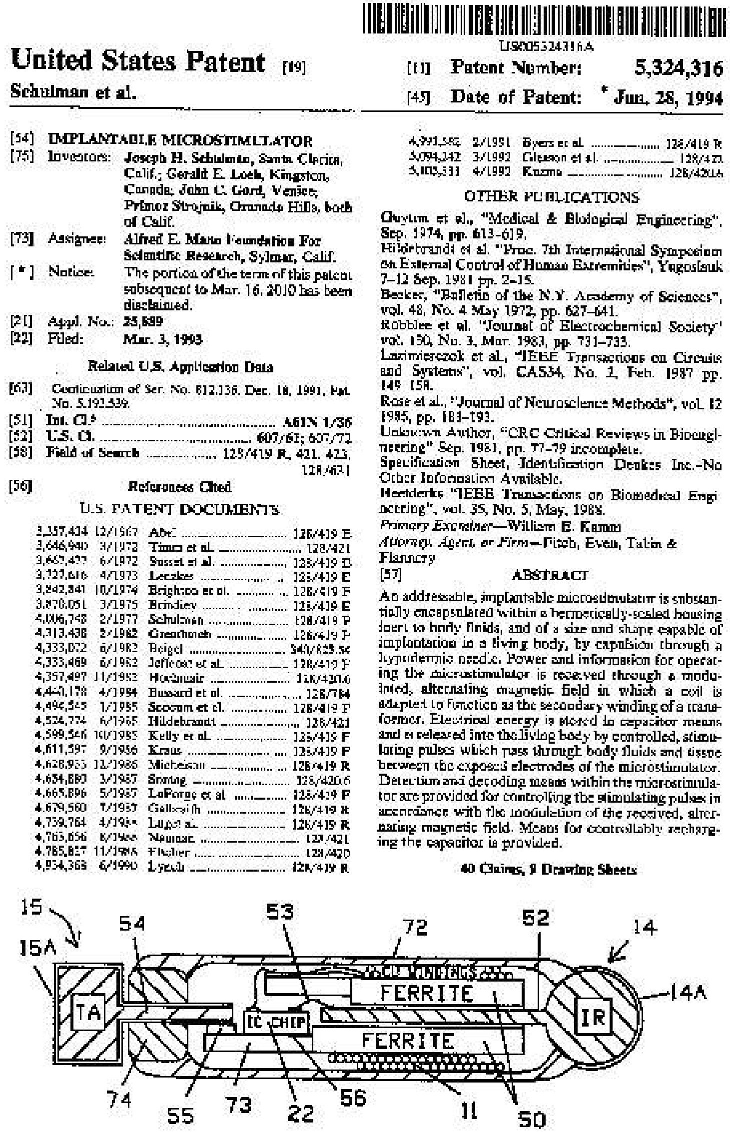
- Perform a literature search on the topic you selected in assignment 1.

- Write a background section (2 pages)
  - For a biomedical research topic discuss what is factually known, the hypotheses that are currently being researched, and what are the remaining open questions (hint: reviews paper).
  - For an engineering topic describe the practical need, state-of-the-art solutions, highlight alternatives if available, and outstanding technical challenges.
  - Make detailed reference to at least 5 relevant papers.

- Write a Executive summary (250-500 word)
  Summarize the results of your literature search. Touch on the broader impacts of this research topic on society.

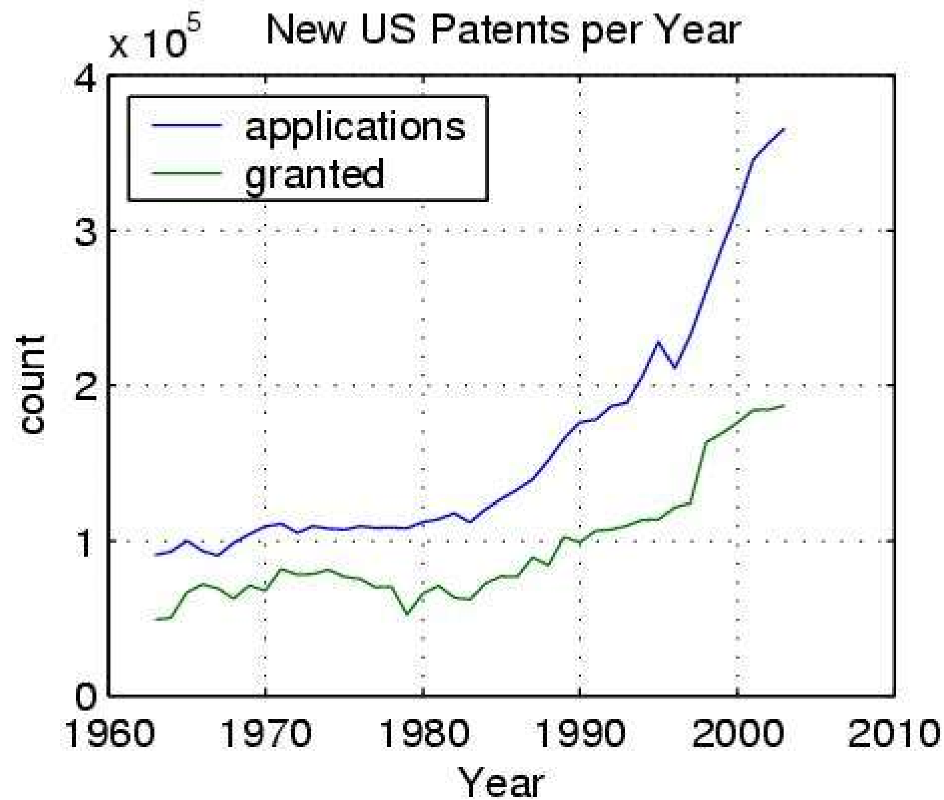
Patents

- Patent gives protection for an idea for 17 years within the US.
- The idea must be:
  1. useful
  2. novel
  3. not obvious
- Must also be doable, e.g. can't patent 'perpetum mobile'.
- Can't patent facts of nature, e.g. $E=mc^2$, unless used in a device.
- Things that can be patented: Machines, exercises, business practices, gene expression, engineered life forms...



Patents

- Most patents would not stand up to peer review process.
- Hardly a way to learn new information.
- Consult patents only if you want to make sure that your idea has not been claimed yet.
- Find patents at USPTO web site.

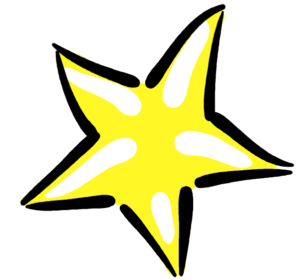


Patent Content

Structure of a Patent:

- **Inventors:** All of them!
- **Assigned institution:** Owns and typically paid the filing fees.
- **Prior art:** Important to establish novelty. What to list and not to list can be tricky.
- **Abstract:** Summary of the description – not always useful and of minor importance.
- **Claims:** This is the core of the invention. Claims try to cover as much as possible yet not cover anything that is prior art. Typically structured as a sequence of claims that build on each other going from the most general to the most specific. The most specific typically describes an actually existing implementation.
- **Detailed description:** Lays out all details needed to understand the claims. Depending on the author they may or may not really help to reproduce the device. Usually you are much better of reading a paper!

Oral presentation



You have seen good examples in BME 101.

Contains:

- Title slide (title, presenter, affiliation, date, venue, logo)
- Problem Statement/Hypothesis (2 slides max)
- Overview (short list of topics headings. 1 slide only in long talks)
- Methods/Results (interleaved in as many slides as needed)
- Conclusions (List of one sentence summaries. 1 slide.)
- Acknowledgments (collaborators and funding)

Recommendations:

- 2 minutes per slide. NO LESS.
- Include as much meaningful images/graphics as possible.
- Do not add "cute" graphics without information content.
- No sound effects.
- Resist the urge to reduce font size! Just so that you can say the same thing with more words than would be otherwise necessary. It is hard for people to realize which text really matters. In particular since they are listening to you while they read.

Poster presentation

See examples in the hallways ...

Contains:
- Title, authors, affiliation, logo
- Abstract (1 slide)
- Problem Statement/Hypothesis (2 slides max)
- Methods/Results (interleaved in as many slides as needed)
- Conclusion/Summary (only one slide!)
- Acknowledgments (collaborators and funding)
- References

Recommendations:
- Same as oral presentation
- Use complete sentences that need no additional explanation (in case the poster is being read in your absence).

Implant Oral Presentation Project

Assignment 5:

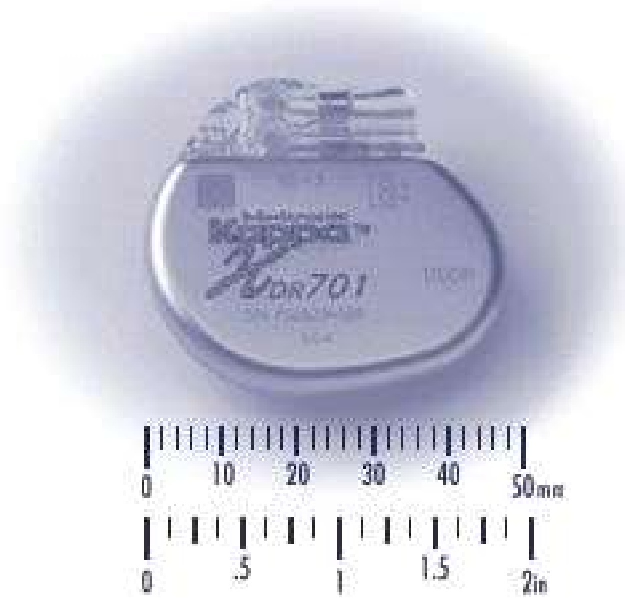
- In groups of 3 prepare 15 minutes oral presentation on one of the implants listed in the following slides. Each person will present 5 minutes. The order will be selected at random at the time of presentation. So be prepared to present all parts.

- Use the format of a oral presentation.

- Address the topics that are typically discussed in engineering papers: (1) Practical need, (2) technical design challenges, (3) proposed solutions, (4) specific implementations, (5) performance evaluation, (6) alternative approaches, (7) benefits and limitations, (8) your suggestion for improvements.

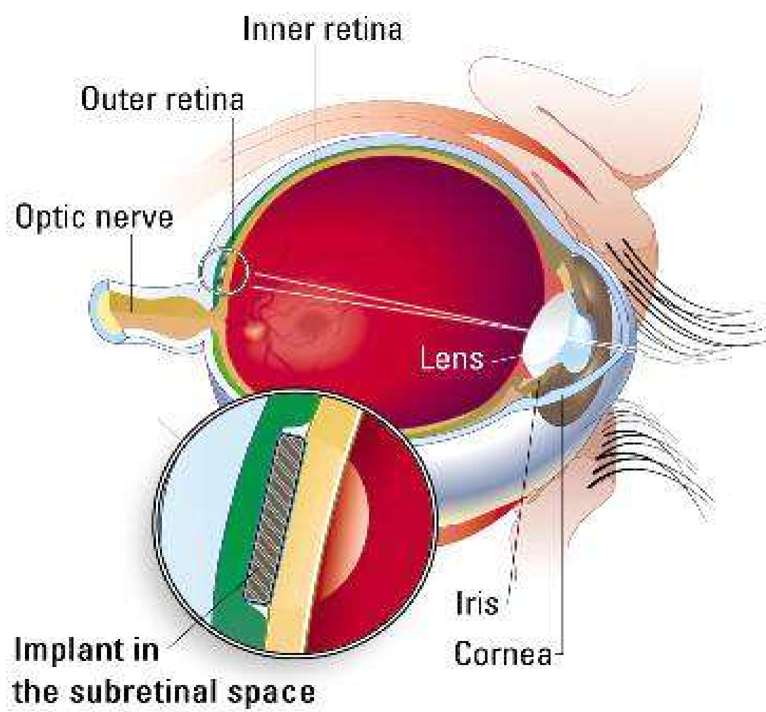
- When discussing needs, benefits, and limitation highlight human and societal factors: health, side-effects, safety, cost, acceptance, comfort, access.

Implant 1: Pacemaker



A pacemaker is a treatment for dangerously slow heart beats, which can result from metabolic abnormalities or blocked arteries to the heart's conduction system. The pacemaker generator contains a lithium battery and what is, essentially, a little computer. The generator can communicate with an external device placed on the skin overlying the pacemaker. Through this device, a physician can change the programming of the pacemaker to best suit the individual patient's needs and investigate the status of the pacemaker. Some pacemakers also report on the performance of the patient's heart. Pacemakers sense every heart beat the patient has and only pace the heart when the patient's heart rate falls below a predetermined limit. Patients are usually completely unaware of when the pacer is pacing their heart. Fortunately, having a pacemaker implanted is only a minor surgical procedure, not open heart surgery. The procedure is performed with mild sedation and a local anesthetic. Patients are not put to sleep. An 2-inch incision is made parallel to and just below a collar bone. Pacer wires are then inserted into a vein that lies just under the collarbone and advanced through that vein under fluoroscopic guidance into the heart. The other end of the pacer wires are connected to a "generator" that is implanted under the skin beneath the collar bone. This generator is about half an inch deep and one and a half inches wide. It is possible to feel the pacer generator under the skin and a slight deformity of the skin can be visually noticed.

Implant 2: Artificial Retina



Human eyes receive light rays and translate then into images via a layer of photosensitive cells that are known collectively as the ***retina***. Light enters the eye and is focused by the cornea and the iris to project a small inverted image of the outside world onto the retina. The area of the retina that receives and processes the detailed images, and then sends them via the optic nerve to the brain, is known as the macula. The macula provides the highest resolution for the images humans interpret as vision. The macula is comprised of multiple layers of cells, which process the initial 'analog' light energy entering the eye into 'digital' electrochemical impulses. The Optobionics Artificial Silicon Retina (ASR) is a microchip designed to stimulate damaged retinal cells to send visual signals to the brain. The chip is 25 microns thick, 2mm in diameter and is powered solely by incident light, thereby eliminating the need for external wires or batteries. The ASR is surgically implanted under the retina so that its approximately 5,000 microscopic solar cells (microphotodiodes) can send photoelectric signals to the brain via the optic nerve.

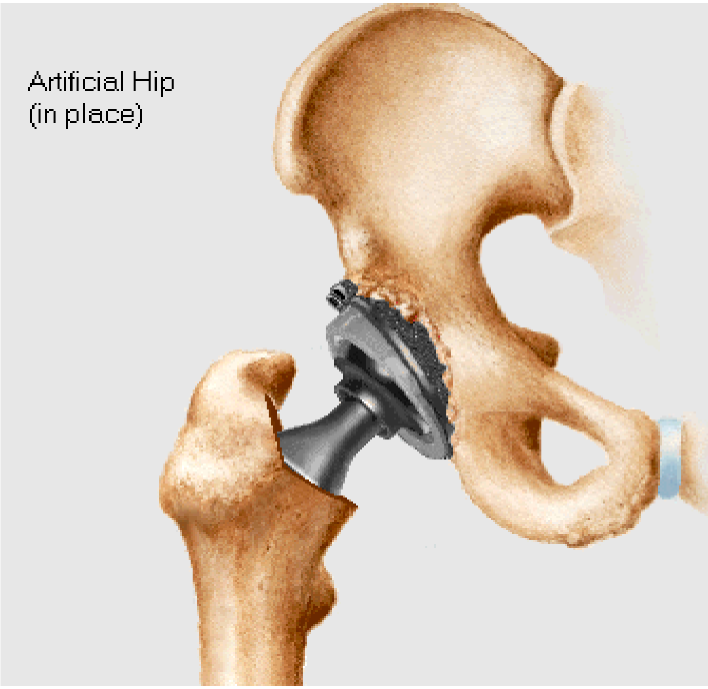
Implant 3: Dental Implants

A dental implant is a man-made replacement for natural teeth that periodontists place into your jaw to hold a replacement tooth or bridge. It is not a transplant, which is taken from another person. Dental implants are manufactured from titanium to be biocompatible, and integrate with the surrounding bone to become part of the body. While high-tech in nature, dental implants are actually more tooth-saving than traditional bridgework, since implants do not rely on neighboring teeth for support. Endosteal implants (in the bone) are the most commonly used type of implant, including screws, cylinders or blades surgically placed into the jawbone. Each implant holds one or more prosthetic teeth. This type of implant is generally used as an alternative for patients with bridges or removable dentures. Subperiosteal implants (on the bone) are placed on top of the jaw with the metal framework's posts protruding through the gum to hold the prosthesis. These types of implants are used for patients who are unable to wear conventional dentures and who have minimal bone height.

Implant 4: Deep Brain Stimulation

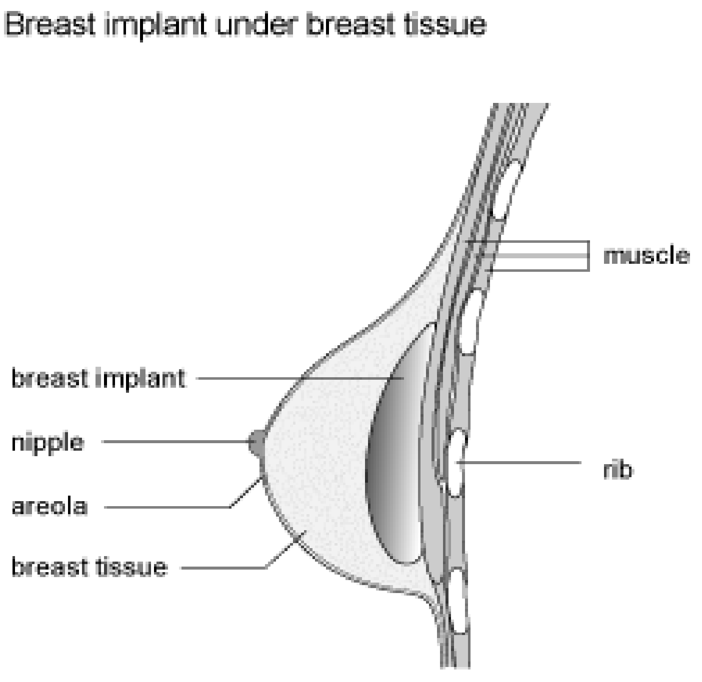
The American Neurological Institute now provides Deep Brain Stimulation (DBS) treatment for patients with Parkinson's Disease. In Parkinson's, and other tremor related-illnesses, patients experience loss of motor control due to uncontrolled synaptic activity within the neurons of the brain. Each uncontrolled activity is like 'an electrical storm' that creates elevated voltage signals in localized parts of the brain. With DBS, electrical signals are delivered to precisely targeted areas within each side of the brain in order to inhibit, or at least control, the unwanted electrical connections between neurons. The DBS involves three implants called a Lead, an Extension and a Neurostimulator. The lead is a thin insulated coil wire with four electrodes at the tip that is implanted into the brain. The extension is a thin coiled wire that is threaded under the skin into the upper chest. Lastly, the neurostimulator is implanted into the patient's chest, near the collar bone. It delivers electrical stimulation to the brain's targeted areas via the extension and the lead.

Implant 5: Total Hip Replacement



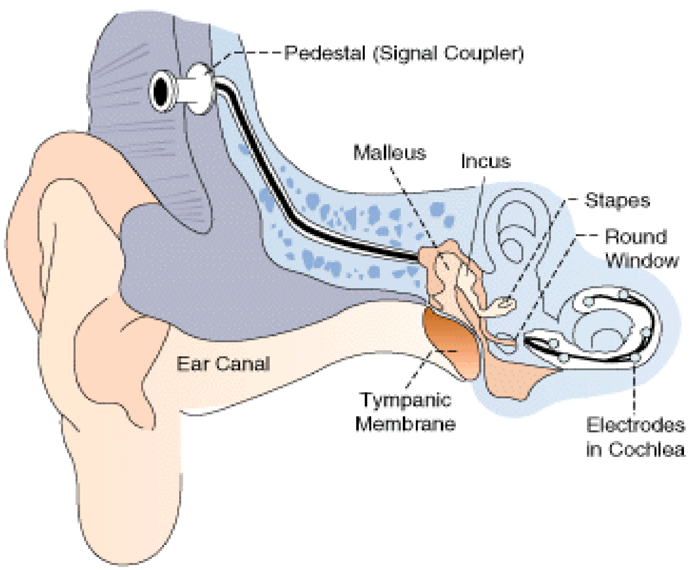
A total hip replacement is a surgical procedure for replacing the hip joint. This joint is composed of two parts; the hip socket (acetabulum, a cup-shaped bone in the pelvis) and the ‘ball’ or head of the thigh bone (femur). During the surgical procedure, these two parts of the hip joint are removed and replaced with smooth artificial surfaces. The artificial socket is made of high-density plastic, while the artificial ball with its stem is made of a strong stainless metal. These artificial pieces are implanted into healthy portions of the pelvis and thigh bones and affixed with a bone cement (methyl methacrylate). An alternative hip prosthesis has been developed that does not require cement. This hip has the potential to allow bone to grow into it, and therefore may last longer than the cemented hip. This is an important consideration for the younger patient.

Implant 6: Breast Implants



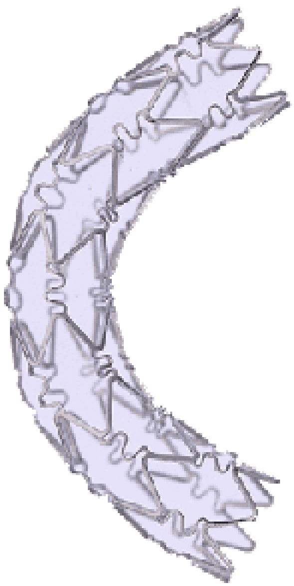
Breast reconstruction is performed for survivors of breast cancer, for women who experience extreme mass loss after pregnancy, and for men/women desiring cosmetic enhancement. Replacement or enlagement is usually performed under general anaesthetic and may be completed without the need for an overnight hospital stay. Beast implants are usually made from silicone, particularly after a special cohesive silicone filling has been developed which is less likely to leak than the silicone in older implants. The implant is inserted through incisions on or near the breasts. The exact position of the incision varies, but can be in the crease under the breast, around the nipple or towards the armpit. After making the incision, the surgeon makes a small space into which the implant is placed. This pocket is beneath the breast skin or under the chest muscle. The incision is closed with stitches, and bandages or dressings are applied over the wound. The procedure usually takes between one and two hours. Some pain and bruising occurs around the breasts for the first few days, but this can usually be controlled with painkillers.

Implant 7: Cochlear Implant



Humans translate the acoustic energy of sound into electrical signals carried to the brain by 30,000 fibers of the auditory nerve. Sound waves travel along the external ear canal and cause the tympanic membrane (i.e. ear drum) to vibrate. The three small bones of the middle ear then conduct these vibrations to the snail-shaped cochlea of the inner ear. The basilar membrane of the cochlea contains rows of hair cells that extend along its length and elicit electrical activity on the auditory nerve fibers when vibrated. Destruction of these hair cells, therefore, results in hearing loss. The cochlear implant seeks to restore partial hearing by bypassing the external and middle ears via electrical stimulation of electrodes implanted in the cochlea to reintroduce the signals carried by the auditory nerve fibers to the brain. A microphone in a behind-the-ear aid case is connected to a package of electronics called a sound processor, that is about the size of a walkman and can be carried in a pocket.

Implant 8: Cardiovascular Stent



Stents are wire mesh devices made from stainless steel or nytinol meshes that look similar to the spring in a pen. Stents are used to prop open an artery that's recently been cleared using angioplasty. Stents are delivered into the coronary artery on a catheter and are 'deployed' by either expansion via balloon, or by a unique 'self expanding' delivery design. They serve as a scaffold to prop the inside of the artery (the lumen) open which increases blood flow to the heart muscle. They are not removed, and remain permanently deployed in the artery. They ultimately become covered with cells and in essence become part of the artery over time. The stent is collapsed to a small diameter and put over a balloon catheter. It's then moved into the area of the blockage. When the balloon is inflated, the stent expands, locks in place and forms a scaffold. Stenting is a fairly common procedure that reduces renarrowing that occurs after balloon angioplasty, or other procedures that use catheters. Stents also help restore normal blood flow and keep an artery open if it's been torn or injured by the balloon catheter. Reclosure (restenosis) has become a problem with the stent procedure. In recent years doctors have used new types of stents called drug-eluting stents (DES) to avoid reclosure problems (restenosis) after the procedure. These DES stents are coated with drugs that are slowly released and help keep the blood vessel from reclosing. These new stents have shown some promise for improving the long-term success of this procedure.