

Considerations for Strategic Planning



Research Frontiers in Medical Cyber-Physical Systems Washington, DC 6 February, 2014

Richard M. Satava, MD FACS



**Professor Emeritus of Surgery**University of Washington

# Disruptive Visions

"The Future is not what it used to be"



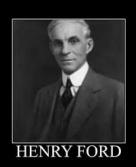


....Yogi Berra

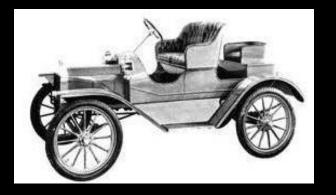
# What is a Disruptive Vision? Rethinking Healthcare

"If I had asked people what they wanted . . . . . . . . . they would have said a faster horse ."









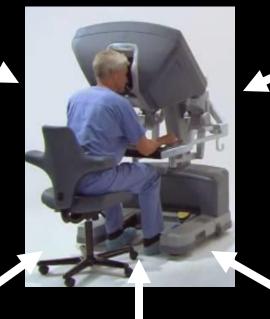
# Expectations are high . . . . challenges are Bigger



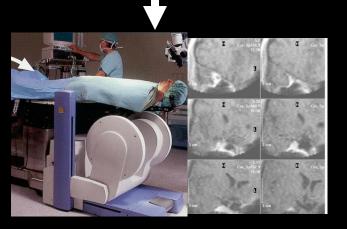
## Total Integration of Surgical Care



Remote Surgery



Pre-operative planning Surgical Rehearsal



Intra-operative navigation



Minimally Invasive & Open Surgery



Simulation & Training Pre-operative Warmup

Courtesy of Joel Jensen, SRI International, Menlo Park, CA

#### **Demonstration of Phase 1**

### **Operating Room with No People**



SRI International, Menlo Park, CA

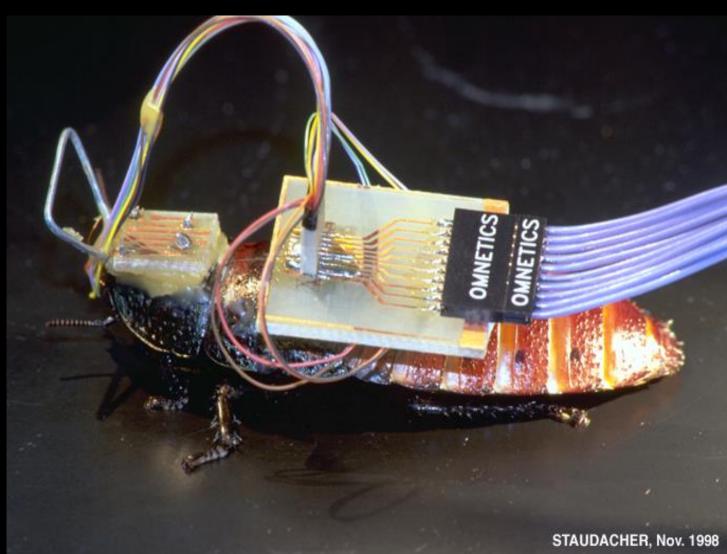
January, 2007

#### **Demonstration of Phase 1**

### **Operating Room with No People**

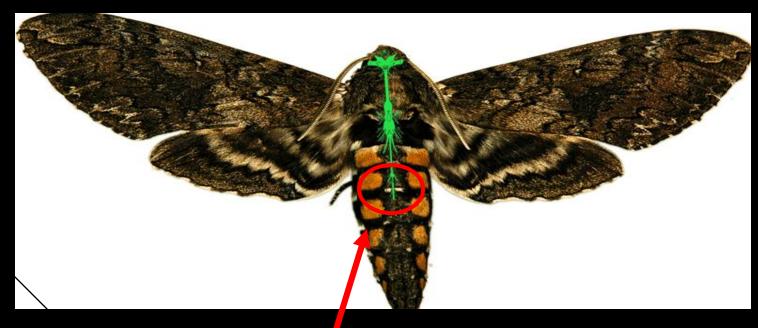


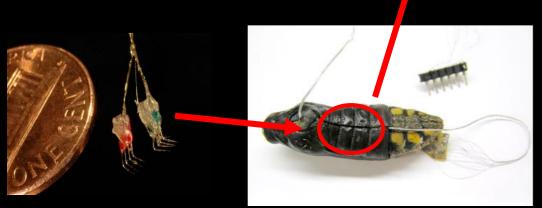
# **Controlling Intervention**





# Direct Control of Muscles







Joel Voldman MIT, John Hildebrand UA

Thomas Daniels, Unv Washington, Seattle



## **Biomimetic** Micro-robot

Courtesy Sandia National Labs



Courtesy Danny Scott Texas Southwestern Dallas, TX



Courtesy D. Oleynkov, Univ Nebraska



Capsule camera for gastrointestinal endoscopy

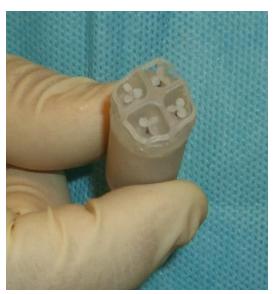
Courtesy Paul Swain, London, England

#### Internal Locomotion Actuators Currently Investigated

Walking robot with legs



Submarine



Vibratory locomotion







Source: M. Sfakiotakis et al., FORTH, Heraklion



Source: A Menciassi et al., CRIM, Scuola Sant'Anna, Pisa

### Femtosecond Laser

 $(1 \times 10^{-15} \text{ sec})$ 





Los Alamos National Labs, Los Alamos NM

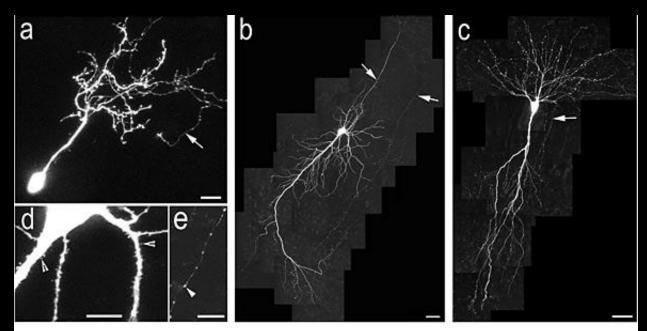
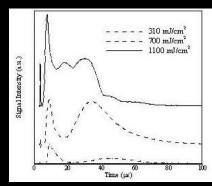
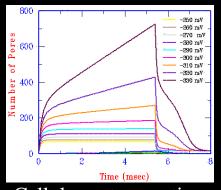


Figure 1. a) Single-cell electroporation of pGFP  $in\ vivo$  in the Xenopus tadpole brain. SCE of CA1 (b) and CA3 (c) pyramidal cells in organotypic rat hippocampal slices. d) Enlargement of the CA1 pyramidal cell showing spines, and axonal varicosities (e).

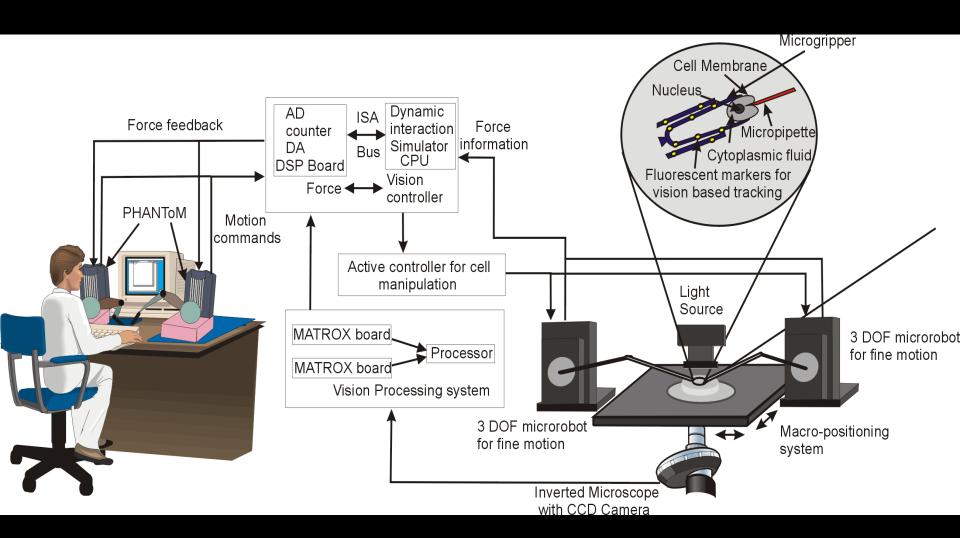


Time of Flight Spectroscopy

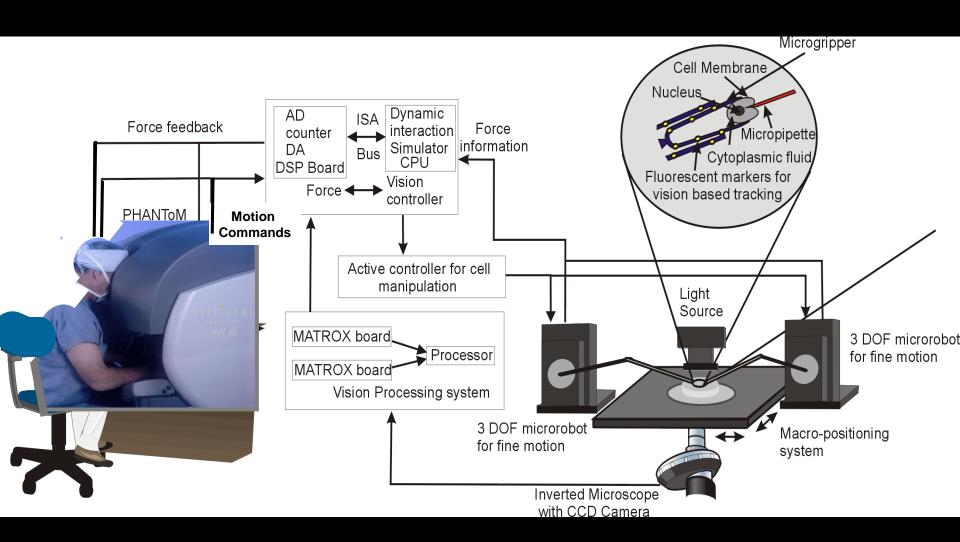


Cellular opto-poration

### Surgical Console for Cellular Surgery



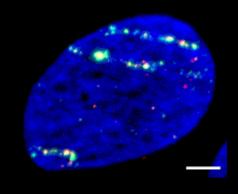
### Surgical Console for Cellular Surgery



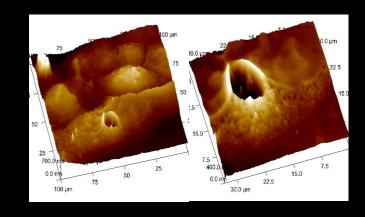
# **New Surgical Tools**



Femtosecond Laser
Specific DNA targeting



Atomic Force Microscopy
Sonoporation of an ion channel



# Radiology or Surgery?

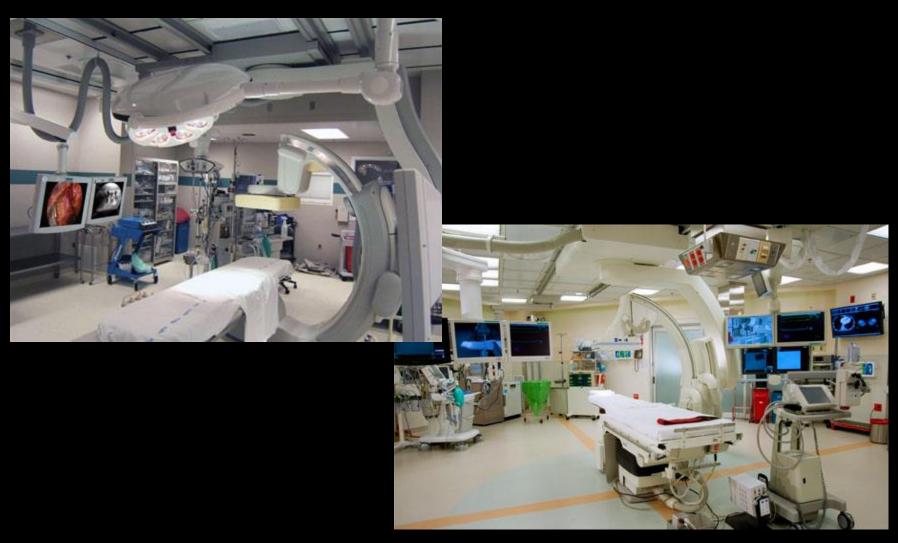


Accuray (Cyberknife)

Non-invasive tumor ablation for solid organs (0.3mm accuracy)
Surgeon should be part of planning and implementation team

Surgeons may want to 'adopt' implementation

# Hybrid Operating Room mage-guided Intervention



# Humanoid Robot Rescue Operations

# DARPA Challenge - Rescue-Bot



In the Rescue Bot - DARPA Robotics Challenge, robots will compete in a variety of tasks, including the use of tools to cut through a wall.

This is a concept of THOR, a humanoid robot to be built by a Virginia Tech–led team.

# **Humanoid Robot - navigation**











The Information Age is NOT the Future

The Information Age is the Present ...

There is something else out there . . . .

## **Current Trend in Intervention**

# Future Direction of Intervention

**Traditional surgery pen surgery Endoluminal** Flexible endoscopy aparoscopic inimal invasive **Multi-invasive** Robotic Non-invasive Directed energy

Each 'niche' will continue to change in proportion

# Rethinking Intervention

It is the flow of information that controls energy which will guide the Future of Interventions

• • EXAMPLES

# The Fundamental Change

(From Industrial Age to the Information Age)

### From tissue and instruments

(Tangible and physical structures and objects)

to

# Information and energy\*

(Intangible and non-visible functional effects)

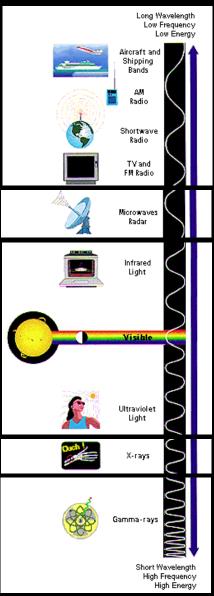
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* "The Information Age is about changing from objects and atoms to bits & bytes" ... Nicholas Negroponte "Being Digital" - 1995
... to photons and electrons! (2013)
```

# t's about Exploiting

Energy Spectrum and

nformation Space

# **Elecromagnetic Spectrum = ENERGY**



Radio: Yes, this is the same kind of energy that radio stations emit into the air for your boom box to capture and turn into your favorite Mozart, Madonna, or Justin Timberlake tunes. But radio waves are also emitted by other things ... such as stars and gases in space. You may not be able to dance to what these objects emit, but you can use it to learn what they are made of

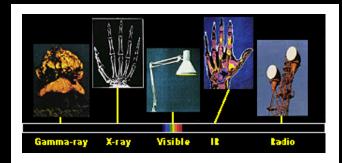
Microwaves: They will cook your popcorn in just a few minutes! Used by astronomers to learn about the structure of nearby galaxies, and our own Milky Way!

Infrared Our skin emits infrared light, which is why we can be seen in the dark by someone using night vision goggles. In space, IR light maps the dust between stars.

Visible: Yes, this is the part that our eyes see. Visible radiation is emitted by everything from fireflies to light bulbs to stars ... also by fast-moving particles hitting other particles. Ultraviolet: We know that the Sun is a source of ultraviolet (or UV) radiation, because it is the UV rays that cause our skin to burn! Stars and other "hot" objects in space emit UV radiation.

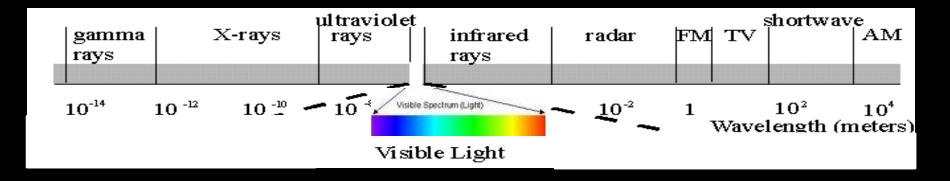
X-rays Your doctor uses them to look at your bones and your dentist to look at your teeth. Hot gases in the Universe also emit X-rays.

Gamma-rays: Radioactive materials (some natural and others made by man in things like nuclear power plants) can emit gamma-rays. Big particle accelerators that scientists use to help them understand what matter is made of can sometimes generate gamma-rays. But the biggest gamma-ray generator of all is the Universe! It makes gamma radiation in all kinds of ways.



Radio waves, visible light, X-rays, and all the other parts of the electromagnetic spectrum are fundamentally the same thing, electromagnetic radiation.

### **Elecromagnetic Spectrum = ENERGY**



#### Medical use of various forms of energy

- Gamma rays
- Xrays
- Ultraviolet

- Visible
- Infrared
- Ultrasound

Healthcare is only using a small % of the energy spectrum

# Directed-energy Weapons

#### 120804-N-ZZ999-001

The Laser Weapon System (LaWS) is a technology demonstrator built by the Naval Sea Systems Command from commercial fiber solid state lasers, utilizing combination methods developed at the Naval Research Laboratory, LaWS can be directed onto targets from the radar track obtained from a MK 15 Phalanx Close-In Weapon system or other targeting source. The Office of Naval Research's Solid State Laser (SSL) portfolio includes LaWS development and upgrades providing a quick reaction capability for the fleet with an affordable SSL weapon prototype. This capability provides Navy ships a method for Sailors to easily defeat small boat threats and aerial targets without using bullets. This video footage shows an exercise conducted by a technical team from the Navai Surface Weapons Center Dahlgren Division and managed & funded by ONR, Naval Sea Systems Command, OSD's High Energy Laser Joint Technology Office and supported by U.S. Fleet Forces Command (U.S. Navy video/Released) abo NEWS

# nformation and Energy

#### **C**ornerstone of **S**ystems **I**ntegration

Single instrument which

- performs both diagnosis & therapy
- in real time
- at point-of-care
- hand-held, portable, low power
- could be autonomous (closed-loop feedback)
- home-based consumer product

#### For about 2500 years

ca 490BC (Protagoras- Greek philosopher) "Man is the measure of al things" 80-15BC (Vitruvius - Greek architect) in architecture, man is the reference measurement

# It's about Interacting on a different scale

From meters and cm ....

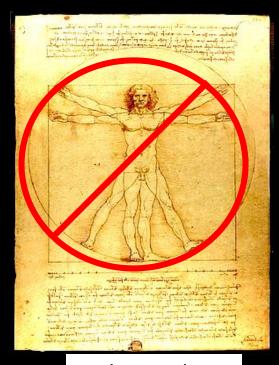
... to microns and nanometers

From seconds and milliseconds

... to micro seconds and femtoseconds (10-15)

From watts and kilowatts

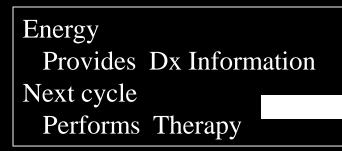
... to milliwatts and microwatts



Leonardo DaVinci Vitruvian Man ca 1490

We now can control molecules, electrons & photons

# t's about Intelligent Systems



# Energy

#### **Controls**

Activates energy devices
Turns on/off systems
Modulates energy

Closed-loop feedback
Enables intelligent control

#### Generates

Diagnostic information
Spectroscopy, fluorescence
Ultrasound, terahertz
or

Therapeutic effect
HIFU, Laser, plasma, etc

Closed-loop feedback

Information

Information
Controls Energy

# If the closed-loop feedback is 50 msec

# Theoretically A physician can perform

in one second in one minute in ten minutes 20 complete procedures 1,200 complete procedures 12,000 complete procedures

therefore, operates at the cellular level

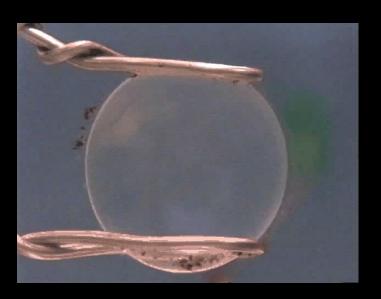
# Intelligent Instruments Point-of-care Non-invasive Therapy

Mechanics to energy



Concentric HIFU around central Doppler solves registration problem

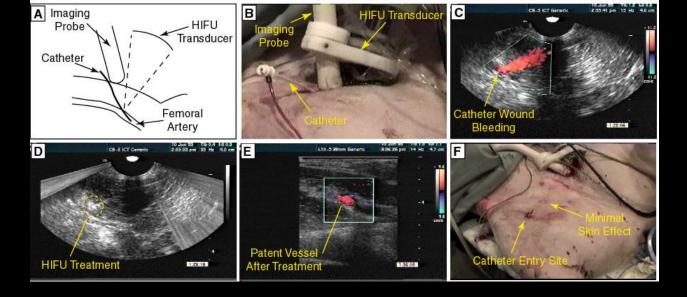






High Intensity Focused Ultrasound for

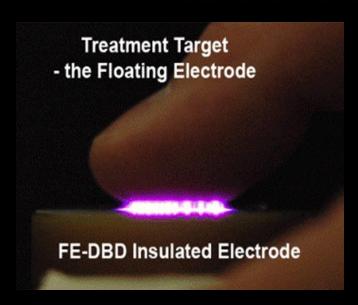
Non-invasive Acoustic hemostasis





Courtesy Larry Crum, Univ Washington Applied Physics Lab 2003

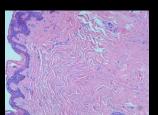
# Plasma Medicine Sterilization without supplies



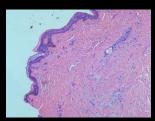








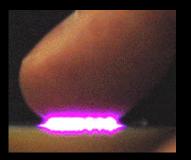




**Insure safety of other cells and tissues** 



100% effective 30 sec, Continuous DBD, 8kHz Power: 0.8 W/cm<sup>2</sup>



### Plasma Medicine



#### The Science of Plasma Physics

Energy is released into a "cloud" by an "electrical discharge"

#### Cloud characteristics

- 1. charged particles free electrons
- 2. free ions reactive nitrogen species (RNS) NO-reactive oxygen species (ROS)
- 3. ultraviolet (UV) and near infrared (NIR)
- 4. visible light esp low level light (LLL)
- 5. high temperature
- 6. electromagnetic radiation (EM)
- 7. pressure pulse wave



# Plasma Medicine



#### The Science

### Biological effects of plasma cloud

- Selectively turn on-off specific molecules
   Prothrombin, cytokines, angiogenisis, VEGF
  - charged particles
     free ions
     UV, NIR and visible light (bio-photonics)
- 2. Induce specific epigenetic phenomenon wound healing, activate coagulation
- 2. charged particles and free ions UV, NIR and visible light (bio-photonics) electromagnetic radiation (EM).

3. Sterilization and debridement

ultra violet (UV)
 High temperature, ROS/RNS

4. Surface etching and electroporation

4. UV light, high temperature

Cell death (cancer)

high temperature Charged particles and free ions

Control cell motility, adhesion integrin, cadherin etc

6. electromagnetic radiation (EM)
UV, NIR, visible (Low Level Light – LLL)

# Plasma Medicine Clinically Relevant Applications

Sterilization & decontamination

Cutting, coagulation & ablation

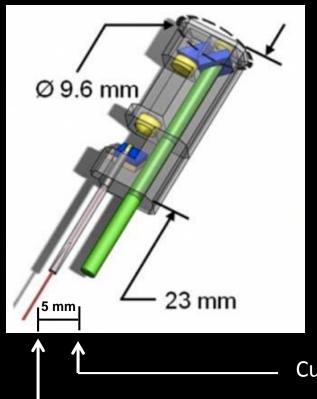
Wound healing & regeneration

Molecular activation & inhibition control

Cancer & disease control/cure

Implant surface specificity to enhance/inhibit

## Intelligent Laser Scalpel



#### **Mechanism of Action**

Cutting/coagulation laser

Dissects tissues (ER:Yag laser)

Diagnostic laser

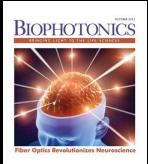
Detects blood vessels (660/910 nm)

Closed loop feedback

Turns off laser when blood vessel detected

Cutting/coagulating laser for dissection

Hyperspectral analysis laser for diagnosis



# Non-invasive Surgery



## Light Penetrates Skull

# Cancer-fighting laser born at Tennessee University space institute

Ashley N. Rice,

October, 2012

TULLAHOMA, Tenn. – A new technique harnesses the power of femtosecond lasers to seek, acutely map and noninvasively destroy cancerous tumors, and it could especially benefit brain cancer patients.

Developed by scientists at the Center for Laser Applications at the University of Tennessee Space Institute, the laser focuses on a specific region to find and destroy tumors.

"Using ultrashort light pulses gives us the ability to focus in a well-confined region and the ability for intense radiation," said Christian Parigger, an associate professor of physics. "This allows us to come in and leave a specific area quickly so we can diagnose and attack tumorous cells fast." The new technology can be especially useful for treating brain cancer patients because it can noninvasively permeate thin layers of bone, such as the skull, and help define a targeted treatment strategy for persistent cancer.

It overcomes the restrictions posed by radiation treatments that damage portions of healthy brain tissue, and also could overcome the limitations of photodynamic therapy that have limited its acceptance and replace surgical options that are unable to remove all carcinogenic tissue.

"If you have a cancerous area such as in the brain, the notion is if you see something and take care of it, it won't spread," Parigger said. "This treatment overcomes difficulties in treating brain cancer and tumors. And it has the promise of application to other areas as well."

The team is working with the University of Tennessee Research Foundation to bring the technology to market

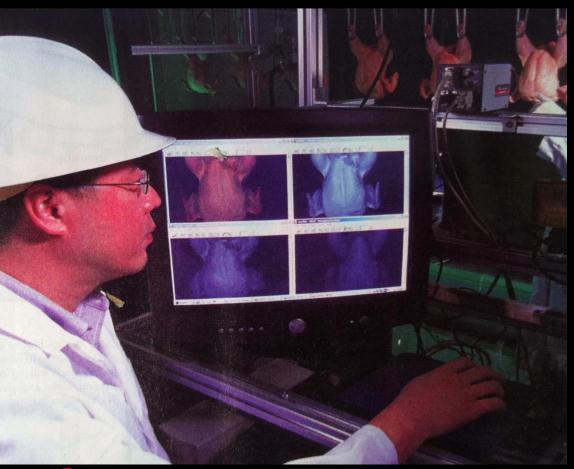
### **BioSensors**

# Hyperspectral Analysis and Automatic Food Inspection

- Laser scans chicken
- Hyperspectral analysis detects bacteria, etc
- Scans 2.5 whole chickens/sec



PETA Supervisor

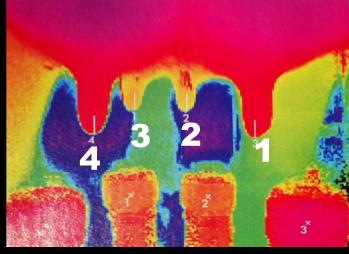


Auto-analysis for infectious bioagents

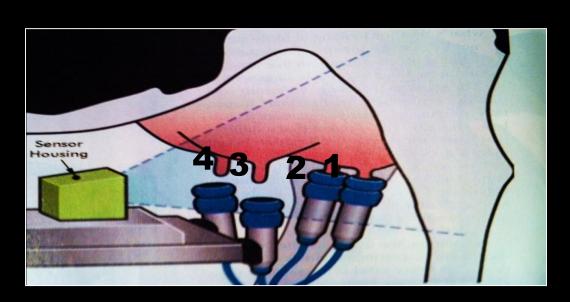
Hogan H. Improving the picture of Food Production. *Photonics Spectra* Nov 2010: 28-30

# Hyperspectral Analysis and Motion Control Automatic Milking Machine





- Hyper spectral identifies udder and teats
- Near-infrared for geometry
- ToF for distance, position
  - Closed loop control for cup guidance
- Robotic arms for placement



Hogan H. Improving the picture of Food Production. *Photonics Spectra* Nov 2010: 28-30

# Hybrid Operating Room Image-guided Surgery

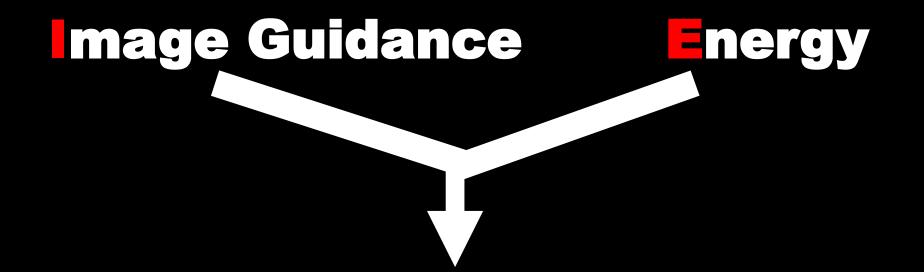






## Surgical Cockpit





# Non-invasive

Directed-Energy Surgery





# s The Future

# **Directed-Energy Intervention?**









# Disruptive Visions

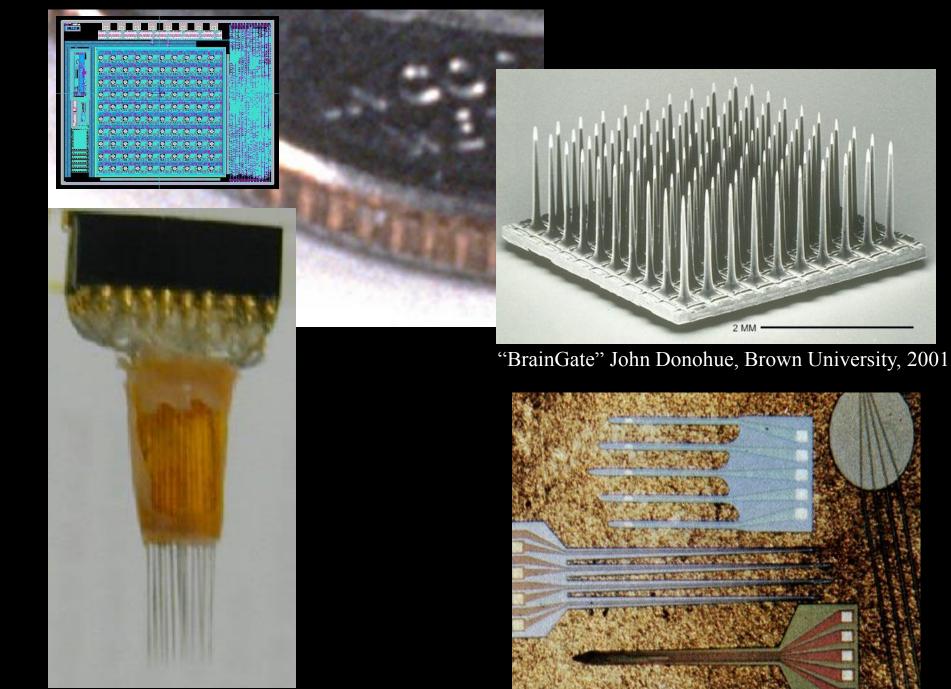
"The Future is not what it used to be!"



- Yogi Berra

# future

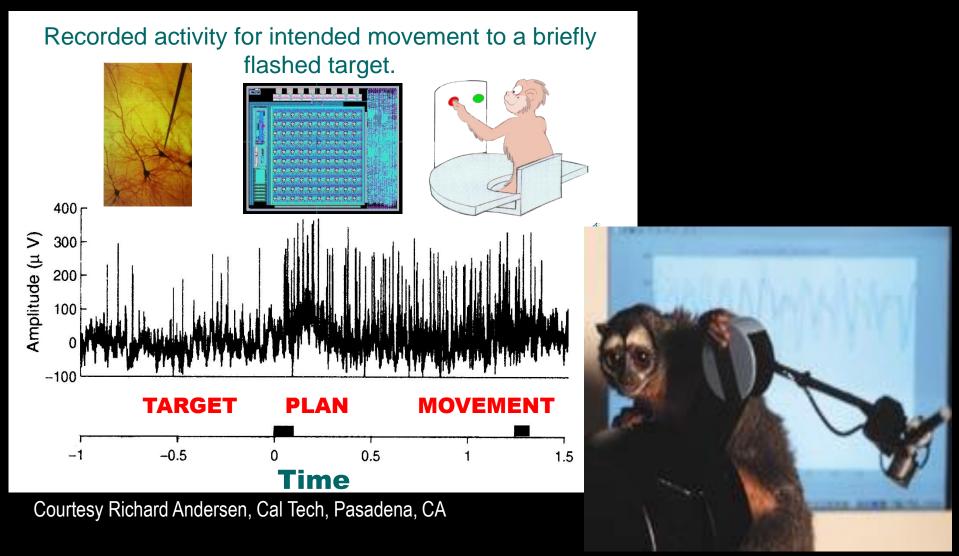
# echnologies



Richard Andersen, CalTech, 2003

Greg Kovacs. Stanford University, 1990

## Brain Machine Interface - Controlling motion with thoughts



Direct brain implant control of robot arm

## **B**rain Machine Interface – **C**ontrolling motion with thoughts



## **B**rain Machine Interface – **C**ontrolling motion with thoughts







Courtesy University of Hawaii 2008

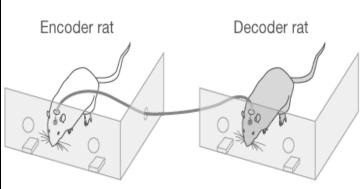


International weekly journal of science



February 28, 2013 DOI 10.038/srep01319





### A Brain-to-Brain Interface for Real-Time Sharing of Sensorimotor Information

Miguel Pais-Vieira<sup>1</sup>, Mikhail Lebedev<sup>1,4</sup>, Carolina Kunicki<sup>5</sup>, Jing Wang<sup>1</sup> \* & Miguel A. L. Nicolelis<sup>1,2,3,4,5</sup>

<sup>1</sup>Department of Neurobiology, Duke University, Durham, NC 27710, USA, <sup>2</sup>Department of Biomedical Engineering, Duke University, Durham, NC 27710, USA, <sup>3</sup>Department of Psychology and Neuroscience, Duke University, Durham, NC 27710, USA, <sup>4</sup>Duke Center for Neuroengineering, Duke University, Durham, NC 27710, USA, <sup>5</sup>Edmond and Lily Safra International Institute for Neuroscience of Natol (ELS-IINN), RN 59066-060, Natol, Brazil,

A brain-to-brain interface (BTBI) enabled a real-time transfer of behaviorally meaningful sensorimotor information between the brains of two rats. In this BTBI, an "encoder" rat performed sensorimotor tasks that required it to select from two choices of tactile or visual stimuli. While the encoder rat performed the task, samples of its cortical activity were transmitted to matching cortical areas of a "decoder" rat using intracortical microstimulation (ICMS). The decoder rat learned to make similar behavioral selections, guided solely by the information provided by the encoder rat's brain. These results demonstrated that a complex system was formed by coupling the animals' brains, suggesting that BTBIs can enable dyads or networks of animal's brains to exchange, process, and store information and, hence, serve as the basis for studies of novel types of social interaction and for biological computing devices.

n his seminal study on information transfer between biological organisms, Ralph Hartley wrote that "in any given communication the sender mentally selects a particular symbol and by some bodily motion, as his vocal mechanism, causes the receiver to be directed to that particular symbol". Brain-machine interfaces (BMIs) have emerged as a new paradigm that allows brain-derived information to control artificial actuators' and communicate the subject's motor intention to the outside world without the interference of the subject's body. For the past decade and a half, numerous studies have shown how brain-derived motor signals can be utilized to control the movements of a variety of mechanical, electronic and even virtual external devices³-6. Recently, intracortical microstimulation (ICMS) has been added to the classical BMI paradigm to allow artificial sensory feedback signals²-8, generated by these brain-controlled actuators, to be delivered back to the subject's brain simultaneously with the extraction of cortical motor commands<sup>9,10</sup>.

In the present study, we took the BMI approach to a new direction altogether and tested whether it could be employed to establish a new artificial communication channel between animals; one capable of transmitting behaviorally relevant sensorimotor information in real-time between two brains that, for all purposes, would from now on act together towards the fulfillment of a particular behavioral task. Previously, we have reported that specific motor<sup>11,12</sup> and sensory parameters<sup>15,14</sup> can be extracted from populations of cortical neurons using linear or nonlinear decoders in real-time. Here, we tested the hypothesis that a similar decoding performed by a "recipient brain" was sufficient to guide behavioral responses in sensorimotor tasks, therefore constituting a Brain-to-Brain Interface (BTBI)<sup>15</sup> (Figure 1). To test this hypothesis, we conducted three experiments in which different patterns of cortical sensorimotor signals, coding a particular behavioral response, were recorded in one rat (heretofore named the "encoder" rat) and then transmitted directly to the brain of another animal (i.e. the "decoder" rat), via intra-cortical microstimulation (ICMS). All BTBI experiments described below were conducted in awake, behaving rats chronically implanted with cortical microelectrode arrays capable of both neuronal ensemble recordings and intracortical microstimulation. We demonstrated that pairs of rats could cooperate through a BTBI to achieve a common behavioral goal.

#### Results

In our training paradigm, animals learned basic elements of the tasks prior to participating in any BTBI experiments. First, prospective encoder rats were trained to respond to either tactile or visual stimuli until they reached 95% correct trials accuracy. Meanwhile, decoder rats were trained to become proficient while receiving ICMS as a stimulus. A train of ICMS pulses instructed the animal to select one of the levers/nose pokes, whereas a single ICMS pulse instructed a response to the other option. Decoder rats reached a  $78.77\% \pm 2.1$  correct trials

# Replacing Human Body Parts

### **Intelligent Prostheses**







a) Rheo Bionic knee Ossur, Reyknavik, Iceland



b) C-leg Otto Bock, Minneapolis, MN

### Tissue Engineering



Artificial Ear



Liver Scaffolding



**Artificial Blood Vessel** 

# rgans which have been grown synthetically

Dozens of biotech companies and university labs are developing ways to replace or regenerate failed body parts. Here are a few of the projects:



Bone-growth factors or stem cells are inserted into a porous material cut to a specific shape, creating new jaws or limbs. A product that creates shinbones is in clinical trials.

COMPANIES: Creative Biomolecules, Orquest, Sulzer Orthopedics Biologics, Genetics Institute Osiris Therapeutics, Regeneron,



#### SKIN

Organogenesis' Apligraf. a human-skin equivalent, is the first engineered body part to win FDA approval. initially for leg

ulcers. Other skins are in the works for foot ulcers and

COMPANIES: Organogenesis. Ad-vanced Tissue Sciences. Integra LifeSciences, LifeCell, Ortec International,



#### **PANCREAS**

Insulin-manufacturing cells are harvested from pigs, encapsulated in membranes, and injected into the abdomen. The method has been tested in animals and could be in human trials in two years.

COMPANIES: BioHybrid Technologies, Neocrin, Circe



#### HEART VALVES, ARTERIES, AND VEINS

A 10-year initiative to build a heart has just started. Genetically engineered proteins have been successfully used to regrow blood vessels.

COMPANIES: Organogenesis, Advanced Tissue Sciences, Genetech, LifeCell, Reprogenesis,

DATA: BUSINESS WEEK, DRUG & MARKET DEVELOPMENT REPORTS



Proteins called aguaporins that allow cells to secrete water are used to recreate

saliva glands damaged by disease successful in mice.

COMPANIES: None yet.



#### URINARY TRACT

Cartilage cells are taken from the patient, packed into a tiny matrix, and injected into

the weakened ureter, where they bulk up the tissue walls to prevent urinary backup and incontinence. The method is in late-phase clinical tri-





#### LADDER

Doctors at Children's Hospital in Boston have grown bladders from skin cells and implanted them in sheep.

They are about to try the same process on a patient

COMPANIES: Reprogenesis.



#### CARTILAGE

A product is already on the market that regrows knee cartilage. A chest has been grown for a boy and a human

ear on a mouse.

COMPANIES: Genzyme Tissue, Biomatrix, Integra LifeSciences, Advanced Tissue Sciences, ReGen Biologics, Osiris Therapeutics



#### TEETH

Enamel matrix proteins are used to fill cavities. It works in dogs; human trials are a few years away.



#### BREAST

In preclinical studies, several companies have been able to create a cosmetic nipple by

inserting a ball of cartilage. Researchers are now trying to grow a whole cosmetic breast.

COMPANIES: Reprogenesis, Integra LifeSciences.



#### LIVER

A spongy membrane is built up and then seeded with liver cells. Organs the size of a dime

have been grown, but a full-size liver could take 10 years due to its complexity.

**COMPANIES:** Advanced Tissue Sciences, Human Organ Sciences, Organogenesis,

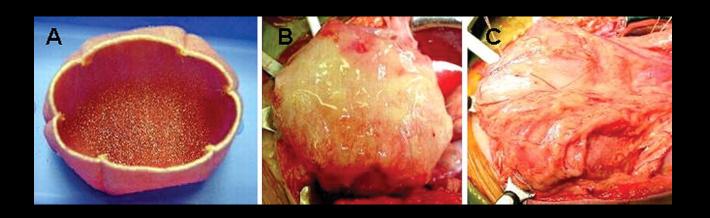


Scientists are in-vestigating nerve-growth factors, inject-

ing them at the site of damage to encourage regeneration or seeding them along biodegradable filaments and implanting them. Rats have been made to walk again.

COMPANIES: Acorda, Regeneron, CytoTherapeutics, Guilford Pharmaceuticals.

# Tissue-engineered Urinary Bladder





Anthony Atala, MD

Pediatric patients n = 12 10 year follow up

End of year 1 all 12 survived, no rejection (no meds)

11/12 spontaneous return bladder control

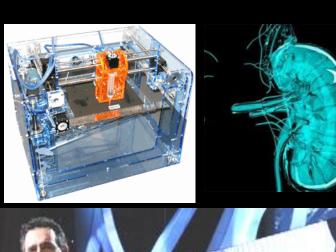
End of year 2 All had complete bladder control

End of year 10 All remained normal & healthy - no rejections

<u>Atala A, Bauer SB, Soker S, Yoo JJ, Retik AB</u>. Tissue-engineered autologous bladders for patients needing cystoplasty. <u>Lancet.</u> 2006 Apr 15;367(9518):1241-6. Atala A. Br Med Bull 2011;97:81-104

Courtesy: Anthony Atala, MD Wake Forest Institute of Regenerative Medicine, 2013

# 3-D Printing (Stereo-lithography) The Future of Surgery

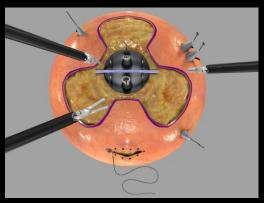


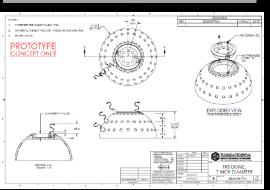




# 3-D Printing (Stereo-lithography)

### Parts for the FRS psychomotor skills







Makerbot Replicator



Physical Dome



Parts for Dome

CAD/CAM model

## Genetically Re-engineering Food & Drugs







Posted on: 27 Jun 2011, 08:43 PM

#### **Test tube-burger coming soon**

London: Coming soon, the world's first test-tube hamburger, say scientists. A team at Maastricht University in the Netherlands claims that the first such laboratory-made burger could be a year away. It will have meat grown from stem cells, paving the way for eating meat without animals being slaughtered.

The Scientists are currently developing the burger which will be grown from 10,000 stem cells extracted from cattle, which are then multiply more than a billion times to produce muscle tissue similar to beef. The product is called "in vitro" meat

Prof Mark Post, who is leading the team, was quoted as saying, "I don't see any way you could rely on old-fashioned livestock in the coming decades. In vitro meat will be the only choice left."

A colleague of Prof Post said, "When we are eating a hamburger we don't think, 'I'm eating a dead cow'. And when people are already far from what they eat, it's not too hard to see them





#### **Tobacco Plants Make HIV Antibody**

For the first time, a plant-produced antibody gets the green light for clinical trials in the United Kingdom.

By Cristina Luiggi | July 21, 2011

Last month, a monoclonal antibody produced in the leaves of tobacco plants entered phase I clinical trials in the United Kingdom. The antibody, known as P2G12, recognizes an HIV surface protein and is expected to help stop the transmission of the virus, although it has never been tested in humans.

This is the first plant-produced antibody to be cleared for clinical trials by the Medicines and Healthcare Products Agency Producing the antibody using tobacco plants grown in a greenhouse in Germany is 10 to 100 times cheaper than using conventional methods employing bacteria or mammalian cells, *Smart Planet* reports

"Monoclonal antibodies can be made in plants to the same quality as those made using existing conventional production systems," Professor Julian Ma from St George's University, London and joint coordinator of the project, told

"That is something many people did not believe could be achieved."

Floss DM, Sack M, Stadlmann J, Rademacher T, Scheller J, Stöger E, Fischer R, Conrad U.. <u>Biochemical and functional characterization of anti-HIV</u> <u>antibody-ELP fusion proteins from transgenic plants.</u> **Plant** Biotechnol J. 2008 May;6(4):379-91.

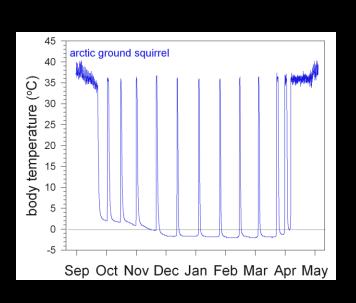
Prof. Mark Post, Maastricht University Netherlands, 2011

# Suspended Animation (Auto-anesthesia – FRAMR)

Institute of Arctic Biology's Toolik Field Station, Alaska's North Slope

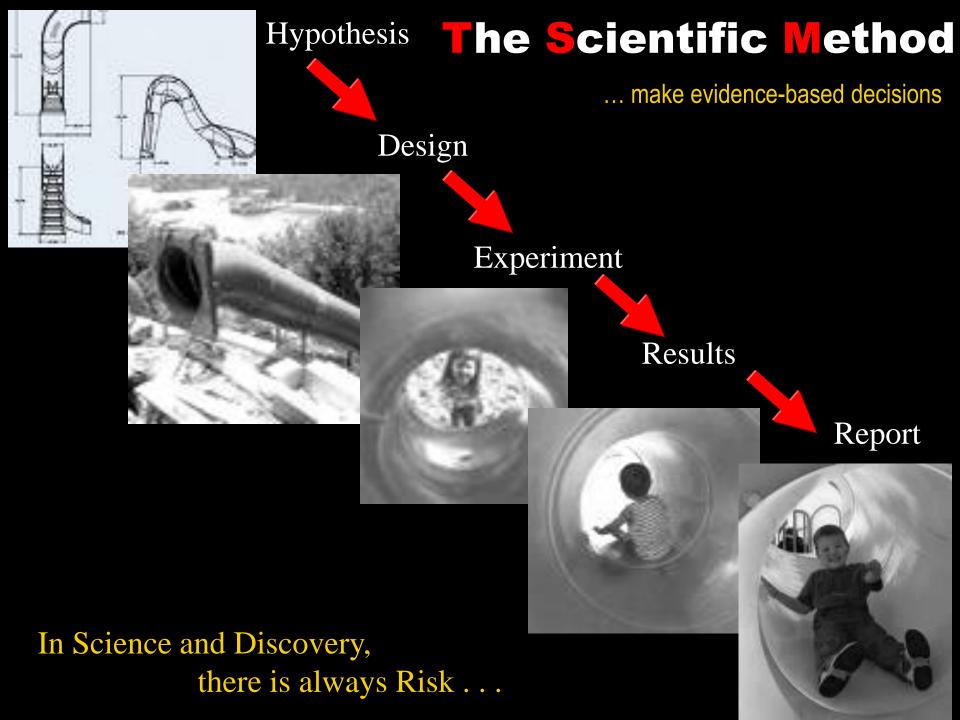






	active	hibernating
heart rate (beats/min)	300	3
resp. rate (breaths/min)	150	<1
body temp.	37°C	-2°C
gene function	ongoing	transcription and translation suppressed
metabolic rate (mlO <sub>2</sub> /g/h)	0.5	0.01 (2%)





# Be careful of unintended consequences

Experience is the name everyone gives to their mistakes - Oscar Wilde

The only thing more dangerous than trying too hard and failing . . . . . is not trying hard enough



# The Moral Dilemma

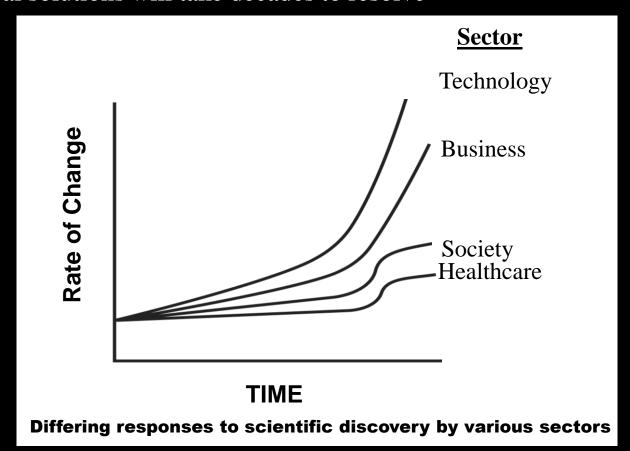
Technology is Neutral - it is neither good or evil

It is up to us to breathe the moral and ethical life into these technologies

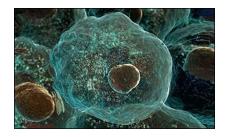
And then apply them with empathy and compassion for each and every patient

# Technologies Will Change the Future

- The rate of new discovery is accelerating exponentially
- The changes raise profound fundamental issues
- Moral and ethical solutions will take decades to resolve







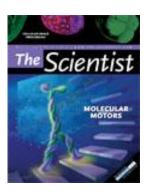
#### **Chinese Cloning Control Required**

Tuesday 16 April, 2002, 10:41 GMT 11:41 UK

Strict ethical guidelines are needed in China to calm public fears about new cell technologies such as cloning, the country's leading scientist said.

Professor Ching-Li Hu, the former deputy director of the World Health Organization, was speaking at the Seventh Human Genome Meeting in Shanghai. His call follows recent reports that Chinese scientists are making fast progress in these research fields.

One group in the Central South University in Changsa is said to be producing human embryo clones, while another team from the Sun Yat-sen University of Medical Sciences in Guangzhou is reported to have fused human and rabbit cells to make tissues for research.



# **Human embryos** cloned

February 12, 2004

South Korean team demonstrates cloning efficiency for humans similar to pigs, cattle | Thersa Tamkins

After outlandish claims, a few media circuses, and some near misses by legitimate researchers, a team of South Korean researchers reports the production of cloned human embryos. The findings, were released Wednesday (*Science*, DOI:10.1126 /science.1094515, February 12, 2004). Wook Suk Hwang and Shin Yong Moon of Seoul National University used somatic cell nuclear transfer to produce 30 human blastocysts and a single embryonic stem cell line; SCNT-hES-1. Using 242 oocytes and cumulus cells from 16 unpaid donors, the group achieved a cloning efficiency of 19 to 29%, on par with that seen in cattle (25%) and pigs (26%).

## Jeffery Steinberg, MD Fertility Institutes of Los Angeles

### **Genetically "designed" child**



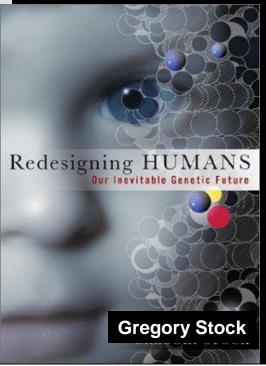
**Preimplantation Genetic Screening General Science: May 13, 2006** 

A British woman has become the first in th country to conceive a "designer baby" sele specifically to avoid an inherited cancer,

The woman, who was not identified, used controversial genetic screening <u>technology</u> to she does not pass on to her child the condition retinoblastoma, an hereditary form of eye cafrom which she suffers.

Doctors tested embryos created by the wo her partner using in-vitro fertilisation (IVF) if for the cancer gene. Only unaffected embryo implanted in her womb, the newspaper said.

It suggested the woman's pregnancy would increase controversy over the procedure -- primplantation genetic diagnosis (PGD) -- becaritics say it involves destroying otherwise hembryos whose conditions are treatable.





# Five "designer babies" created for stem cell harvest

Five healthy babies have been born to provide stem cells for siblings with serious non-heritable conditions. This is the first time "savoir siblings" have been created to treat children whose condition is not genetic, says the medical team. The five babies were born after a technique called preimplantation genetic diagnosis (PGD) was used to test embryos for a tissue type match to the ailing siblings, reports the team, led by Anver Kuliev at the Reproductive Genetics Institute in Chicago, US. The aim in these cases was to provide stem cells for transplantation to children who are suffering from leukaemia "Unlawful and unethical" However, the use of this technology to

Science Vol 315: 1723-25, Mar 2007



# **Emergence of Novel Color Vision in Mice Engineered to Express Human Cone Photo-pigment**

Changes in the genes encoding sensory recptor proteins are an essential step in

the evolution of new sensory capacities "new sensory capacities". In primates, trichromatic color vision evolved aftre changes in x chromosome linked photopigment genes.

Heterogous mouse females human L pigments showed ennanced long-wavelength sensitivity and chromatic discrimination. An inherent plasticity in the mammalian visual system thus permits emergence

# **Extending Longevity**



A strain of mice that have lived . . .

... more than three normal lifespans

Should humans live 200 years?



April 14, 2004

#### Life extension

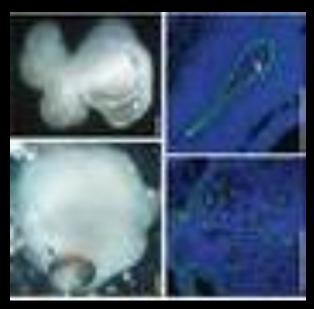
Life extension consists of attempts to extend human life beyond the natural lifespan. So far none has been proven successful in humans.

Several aging mechanisms are known, and antiaging therapies aim to correct one or more of these:

Dr. Leonard Hayflick discovered that mammalian cells divide only a fixed number of times. This "Hayflick limit" was later proven to be caused by telomeres on the ends of chromosomes that shorten with each cell-division. When the telomeres are gone, the DNA can no longer be copied, and cell division ceases. In 2001, experimenters at Geron Corp. lengthened the telomeres of senescent mammalian cells by introducing telomerase to them. They then became youthful cells. Sex and some stem cells regenerate the telomeres by two mechanisms: Telomerase, and ALT (alternative lengthening of telomeres). At least one form of progeria (atypical accelerated aging) is caused by premature telomeric shortening. In 2001, research showed that naturally occurring stem cells must sometimes extend their telomeres, because some stem cells in middle-aged humans had anomalously long telomeres.

# **Growing Human Brains: The First Steps**





## Cerebral organoids model human brain development and microcephaly

Lancaster MA, Renner M, Vartin CA, Wenzel D Bicknell L Hurles M, Homfray T, Penninger JM, Jackson A, Knoblich J

University of Vienna, Austria August 29, 2013



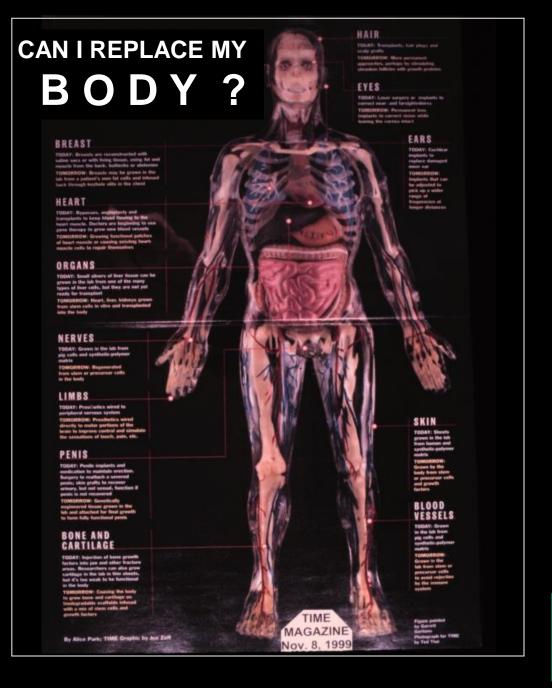
#### **Abstract**

The complexity of the human brain has made it difficult to study many brain disorders in model organisms, highlighting the need for an *in vitro* model of human brain development. Here we have developed a human pluripotent stem cell-derived three-dimensional organoid culture system, termed cerebral organoids, that develop various discrete, although interdependent, brain regions. These include a cerebral cortex containing progenitor populations that organize and produce mature cortical neuron subtypes.

Furthermore, cerebral organoids are shown to recapitulate features of human cortical development, namely characteristic progenitor zone organization with abundant outer radial glial stem cells.

Finally, we use RNA interference and patient-specific induced pluripotent stem cells to model microcephaly, a disorder that has been difficult to recapitulate in mice.

We demonstrate premature neuronal differentiation in patient organoids, a defect that could help to explain the disease phenotype. Together, these data show that three-dimensional organoids can recapitulate development and disease even in this most complex human tissue.



Artificial organs

**Smart Prostheses** 

Genetic engineering

Regeneration

If I replace 95% of my body . . .

... Am I still "human"?

Should there be replacement "parts" for astronauts?

## **Moral and Ethical Issues**

# Raised by Technological Success will take DECADES of debate

Summary of Examples

Should we do research in areas we may not be able to control? (eg, genetics, cloning, nanobots, intelligent machines?)

Will prolonging life result in more disease in the overall population

Can we change medicine from treatment to prevention of disease

In defeating diseases, will technology change a human into a combination of man and machine - what does it mean to be "human"

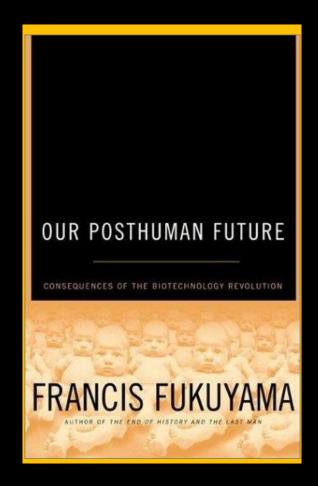
How will we decide who gets the technology, especially in 3rd World

## The Ultimate Ethical Question?

For the first time in history,
there walks upon this planet,
a species so powerful,
that it can control its own evolution,
at its own time of choosing ...

... homo sapiens.

Who will be the next "created" species?





Do Robots Dream? http://depts.washington.edu/biointel