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IBE 2008 Annual Meeting
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A Horror Story!

Editor, Art Johnson

Once upon a time there was a microbe that lived on the skin of humans. Its favorite place to reside was in the warm, humid environment of the nostrils, an environment that it shared with many other microbes of other species. The microbe of which I speak would have liked to have multiplied in number so that it could have this warm, cozy place all to itself, but the other microbes had the same idea, so they all coexisted in an uneasy equilibrium. This arrangement suited them all, because they each had their fair share of space, but, if one microbe moved just a little bit, there followed a melee of jostling to claim the empty territory. Jabbing and elbowing at each other kept them all on guard and gave none an advantage. No microbe dared sleep lest other microbes push him out of the way to claim his space. And so they remained alert, and it kept them busy and tired them, but it was the best they could do.

This constant competition for advantage made all these microbes opportunistic. Should there be a new territory, or a weakened competitor microbe, or a change in the environment more to the liking of one microbe compared to the others, and "Shazam!," that microbe would transform quickly into Capt. Marvel microbe and would take over the joint. In most cases, the human who supplied the nose would never notice. At worst he would sniffle a little more than normal until the balance was restored.

On occasion, however, one of the more dangerous and aggressive microbes would find itself with a rare chance to have some fun. It may have been a cut or skin abrasion, or it may have been a weakened human immune system. Whatever it was, this particular microbe, with its skills sharpened by constant microbial competition over the years, would go crazy. It would grow and multiply in numbers until there were so many they were beyond counting. They were all family and they were all intent on making the most of the situation.

If you get a whole bunch of brothers and sisters working together, then they can do marvelous things. What these microbes could do would be to control their own environment; baking, and making, and staking their collective claim to this new space. Each helped the others, and soon they could become unstoppable. Of course, this did no good for the human upon which they were growing.

So other humans stepped in. Humans are a proud people, and they do not like to admit defeat to a bunch of lowly microbes, no matter how well organized the microbes are. These other humans spied on microbes originally in competition with the deadly microbes and learned their secrets. They learned that one tactic the competitive microbes used was chemical warfare: they produced biochemicals that could kill microbes on contact.

It didn't take these other humans long before they duplicated these chemicals, and they patented them, and they called them "antibiotics." If the competitive

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Symbiotix Management Strategies Now Serving IBE

IBE recently selected Symbiotix Management Strategies (SMS) to serve as its association management company. SMS staff will maintain IBE's headquarters, execute board directives, and provide administrative oversight for the organization's financial, membership, website, and meeting management initiatives.

SMS, founded in 2007, is a specialized firm that uses a network of professionals and a shared-resource model to provide highly specialized, cost-effective professional services for associations and professional societies.

SMS has appointed **Sarah Clements** to serve as the association director for IBE. In this role, she is responsible for overall staff supervision, financial management, committee support, project coordination, creative services and website management. SMS has also appointed **Stephanie Czuhajewski** to serve as IBE's membership director and **Brian Doty** to serve as IBE's director of meetings.

"We are honored to have the opportunity to serve IBE and its members," said Clements. "We believe in IBE's mission and we are committed to providing above-and-beyond service that will advance IBE's goals."

For more information about SMS, visit www.symstrategies.com.

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microbes had known all this, they would have objected to human use of their innovations and hired lawyers to argue their cases. But, as luck would have it, lawyers don't listen to microbes, especially ones in their noses who can't afford retainers.

So, these other humans used these antibiotics against the runaway deadly microbes. Yikes! They were very effective. They killed every microbe in sight—the deadly ones as well as all others. The crisis was over and life went back to normal.

But wait! Lurking in a far corner somewhere was a sinister deadly microbe who had somehow avoided deadly contact with the antibiotic. He survived, and he vowed to get even. So, he went to his lab and cooked up a potion. In his mind was a vision of all his brothers and sisters who had been caught unawares by the antibiotic attack and had succumbed to the deadly chemical onslaught. This thought gave him the will to find the antidote.

If the antibiotic strategy was the only weapon used by the competitive microbes, then they would not have been very competitive at all. There were many such tactics used and they were very successful because they acted as one-two-three punches. One would not be very effective but three might knock out a neighbor microbe.

Unfortunately, the humans did not appreciate this fact, and so relied exclusively on this one chemical punch. And, for a while, this punch continued to be an effective weapon for humans against microbes not to their liking. All too soon, however, the microbes found out how to thwart human intentions. Some developed tougher skins; others changed their habits of hanging out together; still others put on rain coats to keep the deadly biochemicals at bay.

And, when this happened, the humans noticed, and sought other poisons deadly to microbes. The pattern repeated itself over and over: poison discovered, poison used, poison effective for a while, and poison overcome by the microbes.

Eventually, the microbes developed the skills to play this game very well, and considered it to be a challenge to test their mettle. They became so good at it that, for each and every new poison discovered by humans, it took the microbes less and less time to deal with it.

Fortunately, most of the microbes inhabiting the warm, cozy recesses of humans were not particularly dangerous, and so did not draw attention to themselves. When they overcame the challenges thrust upon them by their human hosts, they merely played among themselves or caused a few sniffles, or maybe even produced a few extra vitamins for their human. They were hardly noticed at all by the human.

There were, however, some microbes that liked to cause trouble. When just children, they played malicious pranks, and one prank led to another until they joined gangs and fought with each other and with their neighbors. They painted graffiti on their tenement walls and damaged anything that looked good. They littered in all the open spaces, for they cared not for order and cleanliness. They disdained authority. What they didn't destroy, they stole, and sold for cash. They learned how to make drugs and to use them in bad ways. These were *bad* microbes, and humans soon became aware of their ill natures, and the dangers they posed to the human sense of order and health.

When humans tried to subdue these bad microbes with their antibiotic poisons, they found that they were no longer effective. There was hardly anything that humans could do to beat back these ruffians, and the humans began to be afraid. Some humans even panicked, and cried, and threw up their hands and sought help from the authorities. The newspapers and TV and radio began to call these "flesh-eating microbes," and this caused even more hysteria among the humans who envisioned painful and horrible images of their flesh dropping away upon the ground while the microbes laughed at the expense of their human hosts.

The humans had one more devastating weapon in their arsenal. This was a doomsday weapon developed for the ultimate purpose of destroying all life should the need ever arise. These substances the humans called "disinfectants," and no creature had ever survived being doused with a disinfectant.

So, authoritative humans suggested that disinfectants be used to destroy all the bad microbes in places where they lived. They called for disinfecting hospitals, and locker rooms, and homes wherever these flesh-eating microbes were likely to live.

And so the people were relieved. Disinfection would save the day; disinfection would solve the problem. They relaxed.

But there were two lessons that humans still had not learned. First, microbes and all life is resilient, and when a single weapon is pointed at them, they can duck and avoid being shot. Disinfectants had been used for many years by humans in their homes, in their soaps, in their toilet-bowl cleaners, in their refrigerators, in their deodorants, and in their mouthwashes. The obsessions that people had with cleanliness threatened to make disinfectants just as ineffective as antibiotics. Overuse leads to uselessness. Any microbes not killed by a disinfectant could come back and show the rest how to survive the attack. Any microbe not killed by a disinfectant would find fertile ground not occupied by any other living thing upon which to grow and reproduce.

The second lesson not learned is that these battles against horrible microbes are not waged alone. Humans have always had help from the natives—other microbes that also want to overcome the bad bugs. There has always been a civil war among microbes, and humans have chosen sides based upon the effects these microbes have upon humans. Using disinfectants knocks out human allies as well as human enemies. And so, it is hard to see anything but a temporary victory for humans if they haven't learned these two lessons.

There is no absolute level of safety in the world of biology. There will always be disease and death, because this is how competition works. While humans can move the balance toward their favor, they can't escape the fact that they are still biological creatures subject to many of the same rules and limitations governing all others. And that may be the biggest lesson still to be learned.

Mark R. Riley,
The University of Arizona

Introducing

Journal of Biological Engineering

Biological Engineering is a new and unique discipline that encompasses a wide range of engineering theory and practice connected to and derived from biology. This emerging science-based engineering discipline and related applications are experiencing rapid growth. To nurture and foster this growth, IBE has contracted with BioMed Central to develop a new publication, the *Journal of Biological Engineering* (*JBE*). Our goal in publishing *JBE* is to provide a forum for topics that address the foundational questions that unify all applications of biological engineering. *JBE* can be accessed at: www.jbioleng.org/home/.

One of the reasons for launching *JBE* at this time is that the field is sufficiently mature that higher level discussions can be made amongst practioners to define the foundational core concepts, express the current breadth of the field, and to connect developments from disparate application areas which share a fundamental foundation. An appropriate approach to foster the development of biological engineering is to identify underlying phenomena that govern the behavior of biological and biologically derived systems regardless of scale, environment, or application. This is best brought together through an open access publication in which any interested party can gain full access.

Role and Scope of JBE

JBE manuscripts will integrate engineering with life sciences to generate new quantitative methods, models, and information. Peer reviewed articles will encompass cutting edge research that fully integrates fundamental inquiry, quantitative analysis, and translational design. *JBE* provides a home for the continuum from biological information science, molecules and cells, organismal studies, product formation, wastes and remediation, and education. A description of the broader context of the work and how it connects to other areas must be incorporated into each manuscript.

Topical areas include (but are not be limited to):

- Synthetic biology and cellular design
- Engineering of devices that interface at the biomolecular, cellular, and organismal levels
- Bioproduction and bioproduct engineering,
- Ecological and environmental engineering, and
- Biological engineering education and the biodesign process.

JBE invites manuscript submissions that address theoretical and applied approaches to design, optimize, and use biological systems ranging in scale from molecules, cells, organisms, to ecosystems. *JBE* will incorporate advances in mathematical sciences (including computational and statistical methods) enabling the development of biological engineering, biological engineering design inspired by or in the context of biology, and designs for all scales that include nanometer to ecosystem levels.

We have lofty goals for *JBE*; we aim for this to become the preferred home for cutting edge research in biological engineering. To provide a platform to unify the field it is necessary that all manuscripts in *JBE* not only be of high quality, but that they also present a discussion of how the work advances biological engineering, drives new development and application, or connects disparate areas in new ways. This can be accomplished in many ways and likely will evolve in time. *JBE* also will be a home for educational advances in curriculum content and pedagogy at the undergraduate and graduate-levels.

To foster and nurture the development of biological engineering, we have launched this publication as an open access, online resource. Open access is an important tenet of biological engineering in that information not only is to be freely accessible to the scientific community, but it must be available to the public at large.

Open Access

The publisher, BioMed Central, is an open access provider, where the authors retain copyright of their manuscript. There are no subscription fees or fees to access articles once published; instead articles are freely available immediately

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upon publication. *Anyone, anywhere* can access the publications (as long as they have internet access). To offset the cost of publication authors pay an article-processing charge (APC). Authors who do not have sufficient funds to pay the APC may request a discretionary full or partial waiver from BioMed Central.

Manuscripts published by JBE are assigned a DOI®, or Digital Object Identifier, and will be referenced in PubMed (referencing will take a few months for the first few articles). For example, the first published article in JBE has DOI:10.1186/1754-1611-1-1; the second article has DOI:10.1186/1754-1611-1-2. The DOI® is for labeling content in the digital domain. DOI® names provide current information, including where they (or information about them) can be found on the Internet. Information about a digital object may change over time, including where to find it, but its DOI® name will not change.

Using DO®I names as identifiers simplifies managing intellectual property in a networked environment and allows construction of automated services search processes. Most importantly, this provides a means for permanence of the articles published by JBE. To learn more about DOI® names, see http://www.doi.org/.

Summary data on the initial JBE manuscripts (as of 12/11/07)

Submissions	30
Acceptances	10
Rejections	8
Withdrawn	1
In review	11

Average time to decision: 72 days

Most accessed articles (as of 12/11/07)

1. 1107 Accesses (unique downloads)
Editorial Introducing Journal of Biological Engineering, Mark R Riley, *Journal of Biological Engineering* 2007, 1:1 (10 October 2007) http://www.jbioleng.org/content/pdf/1754-1611-1-1.pdf

2. 536 Accesses
Research Role of reaction kinetics and mass transport in glucose sensing with nanopillar array electrodes, Venkataramani Anandan, Xiaoling Yang, Euihyeon Kim, Yeswanth L Rao, Guigen Zhang, *Journal of Biological Engineering* 2007, 1:5 (10 October 2007) http://www.jbioleng.org/content/pdf/1754-1611-1-5.pdf

3. 527 Accesses
Research Electrospun nitrocellulose and nylon: Design and fabrication of novel high performance platforms for protein blotting applications, Ashley E Manis, James R Bowman, Gary L Bowlin, David G Simpson, *Journal of Biological Engineering* 2007, 1:2 (10 October 2007) http://www.jbioleng.org/content/pdf/1754-1611-1-2.pdf

4. 430 Accesses
Research Amyloglucosidase enzymatic reactivity inside lipid vesicles, Mian Li, Michael J Hanford, Jin-Woo Kim, Tonya L Peeples, *Journal of Biological Engineering* 2007, 1:4 (10 October 2007) http://www.jbioleng.org/content/pdf/1754-1611-1-4.pdf

5. 427 Accesses
Research Development of a Cryptosporidium oocyst assay using an automated fiber optic-based biosensor, Marianne F Kramer, Graham Vesey, Natasha L Look, Ben R Herbert, Joyce M Simpson-Stroot, Daniel V Lim, *Journal of Biological Engineering* 2007, 1:3 (10 October 2007) http://www.jbioleng.org/content/pdf/1754-1611-1-3.pdf

6. 344 Accesses
Letters to the Editor Engineering education in the wake of hurricane Katrina, Marybeth Lima, *Journal of Biological Engineering* 2007, 1:6 (10 October 2007) http://www.jbioleng.org/content/pdf/1754-1611-1-6.pdf

7. 200 Accesses
Methodology Rapid single step subcloning procedure by combined action of type II and type IIs endonucleases with ligase, Tobias Fromme, Martin Klingenspor, *Journal of Biological Engineering* 2007, 1:7 (26 November 2007) http://www.jbioleng.org/content/pdf/1754-1611-1-7.pdf

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The last 2 on this list are provisional pdf files which in the coming days will be converted to type set manuscripts as shown for the first 5.

Total manuscript accesses in November:	1,482
Total manuscript accesses in October:	1,739
Total manuscript accesses	3,221

Clearly, JBE articles are being viewed. The last article on the list above was accessed 123 times in its first 5 days!

A useful aspect of the online publication is the automated links. When one accesses a manuscript "Full Text", the reference list is fully active. That is, to find out more about a reference click on the reference number in the text which takes you to the reference list which is hyperlinked and will direct you to the original material. I have found this to be quite useful and hope you will also.

How to submit a manuscript
Visit: http://www.jbioleng.org/manuscript/ for instructions and the style guide.
Questions or problems: email editor@ibe.org.

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For questions, please email us at: editor@ibe.org.

Honorable Mention Bioethics Essay
2007 IBE Meeting

The Ethics of Human Embryonic Stem Cell Research

Elana Fisher, Cornell University

Cancer, Alzheimer's, Parkinson's, heart disease, and arthritis are some of the most common diseases that are affecting members of society today. Research is ongoing to not only find the causes of these diseases, but hopefully to cure them. Yet much of this research is under scrutiny; specifically it is limited by government funding as well as opposed by many people due to its involvement in the controversial area of human embryonic stem cell research.

Research using human embryonic stem cells is important, particularly to the field of Biological Engineering, because stem cells have the potential to provide us with information on human development and the generation of new cells and tissues for cell-based therapies. Yet, this research has brought up many ethical issues due to its destruction of human embryos during the process of retrieving the stem cells. According to the National Institute of Health, "embryonic stem cells are derived from embryos that develop from eggs that have been fertilized in vitro," and these embryos are "typically four or five days old and are a hollow microscopic ball of cells called a blastocyst." The stem cells are located within the inner cells mass of the blastocyst.

While the potential use of human embryonic stem cells in research is promising, there is a central argument surrounding their use. The ethical controversy poses the question; does the potential for stem cell research to relieve the pain and suffering of others outweigh the destruction of human embryos? This question can be broken down into many areas, yet it ultimately is surrounded by the issue that deals with the moral standing of human embryos. This argument centers on another important question; when does a human life begin? According to the President's Council on Bioethics, in the paper entitled *Monitoring Stem Cell Research*, "under normal circumstances we regard all born human beings (from newborns through adults) as possessing equal moral worth and meriting equal legal protection." The ethical issues of human embryonic stem cell research center around defining the similarities and differences between human embryos and live-born human individuals, which lies in the biological cases for continuity or discontinuity through the fertilization process. Some people argue that from the point of fertilization until the death of that human, there are no lines that can be drawn between embryos and adults, yet others argue that there is a distinct point (or sum of points) of discontinuity that signifies the moral distinction between the embryonic and adult stages of development.

The supporters of the case for biological continuity (the people opposing the use of human embryos to further stem cell research) believe that the human embryo is a living human at its earliest stage of development. This biological continuity is believed because under the appropriate environmental conditions, the embryo has the ability to develop and become a human fetus and then ultimately a human infant. The ethical argument is then that the human embryo deserves the same legal rights and protections as a human being, because each human being started out as an embryo.

The continuity case is also based on the argument of genetic individuality. Sperm and eggs do not have the potential of becoming adults on their own, but when the sperm enters the egg, the oocyte is activated. This represents the official combining of the genetic material, which means a new genome has been formed. Genomes represent the unique identity of organisms, which therefore, according to supporters of the continuity case, means that at its earliest stage of development the embryo has the same identity as the human being that it has the potential of becoming. While the supporters of the continuity argument recognize the fact that the embryos used in stem cell research are frozen and stored outside of the body, they believe that scientists should not ignore their potential for human life.

In contrast to the ethical argument opposing human embryonic stem cell research, those that support the efforts in finding cures for diseases through the use of embryos justify their "side" with important biological and moral discontinuities that occur in the early stages of human development. The case for discontinuity is based on three points surrounding the primitive streak, the nervous system, and the human form.

The primitive streak is the most widely used argument for the discontinuity case. According to the President's Council on Bioethics, in the paper entitled *Monitoring Stem Cell Research*, the primitive streak is the "earliest visible 'structure' that defines the region of the embryo along which the vertebral column will form. The primitive streak generally appears around the 14th day after the first cellular division." Being that the stem cells are removed from a human embryo that is typically only four or five days old, according to many biologists, the individuality of the human being has not yet been achieved since the embryo has not reached the primitive streak in its stages of human development.

Another argument in favor of the use of human embryos in stem cell research deals with the formation of the nervous system. Many people believe that the nervous system defines humanity because the brain and nerves control a human being's activities and sensations (i.e. the sensation of pain). Therefore a justification for the destruction of embryos is that an ethical boundary is not crossed because the embryo has not yet developed the capacity for feeling pain.

The last argument used in supporting the discontinuity case deals with the human form. Many people feel that the

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Honorable Mention Bioethics Essay
2007 IBE Meeting

Ethics of Human Experimentation

Gwen Ellen Owens, Cornell University

Advances in biological engineering are changing the world. By modifying nature- altering genes, developing new energy sources, combating diseases- we are at the forefront of human progress. However, with each daily innovation, each breathtaking increase in engineering capacity and biological knowledge, also comes the growing necessity for society to reexamine how far *should* we go. One of our most pressing concerns within this issue is the ethical treatment of our fellow man. Clinical trials to test the efficacy of novel drugs, to determine of pathogenesis of human diseases, and to elucidate basic principles of human physiology all necessarily involve human experimentation. As professional engineers, we must carefully consider the implications of human experimentation. On a surface level, we must be perpetually aware of how we treat humans in experiments, of how we would like to be treated. On a deeper level, in an era where many commodities are expendable, we must consider how we value the individual human rights versus potential good for society. Where must we draw the line between experimentation and irreparable harm: Altering human genes? Attempting to "grow" humans in artificial facilities? Endangering, or even destroying, human life in order to advance biological knowledge?

Dating back to the early 1700s, the modern era of human experimentation began with human vaccination trials. Edward Jenner, the celebrated inventor of the smallpox vaccine, first tested his theories by infecting his son and neighborhood children with cowpox. Far more serious exploitation of human subjects occurred prominently during World War II; after these war crimes were brought to international attention during the "Doctor's Trials," a series of codes and declarations were enacted to ensure that these blatant violations of human rights would never occur again. Less than thirty years later, one of the most notorious human experiments in U.S. history was exposed by the press: the "Tuskegee Syphilis Study." A group of U.S. researchers had been examining the natural course of untreated syphilis in 150 poor African American men. After penicillin was shown to stop the disease, the researchers actively prevented their subjects from obtaining access to the cure in order to continue their research. By the termination of the study, more than 125 men had died directly of syphilis or of related complications. The intense public backlash in response to this experiment led to the creation of the National Commission for the Protection of Human Subjects and Institutional Review Boards. The ethical tenents adopted by this commission remain the standard considerations for human research today: respect for persons, beneficence, and justice .

Respect for persons means that the researcher has a responsibility to inform participants in human trials of all risks involved, and that their participation must be voluntary. While informed consent has been institutionalized to simply signing off on a form, the need for informed consent today is much broader. One sobering violation occurred during U.S. military experiments to assess vulnerability to biological warfare attack. Clouds of fluorescent aerosol were sprayed over the cities of Minneapolis and St. Louis, and bacteria were disseminated by the army throughout the New York City subway system. During these experiments, the human test populations were not only completely unaware of the risks of inhaled aerosols and bacteria, but were unaware they had been part of a trial at all. Daily human interactions with products of biological engineering- genetically engineered foods, drugs and vaccines produced by bacteria, animal byproducts containing artificial growth hormones- also may involve some risk. These breakthrough products and technologies have generated greater yields, higher quality products, and lowered production costs. However, because the long-term effects these products may have on people is unknown, their use may also may be considered "human experimentation." In order to show respect for persons, we have a responsibility to clearly inform the public about these products, and to ensure that purchase and use is voluntary. Individuals, rather than researchers, should be allowed to determine what level of risk he or she believes is permissible, regardless of the benefits of these products.

Another ethical criteria that researchers must carefully consider is *beneficence*, or "doing good." Double-blinded, placebo-controlled clinical trials are the "gold standard" in biomedicine to provide credible, scientific proof of the efficacy of a new treatment. Controlled clinical trials have created a formal system where researchers must demonstrate that a new treatment is significantly better than a placebo or control, and has produced of thousands of safe, effective drugs. However, when AZT, the single-most effective AIDS treatment to date, began Phase II clinical trials, there arose a bitter conflict between individual good versus benefit to the trial and society at large. In order to conclusively show that AZT was an effective treatment for AIDS, the researchers needed to show, with statistical significance, that there were more deaths in the placebo group than in the group receiving active treatment: patients needed to die for the trial to be successful. It is apparent, therefore, that biomedical researchers have a moral obligation to consider to what extent human health must be protected. Who decides what risks a patient can assume? When does "doing good" for a group outweigh "doing good" for an individual? And does protection of participants extend to preventing their death? *continued on pg. 8*

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embryo must take on a human form before we can consider protecting it as we do with human beings, and at the stage in which the embryo is used in research, the human form has not yet been achieved.

The debate between the continuity and discontinuity of a human embryo during the fertilization process is the leading ethical issue that surrounds the progression of human embryonic stem cell research. While the potential for curing diseases through the differentiation of these embryonic stem cells is shown, the ethical issue of whether or not scientists should use human embryos cannot be ignored. In combating this ethical issue altogether, scientists have found ways to extract human stem cells from adults, as well as from umbilical cords; yet these alternative locations do not provide the same ease for obtaining stem cells that the human embryo offers.

In general though, biological engineering has led to much advancement in science and technology, and whether or not people agree with the ethical issues surrounding these advancements, it cannot be denied that biological engineering has the potential to lead to medical practices which reduce the pain and suffering of millions of human beings.

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A final ethical principle to evaluate is that of *justice*. Development of treatments and devicing particular to groups such as children, certain ethnic minorities, and people with rare diseases are far less profitable than blockbuster drugs that treat depression or mild hypertension. Hence, development of treatments and devicing for these groups has been neglected in the past, while companies have focus instead on products that will generate large profits. Additionally, to be just, people who are placed at risk in clinical trials should also share in the benefits obtained from the trials. For example, several ongoing trials in the Third World have been examining the vertical transmission of AIDS from infected mothers to children. Although there is currently an effective treatment to reduce the rate of this transmission, none of the women are provided access to the treatment. Reminiscent of the Tuskegee Syphilis Study, investigators here have continued to study the natural course of untreated transmission from mother to infant. Rather than merely executing the wishes of the free market, biological engineers should take responsibility for developing treatments and products for under-represented populations, and ensuring that participants in trials are given access to the treatments they aided in developing.

The ethical treatment of human subjects requires evaluation of the conflicts between profit and social good, between benefit for individuals and society, and between developing novel technologies and potential risk. When engaging in human research, there must be less focus on strict experimental results, and more on human subjects engaged in the tests; people must never become a means to an end. Although at times difficult and complex, acting ethically when designing or conducting human experiments combines two of the most critical questions of humanity: how to treat our fellow man and how to modify nature for a brighter future for our species.

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Solid-Mechanics Modeling of Ocular Lenses

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When light rays enter the eye, they are first bent by the refractive cornea and further adjusted by the transparent ocular lens, then pass through the vitreous fluid, before finally reaching the retina, and giving rising to electric signals to the brain. Upon stimulation, the brain triggers the ciliary muscles to either relax or contract, fine-tuning the lens curvature and thus focusing the image on the retina. A complete coverage of the complexity of the intriguing optical, mechanical, physical, chemical, biological, and electrical interplay is obviously beyond the scope of this short article. Rather, we aim to capture the essence of the coupled mechanical and optical behaviors of the ocular lens and how it is governed by the microstructure and micromechanics of the lens constituents, namely, the lens fibers and the lens capsular membrane.

When a lens is relaxed with the maximum natural curvature, the eye focuses on near objects. When the ciliary muscle relaxes, the zonules attached to the lens equator stretch the lens, and the focal length increases, bringing distant objects into focus. The focusing of vision is achieved by such "accommodation mechanics". The simplest microstructure of a typical lens is a thin membrane encapsulating multilayers of arch-like cells that extend from the anterior pole of the optical axis to the posterior pole. The force of the cilary body transmitted by the zonules, causes capsular deformation resulting in altered refractive power. The mechanical properties of the lens materials need to be pliable enough to be molded by the capsular membrane. It is therefore essential to characterize the mechanical and viscoelastic behavior of the macroscopic lens, the micron-thick capsule, and fibers made up of the cell wall components and the fluid proteins (known as crytallins) within each fiber.

To implement these studies, porcine samples from 6-8 month old pigs have been obtained from a nearby Illinois abattoir. Mechanical and optical devices have been designed and constructed to monitor *in-vitro* the simultaneous external load, lens deformation, and the subsequent change in focal length. Materials parameters of the centimeter wide lens such as elastic modulus, viscoelastic storage and loss moduli have been extracted by analyzing the measurements, using pertinent solid mechanics models. These properties will then be related to orchestrated deformation of lens capsule / fibers. The multi-scaling measurements and modeling will ultimately enhance a fundamental understanding of how the ocular lens works, and how various patho-physiological phenomena occur as a result of aging. This work is expected to significantly impact the development of surgical treatments for cataracts, and the presbyopia that affects virtually all of us requiring the use of bifocals by the age of 40-45. Current cataract surgery involves removing the opaque lens contents and replacing it with a preformed lens that possesses a fixed focal length. The focus of the studies at Washington University is the development of polymeric hydrogels as materials for accommodative intraocular lenses, using a surgical procedure previously developed where a sub-millimeter hole is made in the lens capsule to remove the lens contents and replace them with an injected polymer. Should the injected gel exceed the physical strength of the ciliary muscle, accommodation becomes formidable. Mechanical characterization is thus indispensable.

Mechanical measurements have been performed using various techniques. Micro- and nano-force testers with sensitivity down to submicro-Newton and submicron resolution (MTS Nano-Bionix, Texture Technologies Corp TA-XTPlus microforce tester,) have been used to compress a lens in either quasi-static or cyclic loading configurations. Empirical relationships among the applied load, plate separation, and contact radius at the plate-lens interface allow the deduction of materials properties. At Washington University we have designed and fabricated a machine analog of the ciliary body to stretch the sample lens along the equator resulting in an even and natural biaxial stress. An optical device has also been constructed to simultaneously monitor the focal length. These macro-scale measurements allow the opto-mechanical properties of the composite lens to be characterized.

In addition, to probe the micro-scale ultrathin and fragile capsule, new mechanical testing methods are being developed. A lens capsule membrane is surgically removed from a sample lens and is clamped between two rubber O-rings. An external load is then applied to the freestanding membrane center via a cylinder with a spherical cap to prevent piercing in a "shaft-loaded blister" configuration. The load versus displacement relation, which is cubic in mathematical modeling, thus yields an indication of the film stiffness. Again both quasi-static and cyclic loading are possible to extract the apparent linear elastic and time-dependent viscoelastic behaviors.

Dyes have lately been used to stain individual fibers. When a lens sample is compressed between two parallel plates, fiber and suture deformation can be observed in-situ using a simple reflection microscope, or, in a more sophisticated manner, using a confocal microscope capable of mapping the 3-dimensional deformed geometry. With micro- to macro- scale

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solid and liquid properties readily available, a preliminary multi-scaling model can thus be constructed. To add to the complexity, the form factor, or the geometrical arrangement of the fibers and the enclosing capsule, also plays a significant role in the concerted lens deformation. Combining with the biochemical and biomedical information accumulated over the last decades, mechanical characterization of lenses from different age groups and races provides a comprehensive understanding of natural accommodation and patho-physiology (such as presbyopia).

This characterization scheme can also be adopted for phenotypic specifications. For instance, individual fibers and epithelial stem cells for the utero-mouse under external mechanical forces may be imaged with injected fluorescent proteins. Elimination of fiber-fiber adhesion molecules and consequential mechanical modifications allows one to determine the effects of inter-fiber interactions during accommodation. Other interesting ophthalmic features can also be probed. For instance, the distinct point suture in birds (e.g. chickens), the line suture in amphibian (e.g. frogs), and the Y sutures in mammals (e.g. pigs and humans) can be mechanically characterized and distinguished from one another. The scheme is also pertinent in developing biomedical treatments. The aforementioned prosthetic hydrogel is a good example where a combined mechanical and chemical optimization can be assessed that leads to improved products.

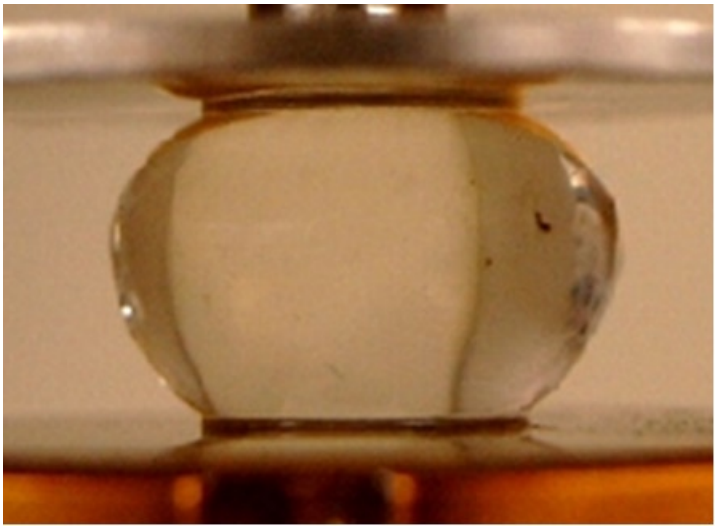

Figure 1. A porcine lens is compressed by two parallel plates.

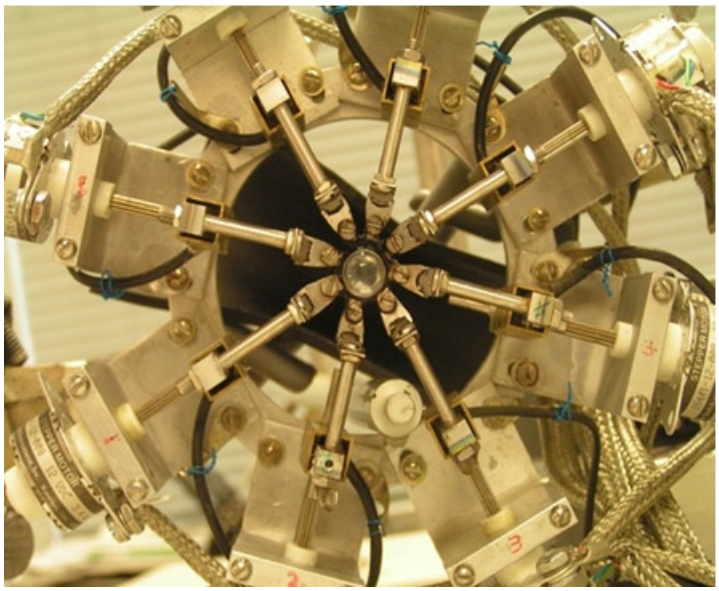

Figure 2. Eight-arm stretcher showing a porcine lens mounted by clamping the ciliary body

The Challenge and Opportunity of Reliability in Ecosystems

Malia Appleford

Ecological engineering, the creation of ecosystems to perform desired tasks, is pushing the boundaries both of our definition of engineering and of our engineering methodology. Fundamentally, engineering is the application of science for utility. However, for many years, engineering has more implied the precise design and control of technological systems. This has been an achievable goal where our understanding of the underlying science has likewise been precise—this is the realm of mechanical, structural, hydrological, and electrical engineering, and, increasingly, biomolecular engineering.

Ecological engineering presents a challenge, however, in that ecosystems are formed from complex interactions between both individuals of the same species and populations of different species. This complexity can make it difficult to predict the behavior of the system as a whole, let alone that of any subgroups within. Therefore, the engineered ecosystems that we use today are operated as a "black box." This includes newer applications such as constructed wetlands but also older systems we might not think of as part of ecological engineering like biological wastewater treatment facilities, composting, and even the whole of agriculture.

The design for these systems is typically based on empirically-determined properties of the system as a whole at a particular operational baseline. In treatment wetlands, we might design for a recommended retention time within the wetland; retention time serves as an amalgamation of processes within the system. For composting, we might instead focus on controlling the carbon-to-nitrogen ratio and moisture content of the mixture.

This method of design, however, disregards a fundamental principle of ecology: dynamism. Although we may be able to control some of the external inputs into an engineered ecosystem—temperature, influent concentrations, etc.—the ecosystem itself is constantly changing, and therefore empirical properties also often change in unpredictable ways. Our classical engineering approach of precise design and control is therefore extremely difficult if not impossible under this scheme.

One particularly difficult question to answer is the reliability of engineered ecosystems. Understanding when and why an ecosystem fails is critical to our ability to design ecosystems, and is specially pressing when the failure of the system would be highly detrimental or even catastrophic. Ecosystem services may be targeted for a wide array of engineered functionality in systems including flood mitigation, surface water quality management, and carbon cycling, among many others. Take, for example, the proposed engineered ecosystem that would provide life support to a space exploration mission to Mars: Unlike our current missions to low Earth orbit, which are managed roughly like a camping trip (packing everything we need for a few days or weeks), a mission to Mars is of sufficient length that essentials like food, oxygen, and clean water must be produced on site. The ecosystem that is proposed uses a combination of biological and mechanical systems to provide life support to the crew, and, because there is no quick "abort-to-earth" option, failure of the system would result in a loss of the crew.

Traditionally, reliability of a system has been estimated through the combined reliability of each of the component parts of the system expressed as a probability of failure. Individual reliabilities for conventionally engineered systems have been fairly easy to determine through laboratory lifetime tests; one might run 100 engines of the same model to breakdown, for example. However, individual reliabilities are not so easy to come by for species, ecological consortia, or whole ecosystems. In addition, there are even times when obtaining experimental reliabilities of even mechanical system components is not practicable. For the Martian life support system, the monetary and time costs are too high for NASA to build and optimize a "test system." They rely, instead, on opinions from expert consultants and determinations of acceptable risk. Designers of most complex systems, however, will not have the time or expertise to build a suitable model. Therefore, we are searching for a simpler way to estimate the reliability of engineered ecosystems and other complex systems.

Because engineering is fundamentally applied science, our approach is to return to the base science of ecological engineering: ecology. Currently we are reviewing ecology literature for theoretical and empirical studies regarding complexity and reliability.

The discussion of the link between complexity and stability has been a major one in the field of ecology. In the 1950s, ecologists Robert MacArthur and Charles Elton both theorized that complexity of an ecosystem begets stability. Other researchers since have used computers to model food webs and have gained a progressively deeper understanding of stability in ecosystems. For example, there appears to be an optimum level of interactions among food web species—too many and the food web is unstable, too few and the system does not have adequate resiliency to survive in the face of external changes. The strength of these interactions also seems to be a critical variable—a majority of low strength interactions is necessary to maintain a food web. Furthermore, the present consensus is that higher levels of ecosystem complexity may cause food web instability, but increase the reliability of "ecosystem services," that is, the overall functions of the ecosys-

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tem. Along the way a fair number of numerical and qualitative metrics have been developed to describe the stability of an ecosystem. These include measures of biodiversity, thermodynamic efficiency, and food web interconnectance, among others. We hope to test whether any of these methods correctly predict the reliability of engineered ecosystems using data from basic engineered ecosystems such as chemostats or other biological reactors used in research and industry. Quantitative information and qualitative assessments of reliability from questionnaires will be sought. We seek a metric that can be applied to purely biological engineered ecosystems, and also to systems like the Mars life support system that also incorporate abiotic components, or "technoecosystems."

We believe that the intersection of biology and engineering is the most exciting area of technology development right now, but that it is crucial to learn how to manage the biological components in a way meaningful to engineers. However, we cannot approach this type of control from the traditional engineering mindset—to learn to manage the biological, we have to go back to the biological. By investigating how ecologists themselves have measured the functions of ecosystems, we hope to be able to take one step towards the goal of reliable design.

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