SUPER CELLS

BUILDING WITH BIOLOGY

TED

NINA TANDON
MITCHELL JOACHIM

Super Cells

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"The time for building with living cells has arrived.

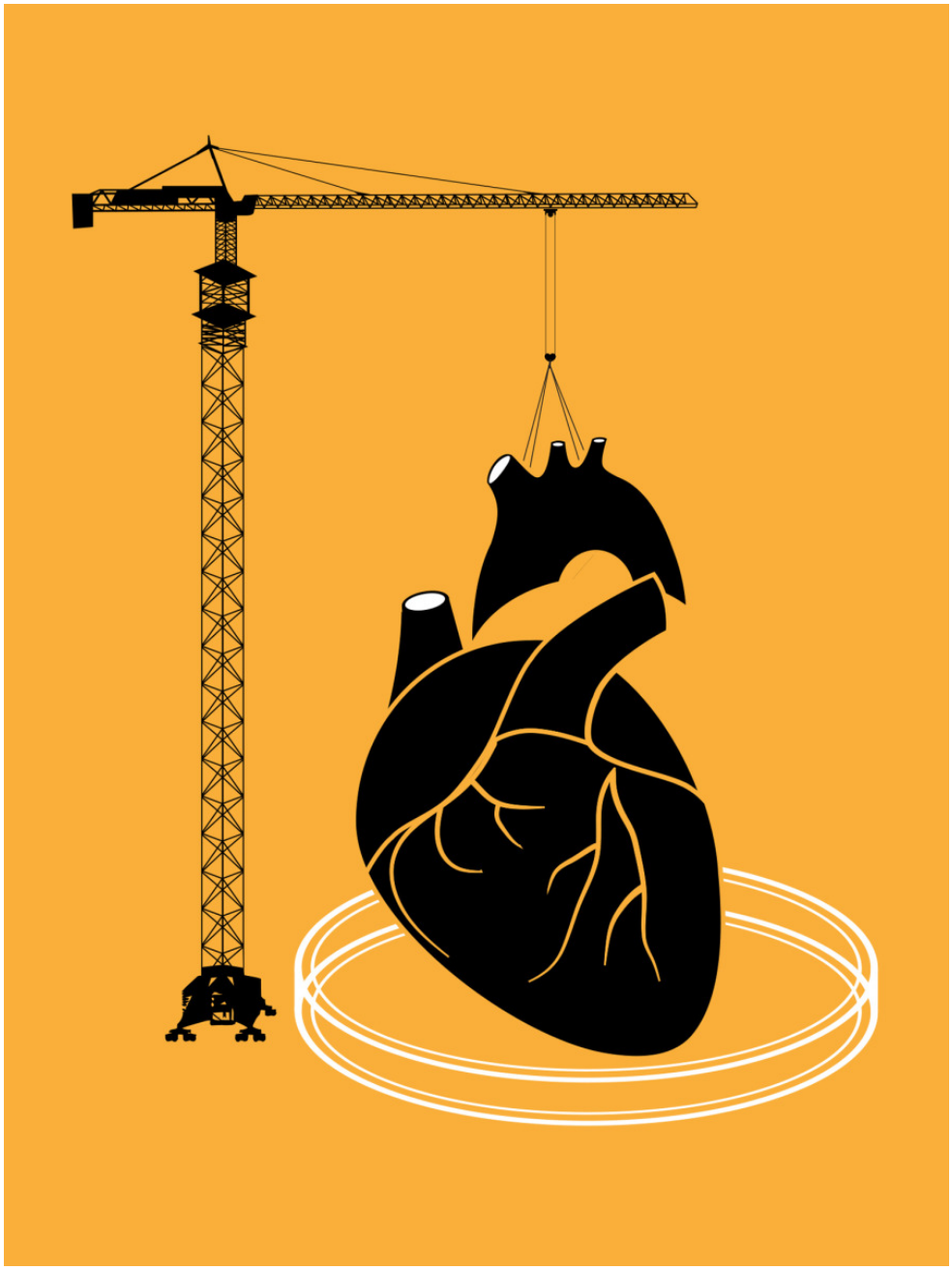
Dedication

From Nina:

To my three families: nuclear (especially my parents, Judi and Sanjiv), lab (especially my "lab mama," Gordana), and TED (especially Tom and Logan). And to James, who's in all three.

From Mitchell:

To my best friend and wife Melanie and two adorable daughters Mia and Maxxa.



Introduction

"Biology has a knack for using what works." —Seth Lloyd, physicist, MIT
"The opposite of nature is impossible." —Buckminster Fuller

Millennia ago, the materials of choice for designers and engineers were clay, stone, wood, and leather. Later we learned to harness the properties of iron and glass. Then we raised buildings and laid down railroads in steel. In the 20th century, we fell in love with plastic, forging from it everything from cups to telephones to medical devices.

Now we are at the cusp of exploring and exploiting a whole new substance, one so dramatically different from all others before it that it opens uncharted possibilities and challenges our very notion of what it means to build.

The main builders and workhorses within the robust, adaptable biological world are cells. These are the most basic structural and functional unit of all known living organisms, the smallest unit of life that is classifiable as a living thing: nature's building block. And yet, since the advent of agriculture, we've never really directly harnessed their power. In fact, it's been only in the last hundred years or so (starting when American biologist and anatomist Ross Granville Harrison first grew tissue explants in the lab) that we even began to culture cells themselves by mimicking the conditions in the body: bathing cells in balanced saline solutions containing nutrients, and controlling their environmental temperature and gas

composition, while keeping the cultures sterile. And although one might argue that beer makers have been harnessing yeast's cellular power for millennia, it's only in the last several decades that we've employed cells in industrial biomanufacturing processes for drugs and other molecules.

Besides the advances in tissue culture, a parallel history of discovery about DNA has also led us here. Within cells, genetic codes stored in DNA are regulated by genetic circuits, and investigations spanning the 20th and 21st centuries have been devoted to decoding and recombining elements of these codes. This quest has led us toward understanding basic biology, but also, increasingly, toward the goal of engineering new biological systems for the benefit of society (called "synthetic biology," a term coined in 1912 by French biologist Stéphane Leduc as "biologie synthétique").

The time of building with living cells has arrived.

Why are we, the authors, particularly excited about this? On the surface, our work appears dramatically different: Mitch designs ecological cities, while Nina is a tissue engineer who has grown living, beating heart tissue and now grows personalized bones for skeletal repair. But when we met in 2011 as TED fellows and began discussing our respective fields, we recognized that our disparate work — growing cities or growing living body parts — included some surprising similarities. We are both, for example, in the business of designing environments that are meant to protect and nurture living things, and even to foster certain activities. But at a deeper level, we realized that we both hold certain views that are considered a bit unconventional for our respective communities — in particular, our view that living systems, and specifically *cells*, could be considered a technological partner in our work. Nina views the cells as the "real engineers" for constructing living tissues, and Mitch has even taken steps toward growing buildings out of living trees and meat.

We are now witnessing a beautiful collision between the worlds of digital fabrication and biology. Digital fabrication (the act of using data to

represent spatial information) isn't new — the inkjet printer, after all, was first developed in the 19th century. But that rudimentary technology has recently spawned some dazzling successors. Beginning in the 1970s, inkjet printers that could reproduce digital files were first developed, and in the 1980s, printers were built that could deposit new materials in successive layers to create three-dimensional objects from digital files. In recent years, innovators have adapted 3-D printing technology to begin printing *living* materials along rationally designed templates.

What this means is that we are at last equipped to guide the growth of responsive, three-dimensional, living, patterned electrical-mechanical structures. And with this (albeit nascent) ability, we are poised to take a radical new approach to technology development and to tackle a broad range of challenges.

It's not farfetched to think that some of this novel work could take place in your own garage. These days, using eBay, Craigslist, and Kickstarter, you can realistically set up your own fully functional genetics lab with affordable, pre-owned, and/or cheap open-source equipment. Or you can use open-source instructions to print versions of expensive parts (e.g., printing a 3-D centrifuge attachment for a rotary tool, dubbed the "dremelfuge") on affordable new 3-D printers (such as the MakerBot). Or, if buying a printer's not your speed, you could hack apart your own printer to print cells for about $150. (It's been done! In winter 2013, a group of biohackers that meets at BioCurious, a community biology laboratory in Sunnyvale, California, published a do-it-yourself inkjet printer that can print living cells.)

This is only the tip of the iceberg; there is already a burgeoning community in the design space working with living materials. Suzanne Lee, fashion designer and founder of BioCouture, has grown "vegetable leather" using bacteria. Ginger Krieg-Dosier, founder and CEO of bioMASON, uses bacteria to grow bricks at room temperature through the process of calcite

precipitation, taking loose aggregate sand and using bacterial solution to harden the material. She earned a €500,000 prize in September 2013 from the Dutch Lottery to test this at the architectural scale. At Bath University, researchers are using bacteria to create self-healing concrete that would fill cracks and prevent decay. At the other end of the life cycle, artist Jae Rhim Lee is focused on decomposition; she's developing the Infinity Burial System, which uses a special strain of fungus to remediate the industrial toxins we store in our bodies, which leach into the earth after death.

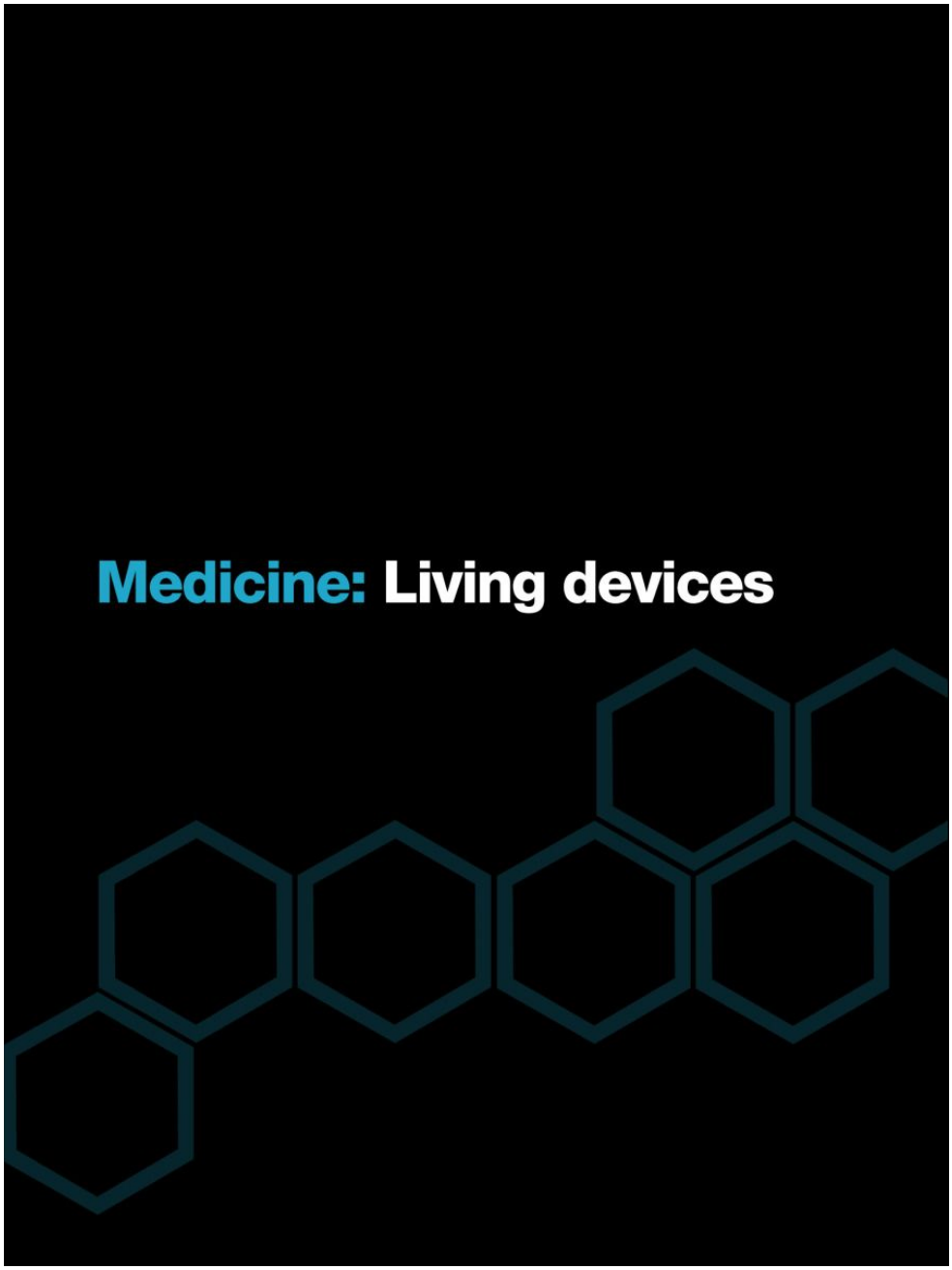
Imagine the possibilities: broken bridges that have the ability to self-heal, one-stop shops for human body parts that render organ donation obsolete, living looms spinning high-tech fabrics, PETA-friendly porterhouse steaks — smarter, more adaptive technologies may form our future arsenal as we confront the looming challenges of the modern day.

If the first industrial revolution was about mechanization of manual processes and the second about mass production, as we find ourselves coming up against challenges of deteriorating infrastructure, globalizing job markets, aging populations, resource shortages, and unpredictable disasters, we are heartened to realize that we are not alone in thinking that biology could be our perfect technological partner.

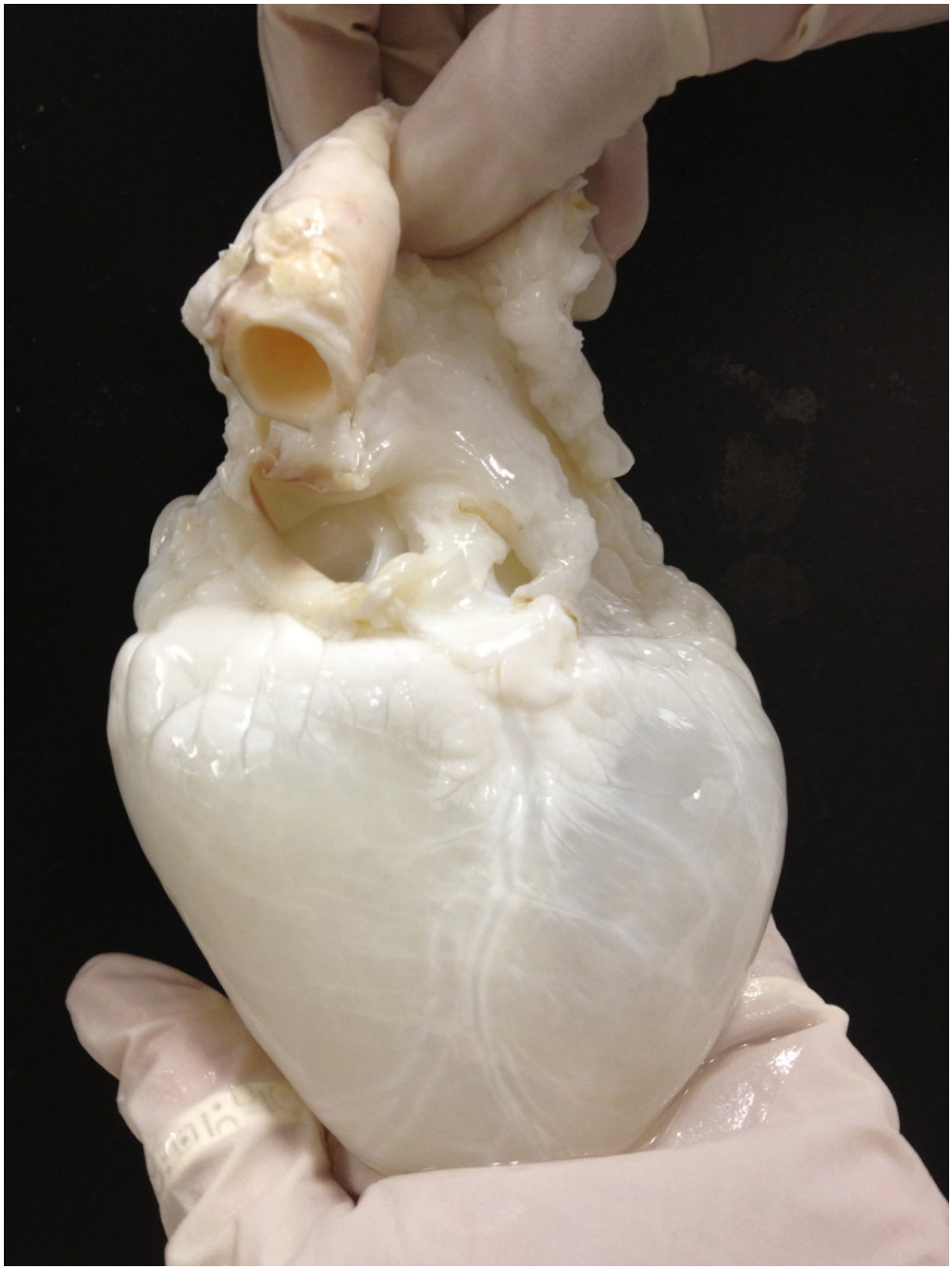
In this book, we have collected case studies from such disparate realms as design, medicine, and engineering to show what the world might look like if more of our technology were to be grown from living cells. We include our own work, in tissue engineering and architecture, as well as dazzling examples of using cells to grow textiles, art, entertainment, and even food.

Through these stories, you'll see that as the diverse fields of biology, design, and digital fabrication collide, we are poised to enter a more efficient, more natural technological revolution. The results are sure to change the way we live — and they may even change the way we think about life itself.

Medicine: Living devices



Scientists at the Wake Forest Institute for Regenerative Medicine are using 3-D printing technology to build organ and tissue scaffolds. Living cells added to the scaffolds then grow into their forms. The scaffolds made of synthetic polymers or hydrogels then biodegrade, leaving just the living material behind. Shown here are scaffolds for prototypes of a finger bone, an ear, and a kidney. All are experimental and not yet ready for patients. Image: Courtesy of Wake Forest University



This decellularized “ghost heart” can serve as a scaffold upon which to grow a working heart from human stem cells. Researchers at the Texas Heart Institute created it by stripping all the living cells from a pig heart with a soap solution, which bursts the cells and leaves only the protein structure behind. The scientists have successfully implanted tissue-engineered hearts into rats and pigs so far. They hope ultimately to create personalized human hearts and thus

relieve the shortage of donor organs. Image: Courtesy of RMR Labs, Texas Heart Institute

Medicine: Living devices

By Nina Tandon

Watch Nina Tandon's TED Talk here.

I have two colorblind sisters and a night-blind brother, so from a very early age I was aware that everyone sees the world quite differently. Certain activities presented an interesting challenge for us siblings to do as a group (roadside bingo, picking out prom shoes, distinguishing between lipstick and eye shadow), while other activities presented an issue about what could be done alone (driving at night). But this interesting mix of perspectives also taught me that the cells that form the very fabric of our being also mediate our experience of life. I understood that these cells, which might compose our eyes and also interpret the neural signals they produce, like any living object, are both miraculous and fallible. It was my first glimpse into biology as a technology.

I was captivated by many pursuits, from legal justice to teaching to sewing. But my parents encouraged me (actually, at the time it felt a little more like bullying) into engineering, because they felt that as a young woman who was good at math, I had an obligation to study it — there just weren't enough girls in STEM fields. So I enrolled at the Cooper Union, where I began studying digital logic and making little games out of electronics (my final project was a physical version of Whac-A-Mole using push buttons, LED lights, timers, and random-number generators). By the end of my freshman year, I was hooked. At an internship in London I began to explore the interaction of electrical systems with the body by building a theremin: an electronic musical instrument played not by touching it, but by waving your hands around its antenna and thereby interfering with its oscillating circuit.

I graduated with a degree in electrical engineering, but I remained fascinated by biology. Even after I went to work as a software engineer at a Bell Labs spinout called Avaya, I still took physiology classes at night at a local community college. The new parallels I saw between nature and the man-made inspired me; DNA, it seemed, was a lot like a hard drive, and the fibers of the nervous system look very much like telephone wires. I still remember the thrill of discovering that this analogy went deeper than what I could see, as I learned that the same equations governing the transmission of information along the transatlantic cable could be applied to transmission along nerve fibers. So I began graduate studies in bioelectrical engineering at MIT under Gordana Vunjak-Novakovic, a pioneer in the field of tissue engineering.

My studies showed me the resident electricity that had been discovered in the body at all stages: during embryonic development, in daily life, in wounds, and in diseases. The focus of my work was the heart, which I'd only recently learned was the body's largest source of bioelectricity, giving off signals more than 100 times stronger than the brain. My research centered on using electricity in tissue engineering, designing and building carefully controlled systems (called "bioreactors") to grow replacement parts for the human body. In order to coax heart cells into forming heart tissue in the lab, we needed to provide the cells with electrical signals to trick them into believing they were living inside a body.

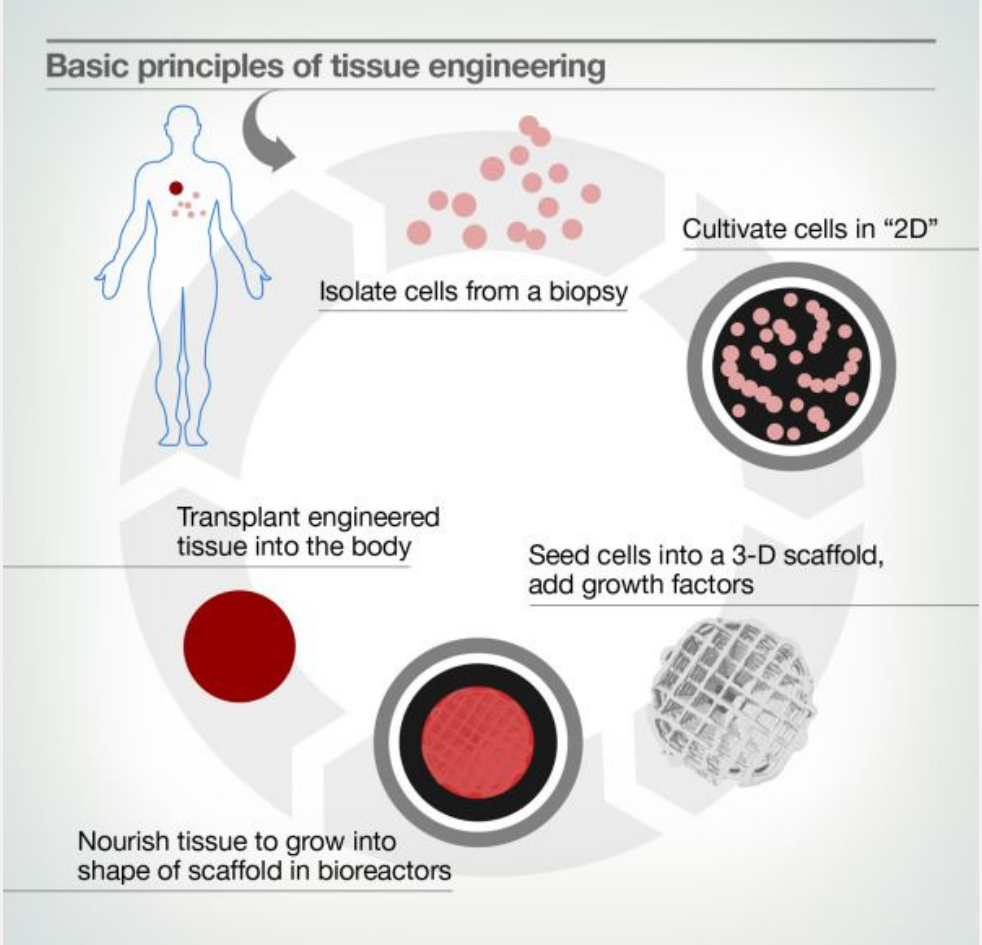
I remember the first time I grew heart tissues in the lab. At first they just looked like mini marshmallows, but after a couple more days, they began to dance in their dish. They were so amazing! I put them under the stereoscope and hooked them up to my stimulator circuit. As I peered down through the oculars, I turned the dial to increase the frequency — and they moved to the beat! I turned the dial the other way, and they slowed down. I'd built circuits before, but this was totally different. This was a piece of living

tissue, and somehow it was interacting with this box that was plugged into the wall.

Now I am cofounding a company called EpiBone to engineer living, personalized bones for skeletal reconstruction. My partners in this venture (which we joke is a sort of family business) are my PhD advisor and "lab mama" Gordana Vunjak-Novakovic, head of the Laboratory for Stem Cells and Tissue Engineering at Columbia University; Sidney Eisig, chair of oral-maxillofacial surgery at Columbia University; and several lab "siblings" of mine, including Sarindr Bhumaritana, Jon Bernhard, and Elisa Cimetta.

How do we grow custom bones? In short, we take CT scans from the patient to engineer a precise anatomical scaffold. Then we harvest cells from the patient, put them together with the scaffold in a bioreactor system, apply certain protocols (like the application of perfusion of fluid throughout the bone to provide mechanical forces to stimulate growth and the delivery of osteogenic cell culture medium), and in three to five weeks the cells mature into human bone.

Our procedure is now being validated in animal models. If we succeed, our bones will be not just the perfect fit, but also a perfect match for the recipient, because they'll be made from the patient's own cells. We believe products like these can revolutionize the treatment of bone defects, whether due to cancer, trauma, or congenital defects.



A poster candidate for such treatment would be the late Roger Ebert, who lost his jawbone due to cancer. The current gold standard treatment for such a loss is an autograft — cutting a piece of bone out of one part of the body and putting it in another. This leads to a whole host of issues, including multiple surgeries and, in Ebert's case, because surgeons cut bone out of his hip and shoulder, a limp for the rest of his life. And with pediatric cases, autografts may be even more difficult, as there's just not enough bone to go

around. But with our technology, we're hoping that, if someday you need new bone, you can grow your own.

People often ask me when engineered tissues will graduate from being a "science project" and actually begin helping real-life patients. The short answer is that it depends, because tissues that are mostly flat and composed of mostly one type of cell, such as human skin, have proven easier to grow than others (say, heart or liver) that incorporate more complex structures with multiple cell types and interact considerably with other organs. It's also important to remember that the field of tissue engineering is still quite young — it was only "officially" established about 25 years ago, at a conference in Lake Tahoe in 1988.

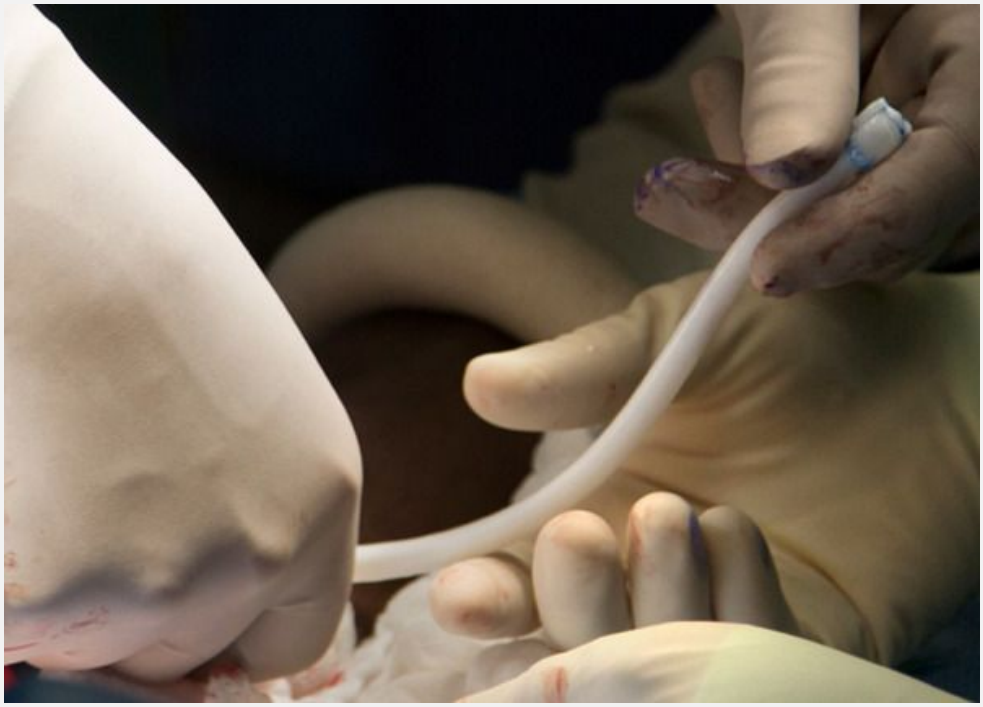
Among the early pioneers of tissue engineering is Wake Forest University's Anthony Atala. He and his team began working in 1990 to grow bladders from patients' own cells (sampled from muscle cells and the cells that line the bladder walls). In 1999, he implanted the first lab-grown bladder in a patient. Over the ensuing years, Atala proceeded carefully and accrued patients slowly, with long-term follow-ups, to best allow his team to modify and improve protocols. With his later implantations, he found improved bladder capacities and continence.

Atala and his colleagues admit that much work remains; restoration of physiologic contraction and voluntary control using tissue-engineered bladders still has yet to be demonstrated. Challenges center around properly aligning the muscle fibers, innervating the tissues, and vascularizing them after implantation.

To date, a few tissue-engineered products have made it to the clinic. Some use cell sources from donated tissues. Dermagraft and Apligraf, for example, are manufactured from human skin cells derived from newborn foreskins, and are used to help in the wound closure of diabetic foot ulcers of unrelated patients. Other products are instead based on harvesting and expanding cells from the patients themselves. Epicel, for instance, is a

permanent skin replacement product for patients with life-threatening burns, and Carticel is a cell-based treatment for large lesions in the cartilage.

In the pipeline of products still being tested is an exciting array of prospects. Researchers at Harald Ott's lab at Massachusetts General Hospital and Harvard University were able to regrow a kidney and then transplant it back — into a rat. Other ventures are further along in testing. Humacyte, for example, coming from the laboratory of Laura Niklason at Yale University, is producing investigational large- and small-diameter tubes grown from human cells. After fabrication, the tubes are stripped of cells (to prevent immune response). These may someday help patients in need of vascular repair or replacement, making invasive patient procedures, such as vein harvests, unnecessary.



Yale University's Laura Niklason and colleagues created this first engineered human artery to be implanted in a patient in the U.S. The artery was grown in the lab from human vascular smooth muscle cells and then decellularized. The surgery took place at Duke University in June 2013, on a patient with kidney failure who needed a vascular graft in order to undergo dialysis. ***Image: Courtesy of Duke University***

Atala's experience with engineered bladders hints at the broader challenges facing the field. The year 2013 marked the five-year anniversary of Paolo Macchiarini's implantation of the first tissue-engineered trachea (for an unnamed 30-year-old Colombian woman suffering from tuberculosis). In 2013 we also saw the implantation of the youngest person

to receive an artificial windpipe: an angelic, pigtailed South Korean toddler, Hannah, born with tracheal agenesis, a rare and usually fatal birth defect. However, despite functional integrity of the implanted grafts, both patients faced significant setbacks. According to her case report, the Colombian woman still has scarring and has gone through 14 different stents to widen her narrowing windpipe. And Hannah, sadly, passed away just three months after her surgery, due to lung complications. Both cases point to the need to understand not just how to engineer better grafts, but how to better integrate the tissues into complex bodies that may be compromised due to disease or prior treatments.

It will likely be decades before we see anything resembling the "body shop" of replacement parts that we often hear about being just around the corner. In the meantime, however, many in my field of tissue engineering believe there is plenty of imminent innovation that can disrupt the practice of medicine.

For instance, while the "spare parts" that researchers are growing from human cells are not yet perfect enough to replace our own body parts, they may still serve as valuable drug-testing platforms, mimicking our bodies better than the animals on which the pharmaceutical industry currently tests drugs. Want to know if a new drug will soothe an irritated nerve without provoking a negative biological reaction? Grow replica tissue and try it! Researchers are already making progress in growing models of conditions such as Lou Gherig's disease (see Kevin Eggan's lab at Harvard) or Long QT syndrome, a genetic cardiac arrhythmia (see Lior Gepstein's lab at the Israel Institute of Technology). A similar technique may also be used for more personalized therapies, as in the case of cancer, where researchers are working to develop three-dimensional models of tumors in the lab. And innovative ways of using lab mice for studying and treating human tumors hint at how lab-grown tumors might be used in the future.

Two such examples are “mouse avatars,” in which mice are implanted with patient tumor samples for subsequent use in drug efficacy studies, and “co-clinical trials,” in which genetically engineered mouse models are used to guide therapy in an ongoing, concurrent human patient trial. We can imagine researchers replacing “mouse avatars” with bioreactors and lab-grown tissues to try a range of treatments on them, as well as developing targeted therapies based on the genetic profile of the tumor and testing those.

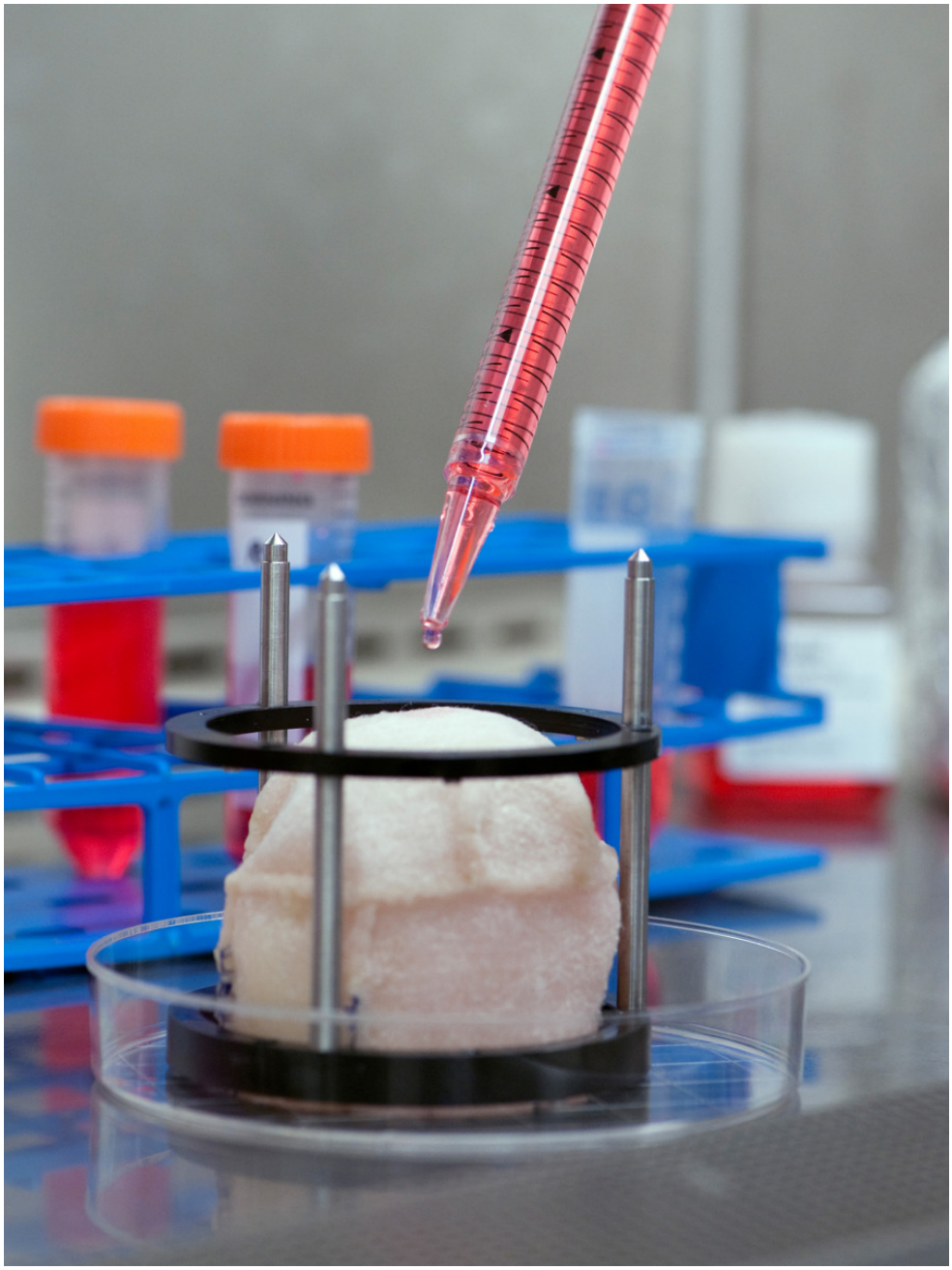
I hope these innovations revolutionize drug screening by helping us discover and evaluate drugs faster, more cheaply, and more effectively, without having to test as many animals or people. The current drug-screening process costs billions of dollars per drug and takes more than 10 years, and even after all that testing, drugs can still act unpredictably and may actually hurt people. Clearly a new method is needed.

We’ll face weighty ethical questions as we pursue these aims. We are blurring the borders of what one considers to be the “real” body. Could patients be exposed to unknown risks (e.g. cancer) post-implantation? In the future of brain tissue engineering, could we potentially engineer truly sentient beings in the dish? People often ask me questions about ownership and the connection of people to their cells that remain alive after biopsy, and which may be used to grow organs outside of themselves. People wonder about what will happen as we continue to add more and more organ systems to the same culture systems. As work continues with growing micro-scale “organoids” on microchips, such as the lung, heart, and intestine (such “organs-on-chips” are being developed at the Wyss Institute, some wonder how sentient (if at all) the systems are. And as progress continues toward growing multiple “organoids” on the same chips (so-called “human-on-chip” applications), some wonder just where making a model of a human ends, and where technologies such as those in the movie *The Island* — where full human clones were grown for organ harvesting —

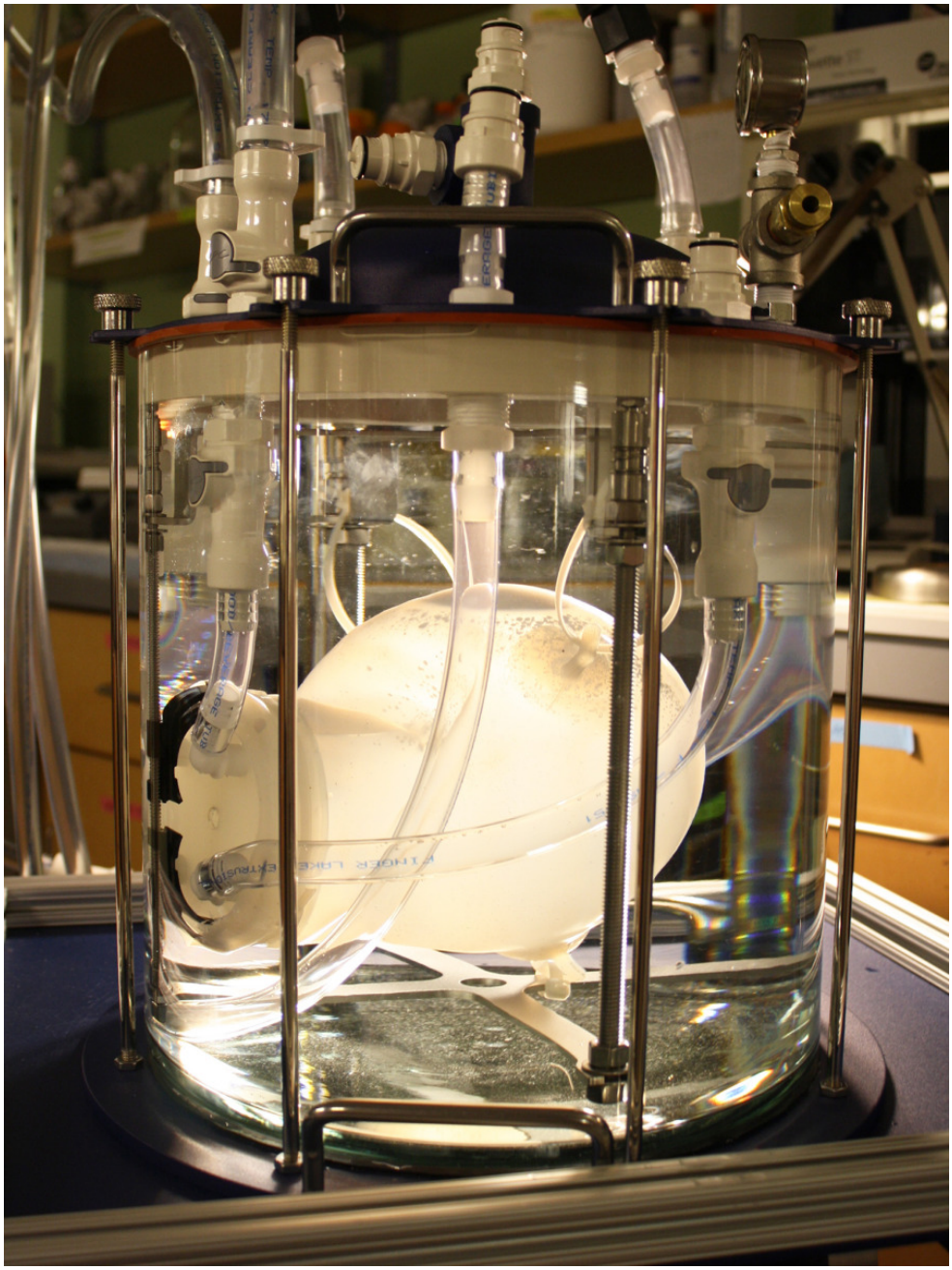
begin. And if we succeed at extending the human lifespan, how will that affect sustainability on the planet? (See the TED.com conversation I hosted about these issues.)

In the last century, the advent of cell culture, organ transplantation, and the development of artificial implants gave birth to the fields of biomaterials and tissue engineering, pushing the development of regulations around informed consent and clinical trials. Current research in tissue engineering and stem-cell science will undoubtedly continue to push the thinking of bioethicists, regulators, clinicians, and regular citizens. After all, we are all likely to be patients, or at least friends and family of patients, sometime in the future. At a minimum, we'll need new regulations to help the FDA cope with tissue-engineering therapies. (The FDA currently regulates medical products under the separate categories of devices, biologics, and drugs, which becomes problematic when "devices" may be alive.)

Nonetheless, I see us striding toward a future that unlocks the power of stem cells to restore the body, leading to living implants, better therapies with higher certainty, and less animal testing. By joining forces with the body's own innate technology, we might guide it to heal.

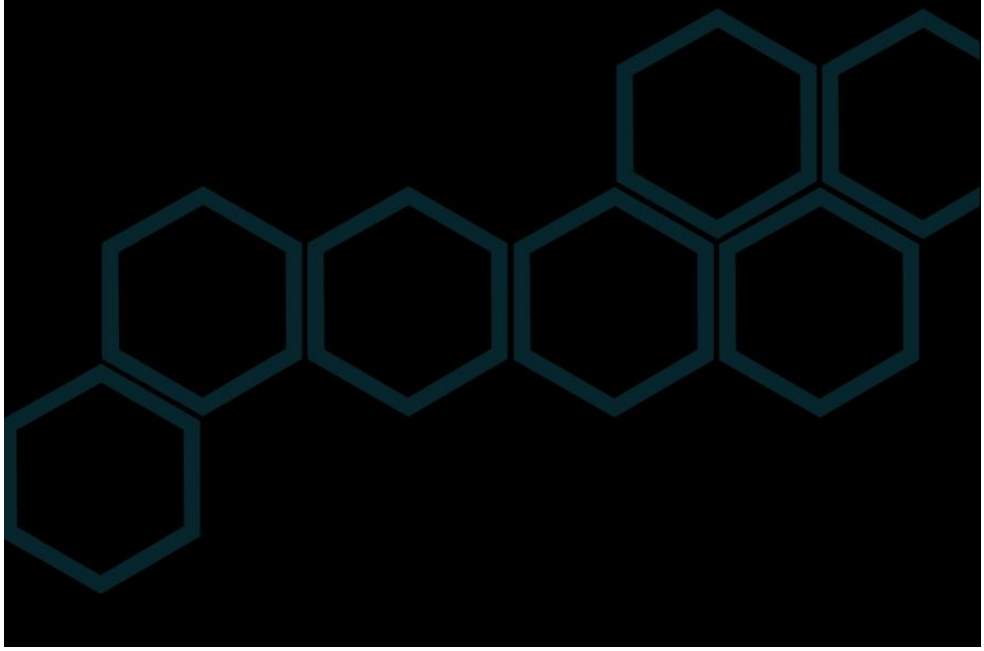


Cells are seeded onto a bladder-shaped scaffold, which can later be implanted in a patient’s body. Scientists at the Wake Forest Institute for Regenerative Medicine were the first to engineer organs in the lab that were implanted in patients. Once the scaffold is implanted, it gradually degrades as the new organ integrates with the body. Image: Courtesy of Wake Forest University



Laura Niklason and colleagues at Yale University developed this human-lung-sized bioreactor to provide a sterile and suitable environment for growing functioning lungs. The bioreactor supports the potential for vascular perfusion through the organ, as well as positive- or negative-pressure breathing movements. Niklason’s lab has so far succeeded at growing rat lungs that functioned for several hours in the animals. Image: Courtesy of Laura Niklason, Yale University

Architecture: Grow a home



Mitchell Joachim and colleagues at Terreform ONE developed the Fab Tree Hab, shown here as a 3-D model (top), to demonstrate that a home could be composed entirely of living materials. The renderings (bottom) show the Fab Tree Hab’s progression of growth. Image: Courtesy of Mitchell Joachim, Terreform ONE

In this rendering of the In Vitro Meat Habitat, bio-designer Mitchell Joachim imagines a house grown of meat cells. Image: Courtesy of Mitchell Joachim, Terreform ONE

Architecture: Grow a home

By Mitchell Joachim

Watch Mitchell Joachim's TED Talk here.

Today the leading trend in design is in groundbreaking prototypes of dwellings that are connected to the ever-shifting needs of the planet. Environmentally driven buildings are going up with stringent new certifications, such as LEED (Leadership in Energy & Environmental Design). Some of the most cutting-edge structures bear high-tech solar cells built into their facades. These technologies are promising improvements, but we can go further. I believe we can completely redefine sustainable building.

Why grow a home? I asked myself this question more than a decade ago when I first started exploring the stimulating possibilities of nature in design. Since then, I have created two prototype homes grown of living materials: One was shaped with living woody plants and the other, grown in a laboratory setting, was made from pig cells.

The initial inspiration for these homes came from Habitat for Humanity. The organization announced that it wanted to rethink the suburban house in order for it to become 300 percent more efficient. To do that, the whole process of building a home, from harvesting lumber to filling landfills with construction waste, needed to be reconfigured.

That was around 2002, and I was then a doctoral researcher at MIT. I proposed to Habitat for Humanity an idea for a home that would be 100 percent made of living matter (shaped trees and woody plants), entitled Fab Tree Hab.

Mitchell Joachim's vision for the Fab Tree Hab includes a circulating water system that irrigates the garden. ***Image: Courtesy of Mitchell Joachim, Terreform ONE***

In my proposal, I argued that a home of living trees is not built, but grown. It is deeply connected to the landscape, not an awkward addition to the ecosystem. A home made of living arboreal matter would scrub the atmosphere by the sequestration of carbon while producing fresh oxygen — a net positive for our environment. I decided to grow a home to prove that it was possible, and to open the door to a greener future.

To rethink the American home is precarious territory. A colossal yet delicate amalgamation of banks and real estate ventures dictate a carefully tuned salable housing unit. Many have tried reimagining it before and failed. Most homes of any perceived "modern" style have difficult resale values and are often marginalized from the outset. But the search for a perfect domicile is not dead. In the last 2,000 years, every culture on our planet has attempted to envision the perfect residence. To simply dismiss

further inquiry is to give up on a better world. The search for this perfect place is usually labeled as utopian, but utopia, in its best incarnation, is a maximal response to real-world problems. We must always strive for the impossible or, at the very least, welcome earnest speculation. What is a more perfect home for humankind and our planet? If not a perfect home, what then is a fundamental reboot of its design?

Using a home-building notion intensely influenced by early 19th century American ecocentric writers Thoreau and Emerson, which looked like a Tolkien elf cottage, I planned an effusively living tree house with its own unique ecosystem. I sought to design the most extreme prototype for a green domicile. I wished to discern the limits of eco-home design, and then generate a sweeping concept that exceeded them. Instead of a typical suburban bungalow sprinkled with solar panels on the roof, I projected beyond normative systems. I thought: Let's grow the material for the home onsite. In place of dead trees harvested from afar, why not use living ones nearby?

To achieve this vision, I used a methodology new to buildings, yet ancient to gardening: pleaching. Pleaching is a method of weaving and/or grafting together tree branches to form living archways, lattices, or screens. The trunks of inosculate, or self-grafting trees, such as elm, live oak, and dogwood, are the load-bearing structure, and the branches form a continuous lattice frame for the walls and roof. Woven along the exterior is a dense protective layer of fast-growing vines, interspersed with soil pockets and growing plants. In essence, the tree trunks of this design provide the structure for an extruded ecosystem whose growth evolves over time.

On a large rooftop in Brooklyn, we grew full-scale, double-curved wall test-sections of the experimental house. To guide plant growth in the early stages, I trained the seedlings along prefabricated scaffolds, cut from 3-D computer files. The vines and willows grew quickly — in a few months

they achieved nine feet in length, and we grafted them in a lattice pattern every six inches. My test wall lasted five years, and a variation still exists today. A clay-and-straw composite called “cob” insulates the latticed vines and blocks moisture (existing homes built with cob demonstrate its longevity and livability as a construction material). And a final layer of smooth clay, applied like a plaster, enhances both comfort and aesthetics.

For windows and doors I used biopolymers or plastics grown from soy-based products. The walls were made of vines spliced together to form a triangulated dome. Infill of living straw thatch is used for insulation at the dome apex because of its lightweight and water-repellent properties. Potable water was captured on the roof and cycled downward into the interior plumbing system by gravity-fed pipes.

Water, integral to the survival of the structure itself, serves as the pulmonary system of the home, circulating from the rooftop collector, through human consumption, and ultimately exiting via transpiration. A gray-water stream irrigates the gardens, which are used mainly for food production, with rows of lettuce extending 3,000 square feet behind the home.

A filtration stream enters a “living machine” (closed anaerobic and aerobic reactors), where bacteria and fish purify it and plants eat the organic waste. Scrubbed water enters the adjoining pond, where it infiltrates the soil or evaporates into the atmosphere. Water consumed by the vegetation ultimately returns to the water cycle through transpiration, simultaneously cooling the home.

Following this vision, instead of felling trees, society will be able to farm them for homes. If we used native seeds, as I did for Fab Tree Hab, these new local dwellings could be part of a completely green community. A dense canopy of leaves and roots shelters numerous mammals and insects. As a groundcover, this is a preferred nesting place for field voles and mice that construct nests for year-round security. Ground-feeding avian

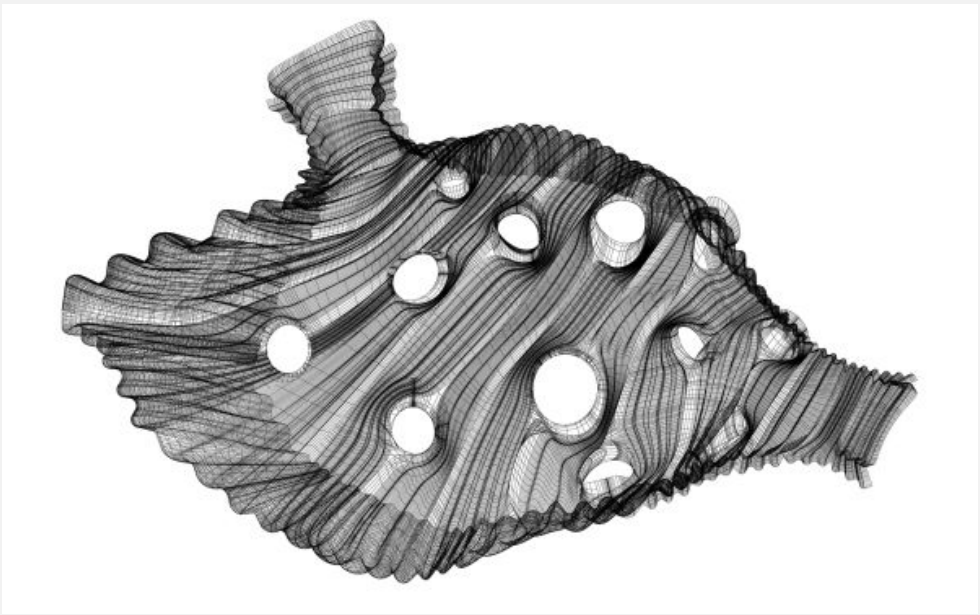
species find insect eggs and other morsels in the leaf litter below. Blackbirds forage on the berries of the mature climbing plants dispersed throughout the house walls; other birds nest or roost in the grafted ivy's thick growth next to a heat source within. In fact, the Fab Tree Hab is a house that is entirely edible, at some stage of its life, for almost every type of organism on the planet. At the end of the house's life, horses can eat the straw, elk can feast on the willows, and termites munch only the dead dry wood cellulose or plant fiber.

After I completed my PhD at MIT in Architecture Design and Computation at the Media Lab Smart Cities Group, I departed Cambridge for New York City, and in 2006 I founded a nonprofit architecture and urban design collaborative called Terreform ONE. I had spent years working on ecological skyscraper design and future mobility systems. My lab research, with Frank Gehry and William J. Mitchell, was on a future city car that was super soft, stackable, networked, and omnidirectional. I was also working on an Extreme Expeditionary Rover for NASA. But I wanted to get back to living home design.

For the architect, nature has long been a point of departure. And so from the Fab Tree Hab I leapt to my next inspiration, the newest intersection of nature and artificial fabrication: synthetic biology. Now that the power to control design at the cellular level is an everyday reality, my materials shifted from whole organisms (trees) to their tiniest component: cells. I decided to grow a house of meat.

The idea sprouted directly from the Fab Tree Hab. I had occasionally been teased for being the "vegetable house guy," and one heckler had proclaimed that the veggie house would never last, so why didn't I make one out of meat? He was being ironic, but I understood it differently, as a real question: Why limit living organic homes to only materials made of plant life? Tissue engineering offered another way.

The In Vitro Meat Habitat, nicknamed the “meat house,” would be bioengineered through in vitro replication of mammalian pig cells. I crafted the plan so that sentient creatures would not be harmed in the tissue growth of the dwelling; it was essentially a victimless shelter.



This diagram shows the design concept for the In Vitro Meat Habitat, to be grown from pig cells. ***Image: Courtesy of Mitchell Joachim, Terreform ONE***

My house of cells was similar in technique to the synthetic hamburger grown in 2013 from cells derived from the meaty shoulder of a cow. I didn’t want to grow a full-size house, but rather to test the potential architectural implications. Breakthroughs in regenerative medicine, such as the creation

of living replacement bladders in a laboratory, had already shown that it was possible to grow tissue into a specific geometry. So could we grow materials that would work for everyday domestic use?

Following the methods of tissue engineering, my colleagues and I isolated the pig skin cells and reproduced them in a culture. We established an immortalized cell line to replicate as much material as needed. Then we washed the cells onto a polyglycolic acid (PGA) fibrous scaffold to promote cell adhesion, growth, and viability, and to provide geometric shape for building. It looked like a punctured football and was about the same size.

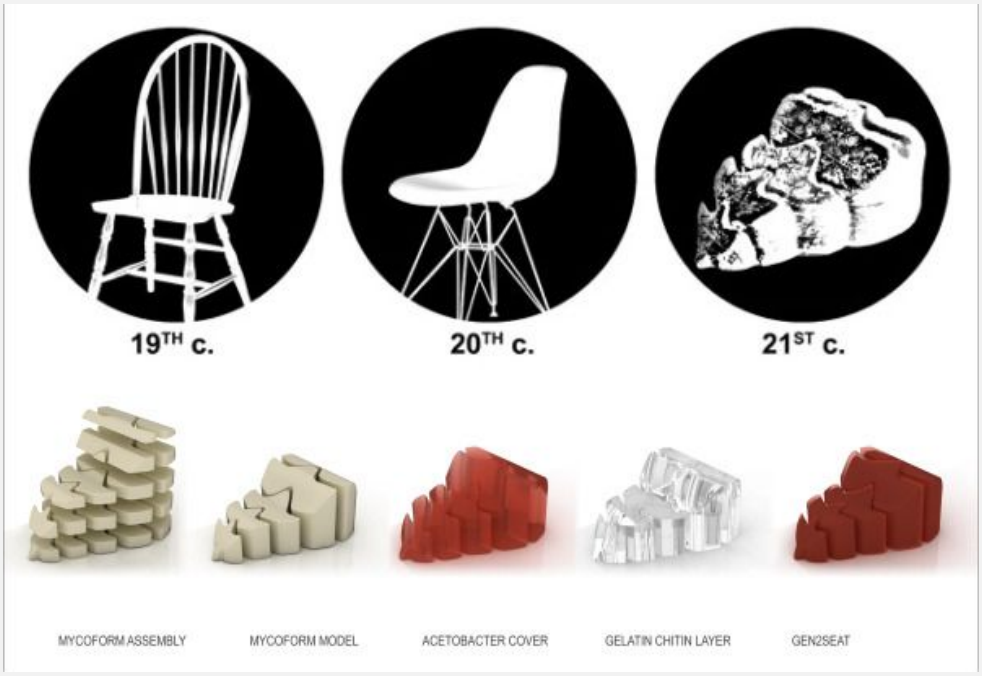
As of now, the concept model consists of essentially very expensive fitted cured pork, or articulated swine leather with an extensive shelf life. The actual size of the desiccated and arid-smelling non-perishable prototype is 11 by 3 by 7 inches. It's important to declare that the maquette is both a vehicle for propaganda and a mechanism for awareness of the potentials for building with cells. It's as much a parody of yesterday's bio-formalist architecture, as it is factual biological material. It's not meant to be actualized as a full house, but it serves as a highly informed case study for growing large volumes of in vitro material en masse.

To me, the house illustrated the biological supremacy achieved by using real organic materials grown from scratch. This is different than, say, using bamboo as a building material and replenishing the harvested supply. Instead, it's inventing a new material and fully integrating it into nature's metabolism. The In Vitro Meat Habitat is neither a copy or a mimicry of nature. It is unsullied nature itself.

Creative people have often looked to biologists for groundbreaking design solutions. The new availability of biological expertise, through DIY toolkits and access to community/citizen science labs, has enabled a paradigm shift to more cross-disciplinary collaboration in design. Biological methods are an exciting driver for new inventiveness within art — my own included. For example, with merely $3,000, I was able to build

from scratch my own biology lab, called Bioworks. The Brooklyn lab evolved into Genspace, a nonprofit science outreach group. I completed it with my former roommate and colleague, Oliver Medvedik, with the inspiration to apply synthetic biology techniques to ideas on an architectural scale. We ordered all the machine parts and lab equipment online from eBay, Craigslist, and other e-commerce sites. My aim was to produce a palpable organic architecture seen only in film, as in the blockbuster *Avatar*. In that movie's vivid and limitless world, everything from birds and plants to the whole ecosystem was designed through biological imagination. It inspired me to lead an investigation into biologically produced projects. The In Vitro Meat Habitat was the first real accomplishment from this exertion.

I completed a second, longer-term effort called the Gen2Seat for the iGEM (International Genetically Engineered Machine) competition. For that project, I grew a chair.



This graphic from Terreform ONE illustrates the Gen2Seat's concept and construction. ***Image: Courtesy of Mitchell Joachim, Terreform ONE***

I'd always sought a chair, from the very start. A chair is so ubiquitous in our society, and its shape has changed throughout various eras to resonate with current necessities and standards. I wanted to not only redesign the notion of a chair, but to revamp its formation to an organic and possibly home-based procedure where goods are not artificially put together, but grown. Charles and Ray Eames couldn't duplicate or conceive of this chair. It's not an everyday project, slapping together some steel or wood or fiberglass. It's a total departure from "modern" design.

To make parts of the chair, I genetically engineered the naturally occurring bacterium Acetobacter xylinum. This bacterium secretes copious

amounts of cellulose, which can then be harvested and used directly as a structural material. Eventually, our goal is to create a novel strain that can also secrete the biopolymer chitin, which is normally produced by arthropods, such as insects and crustaceans. In addition, we fused mycelium blocks with the modified acetobacter to create a new biopolymer. Applying the tools of synthetic biology alongside other biological disciplines, such as microbiology and tissue engineering, will allow us to create products more organically, with minimal waste and energy expenditure.

Our chair might be the first household product that can be grown rather than manufactured, but it won't be the last. Gen2Seat grows in a mold in seven days. Inspired by the design of our own tailbones, Gen2Seat is customizable in height and form, due to the different articulated sections that give it flexibility and ease of transportation. Funding for the project was provided by the Open Science Challenge grant, and interest from manufacturers such as Ecovative means that the Gen2Seat could become a real product in an emerging techno-industrial revolution where products are designed with not only efficiency and profitability in mind, but also sustainability and disposability. When you're done with the Gen2Seat, it's composted in a garden, not tossed into a landfill like an Ikea product.

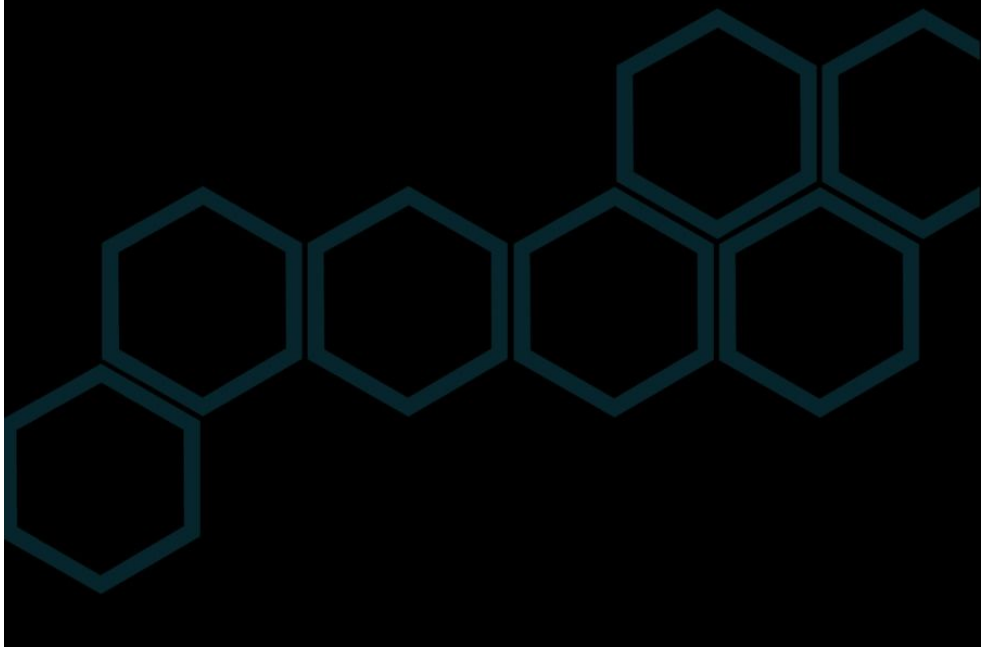
The primary goal of the meat house was to set the minds of industrial designers and architects on fire. Bio-design represents an all-inclusive reset on today's manufacturing techniques. Why not grow parts of your home instead of extracting vital planetary resources? This sort of question should be the spark of the next industrial revolution, especially as it relates to the production of utilitarian objects. Our materials could be genuinely interdependent with one another and with the environment. The utopia of this pursuit would be an approach to design that makes no distinction between nature and the human body, or between nature and the human environment. A human house would be just another phenotype of a bird's nest, a spider web, a beehive, or a termite mound.

Living architecture is a long way from becoming a mainstream practice. Yet the ability to mitigate climate change is of the utmost importance to every architect. In the United States we suffer from a lifestyle that absorbs too much of Earth's resources within a rampant culture of affluenza. Searching for innovative strategies to help solve our current eco-crisis is vital to human survival. New directions in biological design are a magnificent approach to going beyond survivalist routines. Bio-design is the next step toward a resilient harmony where humankind and nature seamlessly blend.

Pig skin cells, grown into this shape in Terreform ONE’s lab, make up the walls, floor, and ceiling of this prototype home. The model is non-perishable and measures 11 inches long. Image: Courtesy of Mitchell Joachim, Terreform ONE

The Gen2Seat, a chair made from the cellulose produced by Acetobacter xylinum bacteria, may be the first household product that can be grown rather than manufactured. Image: Courtesy of Mitchell Joachim, Terreform ONE

Fashion: Cellular ateliers



BioBiker jacket: a “negative” of the classic black leather biker jacket, made with replaced metal studs with black oxidation (a dye- and chemical-free process). This garment and those on the following pages are made by Suzanne Lee from all-natural bacterial cellulose fabric. Image ©Biocouture Ltd. 2014, photo by Gary Wallis

BioShirt: Lee’s first grown garment prototype, created in collaboration with David Hepworth of Cellucomp, 2004.
Image ©Biocouture Ltd. 2014

Fashion: Cellular ateliers

By Nina Tandon

If you peruse a typical fashion design course catalog, you'll see that students have thousands of classes from which to choose: accessories, entrepreneurship, history of art and interior design, patternmaking, textiles, toy design — just to name a few. But if you talk to London-based fashion designer Suzanne Lee, she'd suggest that students who want to be the designers of the future should also study ecology, cell culture, and perhaps even genetics.

Designer Suzanne Lee examines a sheet of microbial cellulose to be used as biofabric. Still image from the forthcoming documentary film "The New Black" by Scandinavian production company House of Radon. ***Image: ©Biocouture Ltd. 2014, photo by House Of Radon***

Why ecology? Because the materials designers use are often toxic to the environment. Take leather, for example. "An animal has an expensive environmental footprint," Lee told me. "It uses valuable land, food, and water, and that's before you get to the toxic chemicals required for processing the hides." Not that agriculturally based fibers are much better — the World Wildlife Fund reports that cotton covers 2.4 percent of the world's crop land, yet accounts for 11 percent of global sales of pesticide. It also takes more than 20,000 liters of water to produce 1 kg of cotton, which is equivalent to one t-shirt and a pair of jeans.

Because we are using more materials for fashion than ever before, this is an ever-increasing problem. Lee explains that with the rapid rise of "fast fashion," the time it takes for a garment to get to market has been reduced from months in the early 2000s to a matter of days now. "Instead of delivering new collections twice yearly," she reports, "some companies now deliver new designs twice *weekly*!" And while this certainly has implications for the quality of the designs, these trendy, inexpensive clothes are also being discarded at an alarming rate, filling up landfills, causing pollution, and depleting precious natural resources. According to the Environmental Protection Agency, Americans throw away about 13.1 million tons of clothes every year (an estimated 83 pounds of clothes per person). And many "fast fashion" clothes are made not from cotton but from polyester, a petroleum-based fiber, which, despite efforts to incorporate closed-loop production methods and recycling, is still one of fashion's largest and worsening source of carbon emissions. Blended fabrics

pose additional complexities with regards to processing for recycling.

BioRuff detail. ***Image: ©Biocouture Ltd. 2014, Photo by Santiago Arribas***

What does all this have to do with cell culture?

Back in 2003, while researching her book *Fashioning the Future: Tomorrow's Wardrobe*, Lee was looking for new ways to create materials and products by "thinking 50 years ahead, as opposed to thinking [only] two years or two seasons ahead," she says. She found herself interviewing scientists and engineers, and one of the people she met was biologist and

material scientist David Hepworth, co-founder of the sustainable-materials company CelluComp, based in Scotland. He told her, “If you really want to think radically, think about getting cellulose by culturing bacteria,” particularly Acetobacter, which is found in symbiotic relationships with many plants, such as sugarcane and coffee, and is used in fermenting vinegar.

Lee began to envision fashioning a dress from microbes, and a collaboration was born. She and Hepworth started growing material in 2003, and they grew their first garment — a simple, classic shirt, in her size — in 2004. “I was insanely excited,” Lee recalls. “I couldn’t believe I was able to grow the fiber into a material and sew it into a garment.” She’ll be the first to admit that the product wasn’t perfect: “The textures and colors on the left and right sides were different, the collar was thinner. But it was wearable!” Still, she was reluctant to wear it out and about too much, as this precious garment was one of a kind.

Bio material. ***Image: ©Biocouture Ltd. 2014***

Lee begins her fabric-growing process by brewing tea. Not for herself, but to nourish the living organisms she's about to cultivate. Into about 30 liters of green tea she dissolves a couple kilograms of sugar — food for growing microbes. She then adds acetic acid and the live culture of bacteria and yeast, keeping the mixture warm. And voilà: a mini fabric farm!

After about three days, the mixture begins to bubble and ferment. This means the bacteria are feeding on the sugar, and as they do, they spin tiny nanofibrils. These minute threads are about 3 to 8 nanometers in diameter — about 1,000 times narrower than a cotton fiber and 10,000 times narrower than a thin human hair. Unlike cellulose from plants, this version

contains virtually no impurities. The fibers stick together, forming a flat layer on the liquid's surface. Two to three weeks later, this natural "fabric" is about an inch thick. Lee rinses it and spreads it out to dry. The material thins as its water content evaporates. The result? Depending on the recipe, Lee says, it's "either like a really lightweight, transparent paper, or something much more like a flexible vegetable leather." She can cut and sew it conventionally or mold the wet fabric around a three-dimensional shape, and as it dries it naturally knits itself together, forming seams.

Cellulose, essentially a chain of sugars (i.e., a polysaccharide), is an important component of the cell walls of green plants, many algae, and other microorganisms. Cotton and wood are currently the major resource for cellulose products, such as paper, textiles, and construction materials. However, the abundance and purity of the cellulose from bacterial sources hints at the robustness with which it may be grown and its promise to more sustainably produce materials.

Until about 30 years ago, when the remarkable material properties of bacterial cellulose began to be discovered, its use was limited largely to the manufacture of *nata de coco*, an indigenous dessert food in the Philippines, in which cubes cut from thick gel sheets fermented in coconut water are immersed in a sugary syrup. Since then, its stiff fibers — whose strength approaches that of titanium or aluminum — have been used to reinforce paper, as bandages for burns and wounds, and to construct the speaker-driver diaphragms in high-fidelity speakers. Clearly there is much more to come.

Cellulose growth trays. ***Image: ©Biocouture Ltd. 2014***

Lee and her team have made a series of clothing prototypes, grown as experiments or for commissions and exhibitions, including jackets, a kimono, and a shoe. They're currently growing a skirt for the Festival of Imagination, which is hosted by the high-end London department store Selfridges. Lee is quick to point out the reduced ecological footprint of these materials: "If you were to compare a jacket made of our material with one of cotton, ours takes 50 liters of water, and the other takes thousands of gallons."

In addition, the cell culture is static, requiring minimal supervision. "Your costs are literally nothing once it's set up," she says. "You don't need a biolab. You don't need to be a scientist."

However, the nano-structure of the material does create certain limitations on the types of garments that would be suitable to produce. “It only makes sense to fashion it into articles that that work with the qualities of the material, so you wouldn’t try to create a t-shirt,” Lee cautions. Instead, she says, “It would be more desirable to shape accessories or garment types requiring more structure, for example outerwear, as opposed to something worn next to your skin.” Other challenges include the lingering aroma of fermentation and the material’s high absorbency. Lee says, “In a dry environment it would be a bit crispier, and in a humid environment it would kind of soften up. If you went out in the rain, it would soak up and get heavy. It’s essentially a super-absorbent sponge.”

Furthermore, without access to sustainable sources of feedstock, the production remains reliant on the availability of sugar, “an expensive commodity with fluctuating price.”

There are ways around these challenges. Some fixes, such as Teflon coating, are easy but too industrial for Lee’s tastes. She continues looking for alternative, more biological approaches, such as nano-organic coatings based on silica and free waste streams to provide a feedstock. In the process, she has become interested in changing the inherent characteristics of the material itself.

So is this where genetics come in?

Yes. If we think of the microbes as “factories,” Lee explains, we can begin to imagine engineering them to produce cellulose that’s not just hydrophobic, but that possesses any other attributes we could desire. The advances being made in synthetic biology, in which gene splicing and other techniques are used to reprogram cells to express different traits than what they have evolved to express, will enable this.

What sorts of future fabrics could grace our fashion runways? Lee presented me with a captivating collection of possibilities, like nourishing, biocompatible textiles that “deliver something beneficial to the skin” as a

kind of “cosmeceutical hybrid of cosmetics and apparel.” Or materials with built-in electronic functionality that could sense the body or surrounding environment and relay information, thus incorporating apparel into the expanding “internet of things.”

Where we’re heading, Lee proposes, is the development of more sophisticated technologies that will enable us to “actually bio-print and lay down biological materials in a designed, structural way. Further down the line, I imagine we could print an entire bio-shoe.”

BioKimono, commissioned by Toyko Design Centre for the exhibition “Warp Factor,” color transformation achieved with iron oxidation on

kakishibu, a persimmon tannin juice. ***Image: ©Biocouture Ltd. 2014, Photo by Gary Wallis***

How many different industries did we just combine?

As Lee's work has garnered more attention, it has attracted interest from all sorts of design fields, including accessories, furniture, and architecture. Or, as she says, "every field where people were looking for new sustainable materials." Many of them actually wanted to buy materials from her — far more than she could assist or supply.

Lee realized that she was occupying a unique seat at the juncture of design and living material manufacture. Rather than produce material only for her own work, she expanded her aims to form Biocouture, the first living-material consultancy. She describes Biocouture as a catalyst for getting living materials into the consumer space. The company experiments and informs R&D, as well as brokering relationships between design brands looking for new materials and the material innovators themselves. In addition, she is building an online platform (still in conceptual development) that brings together an open-source community of biological innovators sharing recipes, methods, documentation, and educational tools.

Ultimately, Lee hopes to "cause an explosion of innovation around grown materials."

The demand is definitely there: Lee is constantly fielding calls asking for prices on her prototype materials and products. Yet a critical set of economic and scale-up challenges remain before cultured materials can graduate from the laboratory into the production line. These technologies are still young, and our current bio-fabric infrastructure produces relatively small quantities, resulting in high prices. For mass fashion, we need the opposite.

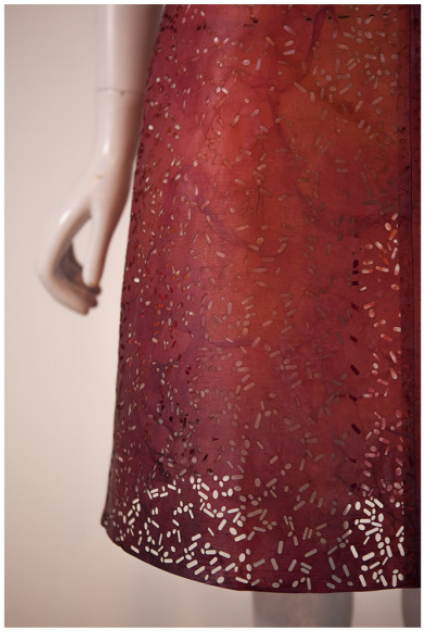
In addition, material scientists are still working to *match* the fabrics already made by nature. To truly compete with petrochemical materials that

churn through big-box stores at rock-bottom prices, we'll need to go *beyond* it.

BioBomber jacket, its engineered print created with fruit and vegetable stains from beetroot, blueberry, and raspberry. Image ©Biocouture Ltd. 2014, photo by Gary Wallis

BioRuff jacket, commissioned by the Science Museum London for its exhibition “Trash Fashion: Designing Out Waste,” in collaboration with Imperial College London. Image ©Biocouture Ltd. 2014, photo by Santiago Arribas

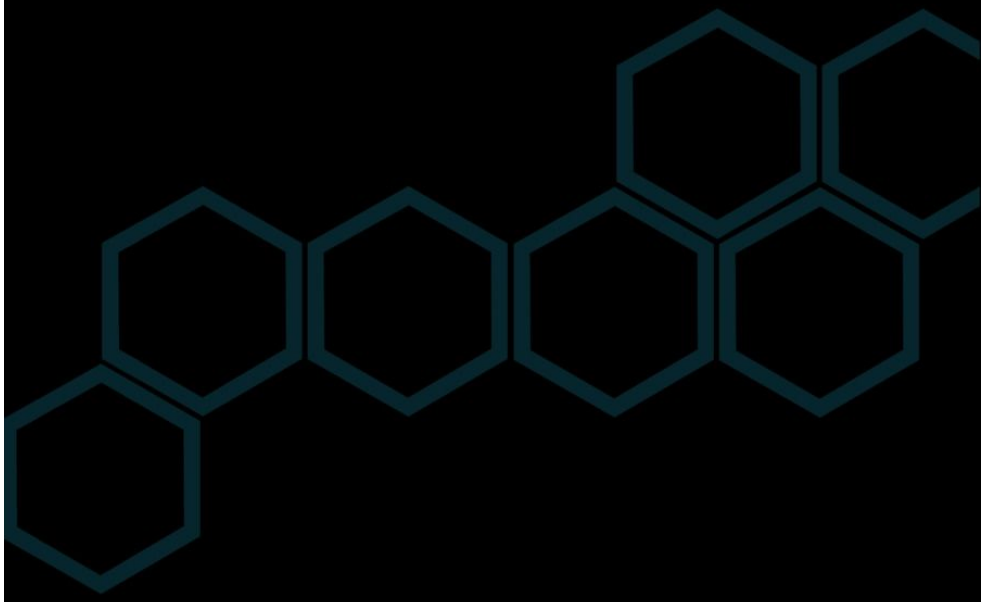
BioShoe, commissioned by Espace Foundation EDF for the exhibition “Alive/En Vie,” Paris 2013. Image ©Biocouture Ltd. 2014, photo by Bill Waters



BioSkirt, commissioned by Selfridges department store for its “Growing the Future” exhibit and workshops given in early 2014 as part of the store’s “Festival of Imagination.” Lasercut motif taken from microbes (rod-shaped bacteria and ovoid yeast cells) that grew the material. Image ©Biocouture Ltd. 2014, skirt photos by House of Radon

BioDenim jacket, garment-dyed in indigo to preserve and render the cellulosic fibers anti-microbial. Image ©Biocouture Ltd. 2014, photo by Gary Wallis

Food: Ranch in a lab



Food: Ranch in a lab

By Nina Tandon

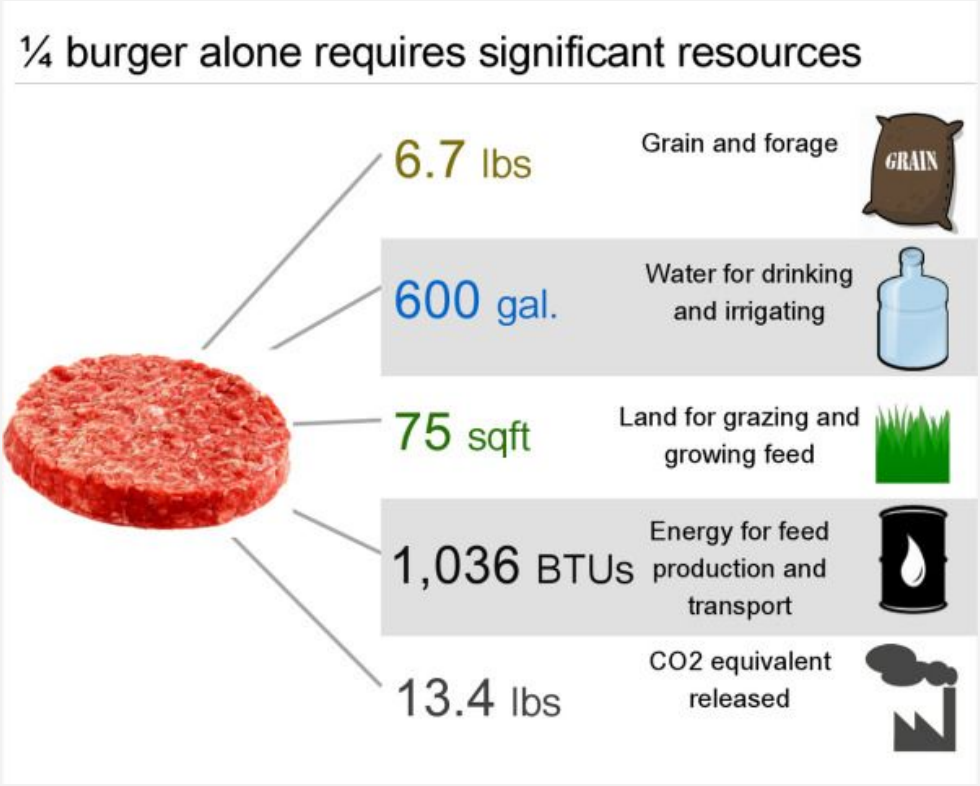
Andras Forgacs, delivering a TED Talk, displays a piece of leather he grew in the lab. ***Image: James Duncan Davidson/TED***

Andras Forgacs, an entrepreneur turned rancher, arrived in agriculture by way of medicine.

In 2007, he and his father Gabor Forgacs founded Organovo, a San Diego company using 3-D bioprinting to engineer human tissues for pharmaceutical research and medical applications. Forgacs admits that,

back then, people often thought they were “a little crazy.” But as their lab and others like it made progress printing simple human body parts (see Anthony Atala’s TED Talk), they started getting questions like, “If you can grow human body parts, can you also grow animal products like meat and leather?” This time they were the ones to find the idea a little crazy. But after some consideration, they began to think that what was craziest of all were our current methods of producing these goods.

The environmental costs of maintaining the herds that provide the world’s meat and other decidedly un-vegan things are staggering. By 2050, when the UN predicts the population will reach approximately 10 billion people, Forgacs predicts that it will take 100 billion animals to satisfy the world’s demand for meat, dairy, eggs, and leather goods. Meeting that demand will require some seriously huge supplies of grain; presently more than 35 percent of the world’s grain crop is fed to livestock. And given that economic development tends to lead to increased meat consumption, a growing, globalizing population will likely have a bigger hunger for meat. The sum total of these factors is a double increase in need for agricultural outputs for human food and livestock feed. “Maintaining this herd will take a huge, potentially unsustainable toll on the planet,” Forgacs says.



Forgacs' company, Modern Meadow, created this illustration of the environmental costs of a quarter-pound burger grown the traditional way. ***Image: Courtesy of Modern Meadow***

There are also food security risks and public health risks from the high concentrations of animals found in modern agriculture, which create breeding grounds for disease and increasing vulnerability to livestock-targeted bioterrorism. Outbreaks such as swine flu, foot-and-mouth disease, salmonella, and BSE (mad cow disease) are particularly prevalent where animals and people exist in close concentration.

Forgacs wondered if he could find a better way — especially considering that "essentially, animal products are just collections of tissues, and right now we breed and raise highly complex animals only to create products that are made of relatively simple tissues." What if, instead of starting with a complex and sentient animal, we started with what the tissues are made of, the basic unit of life, the cell? This was just what Forgacs and his father had done with Organovo. They could use the same techniques of biofabrication, guiding cells to replicate themselves to grow tissues and organs, in order to instead grow biomaterials that could form the basis of a humane, sustainable, and scalable new industry.

The idea of culturing animal products is not new — humans have been harnessing the power of cells for making wine, beer, and yogurt for millennia. In fact, Winston Churchill wrote about the practice in his essay "Fifty Years Hence," published in *Strand* magazine in 1931, where he predicted a future of cultured meat, saying, "We shall escape the absurdity of growing a whole chicken in order to eat the breast or wing, by growing these parts separately under a suitable medium."

However, although a brewery is essentially a bioreactor, "brewing" leather or meat requires the development of different advanced systems for cell culture. Churchill's prediction was in a sense on target, but it wasn't until 60 years hence that experimenters began culturing meat in earnest. The FDA first approved NASA's production techniques for in vitro meats in 1995, and NASA researchers subsequently began experimenting with cultured meat as long-duration food for astronauts on space missions. The first edible sample NASA engineers produced were "fish fillets" made from goldfish cells in 2002, in collaboration with the Touro Applied Bio Science Research Consortium.

Interestingly, scientists weren't the only ones experimenting with lab-grown meat. Artists Oron Catts and Ionat Zurr — the artistic and academic directors, respectively, of SymbioticA, a collaborative art and science lab at

the University of Western Australia (see the "Art" chapter) — were also growing in vitro meat as far back as 2000. When Catts and Zurr were research fellows at Harvard Medical School, they grew "victimless lamb steaks" from prenatal sheep cells. Later, in 2003, they grew and ate "frog steaks" for an exhibition titled "Disembodied Cuisine" in France — culminating in a feast where the frogs from which the cells had been taken were exhibited, alive, alongside the dinner. The artists ate the frog steak fried in a sauce of honey and garlic, condiments well known for their antibacterial properties. The goal, rather than engineering food, was to "generate evocative objects for cultural debate" about current biotech research. "Many think the French habit of eating frogs is disgusting," Catts said, "and many French think the idea of eating engineered food is revolting. So we decided to combine the two."

The idea of starting a business around lab-grown meat also dates from this time. In 1999, three Dutchmen filed for a worldwide patent on a process to produce in vitro meat. In 2004, an American named Jon F. Vein filed a patent for in vitro meats for human consumption. However, these patents are "essentially meaningless," Forgacs asserts, as "none of these people are in the business of growing meat commercially, or at scale." Meanwhile, in 2008, PETA offered a reward of $1 million to the first person who made commercially viable in vitro chicken meat by March 1, 2014.

Forgacs founded his cultured meat and leather company, Modern Meadow, in fall 2011 in Columbia, Missouri, the city where his father and co-founder Gabor Forgacs' academic laboratory is based. Not surprisingly, the team's methods for growing animal products from cells closely parallel those used for growing replacement organs and tissues. They begin with animal cells, multiply (i.e., "expand") them in the lab, form them into tissues, and mature them in bioreactors into muscle and skin, the main ingredients of meat and leather.

How big a steak might they serve? For now, they're expanding cells in cell culture roller bottles, traditionally used for high-quality, reproducible antibody production for laboratory reagents and antibody-based therapies and vaccines. These have limited yields, fitting around 100 million cells each (enough for an inch-size patch of meat about a millimeter thick). Soon, however, they'll begin using next-generation cell culture systems that allow sterile fluid and air manipulations, increase cell yields, and requiring less labor. Looking ahead, they envision scaling up further to use cell culture bioreactors for high yield at scale, first to billions of cells producing enough meat or leather for kilogram quantities of product, and ultimately, they expect, in the thousands of kilograms.

Karoly Jakab, senior scientist at Modern Meadow, examines cell cultures as they grow in an incubator. ***Image: Courtesy of Modern Meadow***

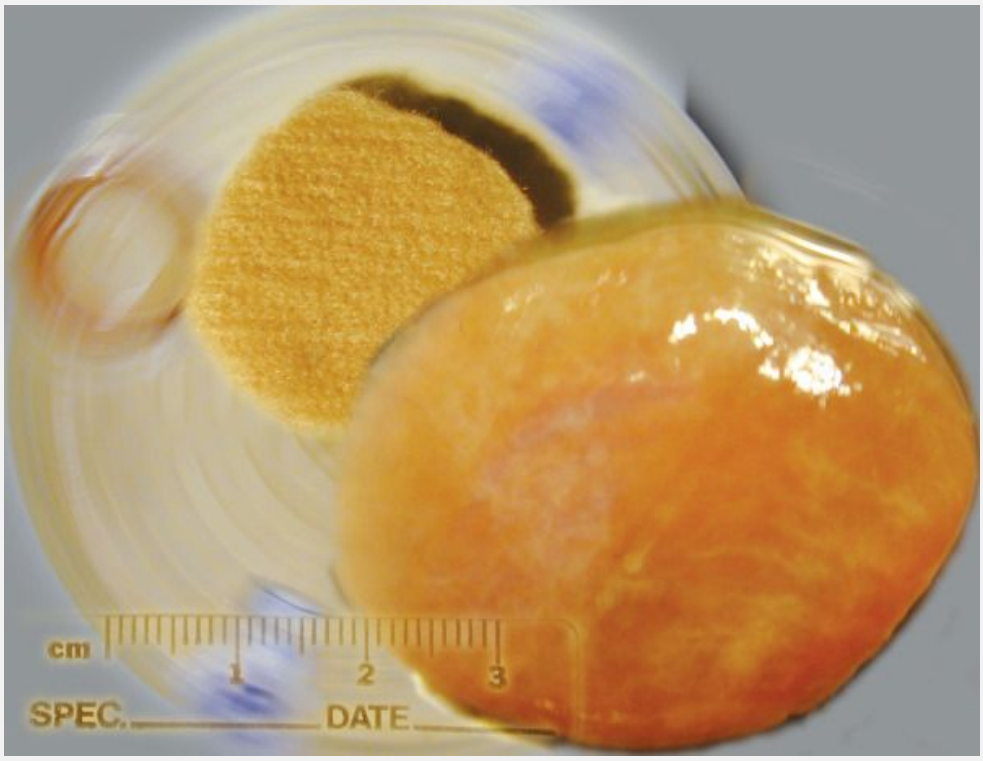
Once they've grown the cells, the researchers harvest them and assemble them into tissues. For leather, they spread out the cells and their collagen to form thin sheets, layering the sheets on top of each other like phyllo pastry. The process for assembling a meat product is a bit more complex. For starters, Forgacs' current meat model is composed of four distinct cell populations: muscle, fat, endothelial (lining the blood vessels), and fibroblast (the main cell type in skin, which forms the basis of their leather product). The expansion of each cell type needs to be optimized individually, as each one multiplies at a different rate and under slightly different ideal conditions. In addition, proper meat, unlike leather, must be marbleized rather than layered. Finally, there's an additional downstream bioreactor conditioning (like laboratory cellular "exercise") needed for meat, lest it come out as limp muscle with a lackluster mouth-feel. (This is where my research ties into theirs; I develop systems to perform this exercise in bioreactors.)

So what does lab-grown meat taste like?

Forgacs first tasted meat grown in Modern Meadow's lab around Thanksgiving 2012. As he describes it, the whole day was quite ceremonial. He bought a little pan, olive oil, salt, and pepper — kitchen essentials not typically stocked in a lab. Then he donned a costume: a white lab coat. He remembers "a little sausage the size of a pinky," which the team cooked up on a hotplate in the lab. In an effort to be scientific, he did a first tasting unsalted, and a second with salt and pepper. "Flavor-wise, it was very mild, and it didn't taste bad at all," he recalls. "We just wanted to demonstrate that it was edible." Ultimately, Forgacs aims higher than "edible," of

course. He says his team is collaborating with chefs and making tasty progress.

Other experimenters agree that chefs will play an important role in making the flavor and texture of the meat more ready for the palate. Oron Catts, for instance, said his frog steak was gelatinous, with the texture of fabric, since the polymers on which they grew the cells hadn't yet completely degraded and the cells also hadn't been "exercised." When asked about the taste, he replied, "The sauce was good."



Artwork entitled "Tissue Engineered Steak No. 1," grown from prenatal sheep skeletal muscle in 2000 by the Tissue Culture and Art Project as a study for the exhibit "Disembodied Cuisine." ***Image: Courtesy of the Tissue Culture & Art Project (Oron Catts and Ionat Zurr)***

The first lab-grown beef burger was fried and eaten in London in August 2013. How'd it go down? "Like an animal-protein cake," said Chicago-based food author Josh Schonwald.

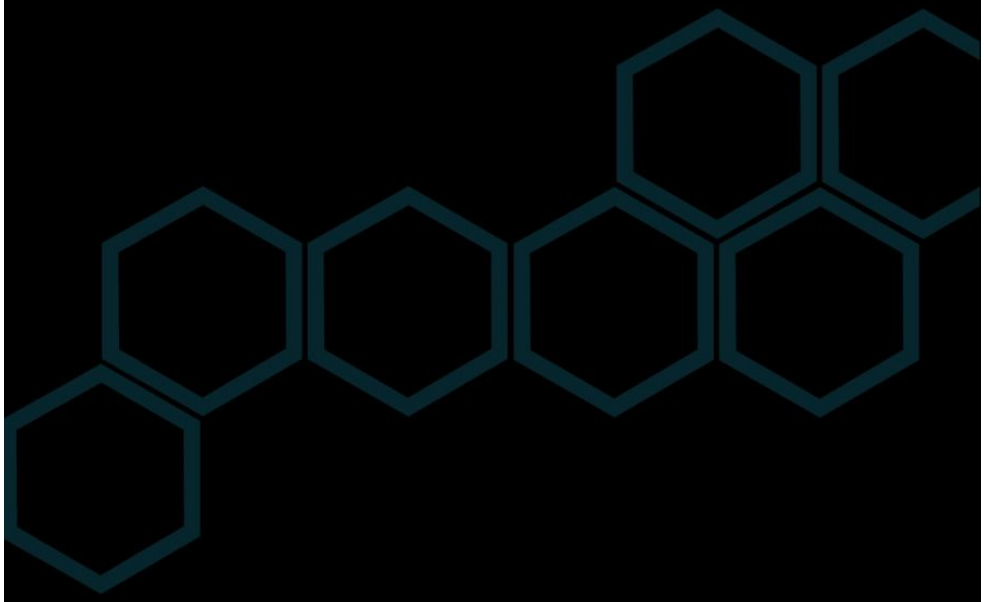
Beyond taste, other questions remain. Would lab-grown meat be considered Kosher or Halal? Organic? Could vegetarians and vegans eat it? Growing animal products for possible ingestion will also present a very different set of regulatory questions than biological therapeutics intended for implantation. So, for the time being, Forgacs considers novel bio-textiles for apparel as a kind of "gateway material," opening up the possibilities for the biofabrication industry. He says, "Initially at least, more people would be willing to wear novel materials than would be willing to eat novel foods, no matter how delicious."

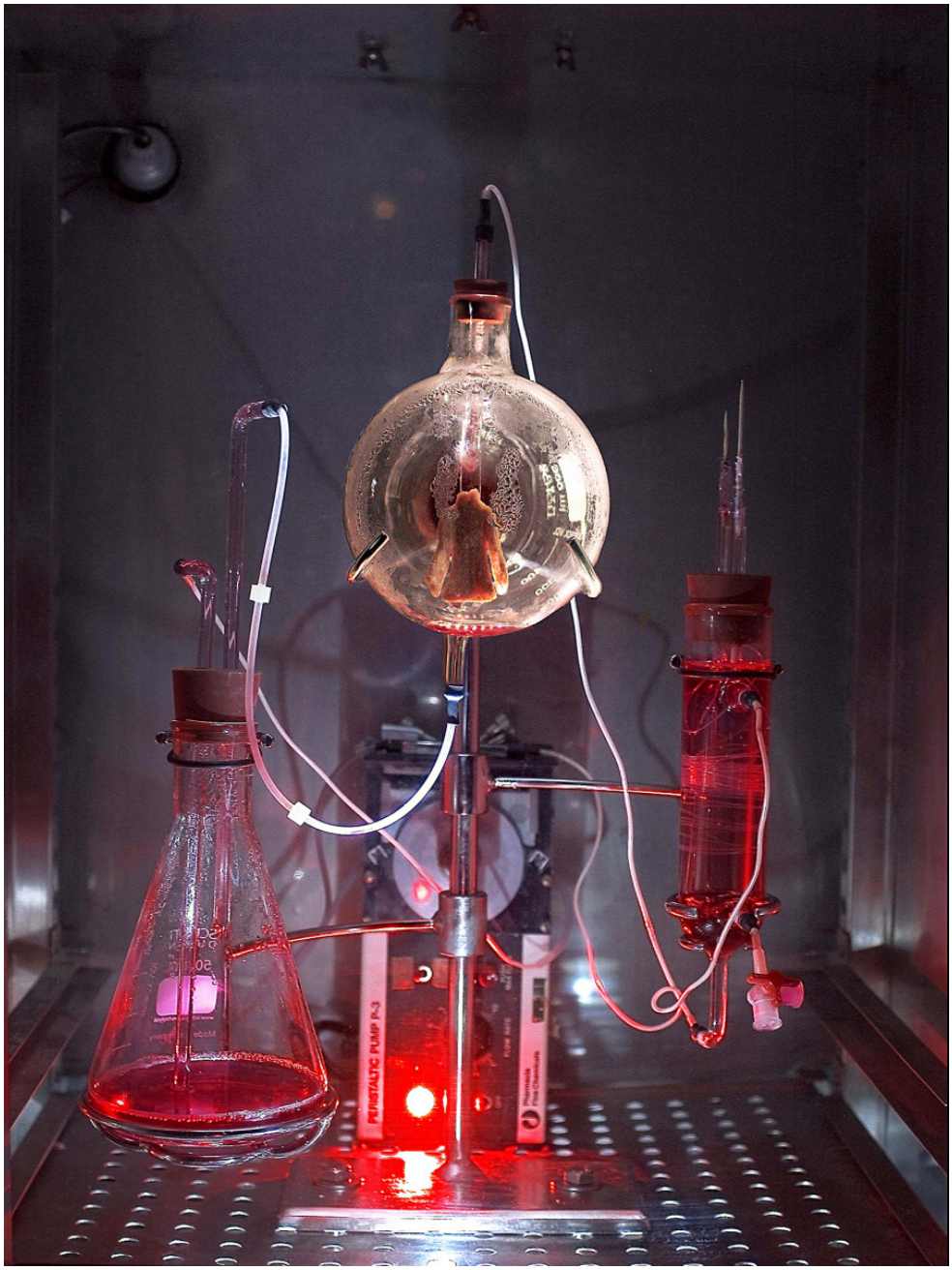
But all these questions are essentially moot unless the biggest question of all is answered: Will it ever be economically viable to culture meat at scale? There are numerous small obstacles, Forgacs says, but "we're systematically knocking them down." If he and others succeed, cultured meat production could potentially deliver vast environmental efficiencies over cultivated meat. Forgacs believes that meat grown with his methods can hit the most optimistic projections of Oxford University researchers for reduced environmental impact via cultured meat: using up to 99 percent less land and 96 percent less water, producing 96 percent fewer greenhouse gas emissions, and consuming 45 percent less energy.

As a tissue engineer myself, and as an entrepreneur considering the challenges our field faces, I can't help but think that some of the questions Modern Meadow is tackling also apply to our investigations in health. How

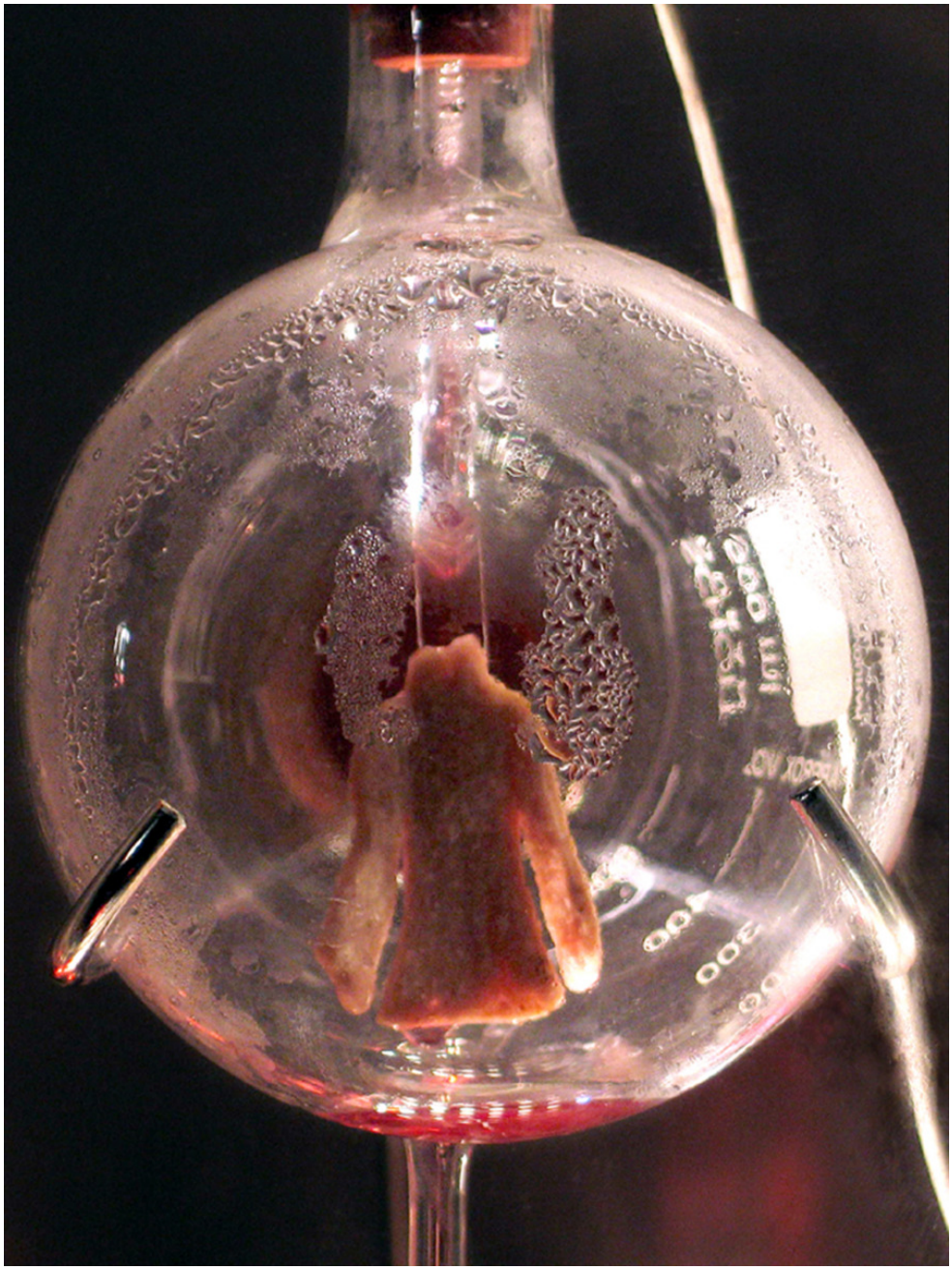
do you master scalability and quality control when cells are the "employees" on the production line, and where safety and quality are of the utmost importance? Perhaps Forgacs' foray into agriculture will, in turn, fuel our advances in medicine and beyond.

Art: Cellular muses

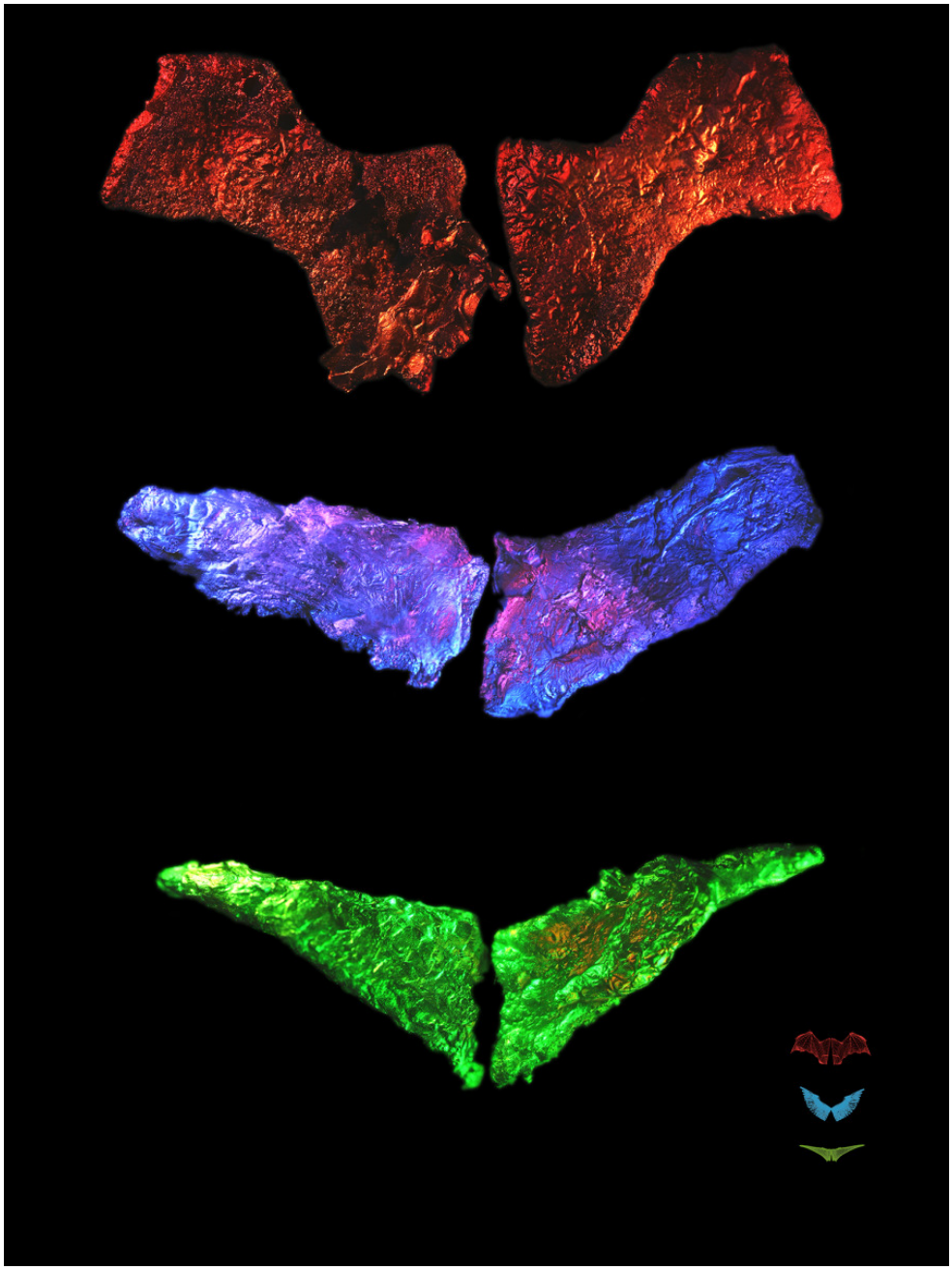




Victimless Leather, a piece created by Oron Catts and Ionat Zurr of the Tissue Culture and Art Project in 2004, is a miniature coat grown of cells inside a custom-made perfusion chamber. Image: Courtesy of the Tissue Culture & Art Project (Oron Catts and Ionat Zurr)



Victimless Leather, Tissue Culture and Art Project, 2004. Image: Courtesy of the Tissue Culture & Art Project (Oron Catts and Ionat Zurr)

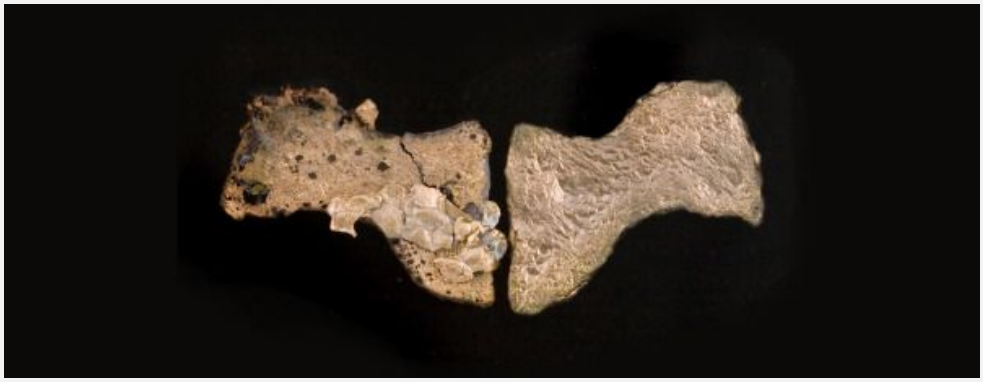


These tiny “wings,” called Pig Wings, are grown from pig-bone-marrow stem cells and illuminated with colored LED lights. Image: Courtesy of the Tissue Culture & Art Project (Oron Catts and Ionat Zurr)

The Semi-Living Worry Dolls, Tissue Culture and Art Project, 2012. Image: Krzysztof Miękus, courtesy of the Tissue Culture & Art Project (Oron Catts and Ionat Zurr)

Art: Cellular muses

By Mitchell Joachim



Pig Wings. ***Image: Courtesy of the Tissue Culture & Art Project (Oron Catts and Ionat Zurr)***

The old adage that art imitates life has been officially subverted. Now art literally *is* life.

In a handful of unconventional labs and studios around the globe, artists and scientists are hybridizing their expertise to create a whole new form: bioart. Their materials are living cells, proteins, tissues, and DNA. Their tools include electrodes, centrifuges, incubators, and sterile test tubes.

The purpose is to explore the possible expressions of life, manipulated, and to challenge us to consider the implications of manipulating life in the first place.

Consider the creations of SymbioticA, a lab/studio at the University of Western Australia that is among the field's most trailblazing pioneers. For the *semipermeable (+)* exhibit at Powerhouse Museum in Sydney in summer 2013, bioartists Guy Ben-Ary, Kirsten Hudson, and Mark Lawson created a piece based on the technology of induced pluripotent stem cells (iPS cells). Their piece was entitled "In Potentia." The technique they used (based on Nobel prize–winning science) was to take non-stem cells (e.g., foreskin cells) and re-program them into an embryonic-like state (sort of like "cellular amnesia") by applying a cocktail of genes to them. Induced pluripotent stem cells have generated a lot of interest because, like embryonic stem cells, they can be directed into different lineages, like neuron, muscle, bone, etc., but without the controversy that comes with being derived from embryonic tissue. In this case, the bioartists reprogrammed foreskin cells into iPS cells. Then they directed the differentiation of the cells into neurons and grew them into neural tissue that generated neural impulses. The artists encased this "biological brain" in a custom sculptural incubator, complete with a life-support system, an electrophysiological device, and a custom-made electrophysiological recording setup consisting of an array of micro-electrodes that measured neural activity. (They developed this in collaboration with Backyard Brains; see co-founder Greg Gage's TED Talk about making a "beatbox" from cockroach electrophysiological recordings.) The electrical pulses were then converted into digital signals and linked to a musical tone that sounded like a haunting soundscape. The goal? As the artists said, it's to challenge "Western culture's fetishisation of consciousness" by transforming foreskin cells into a "brain."

Andre Brodyk's artwork, "proto-animate^{tp20}," incorporates the APOE 4 gene known for its role in Alzheimer's disease. ***Image: Ian Hobbs***

Another bioartist in the same exhibit, Andre Brodyk, derived a code sequence of 158 DNA base pairs from the human gene APOE4 (Apolipoprotein E4). He was particularly interested in this specific gene because mutations in it have been associated with late-onset Alzheimer's disease. Brodyk used a particular area of APOE4 sequence, along with a gene for a glowing protein, to double-transform E. coli bacteria. "Transformation" is an engineering process by which bacteria, for example are altered to incorporate foreign genetic material (DNA) from another organism or environment. Brodyk used the transformed bacteria to draw red glowing images that gradually deteriorate and fade over time, in reference

to the pattern of memory loss seen in many who suffer from late-onset Alzheimer's, in which people tend to more accurately recall memories from the distant past but have difficulty recalling the immediate past. These images formed part of a poetic bioart installation.

"I'm an artist, I'm a storyteller," explains SymbioticA cofounder and director Oron Catts. As the "gap that makes most of us uneasy" between our cultural perceptions of life and what we are able to do to it through technology widens, Catts wants people "to be confronted and challenged."

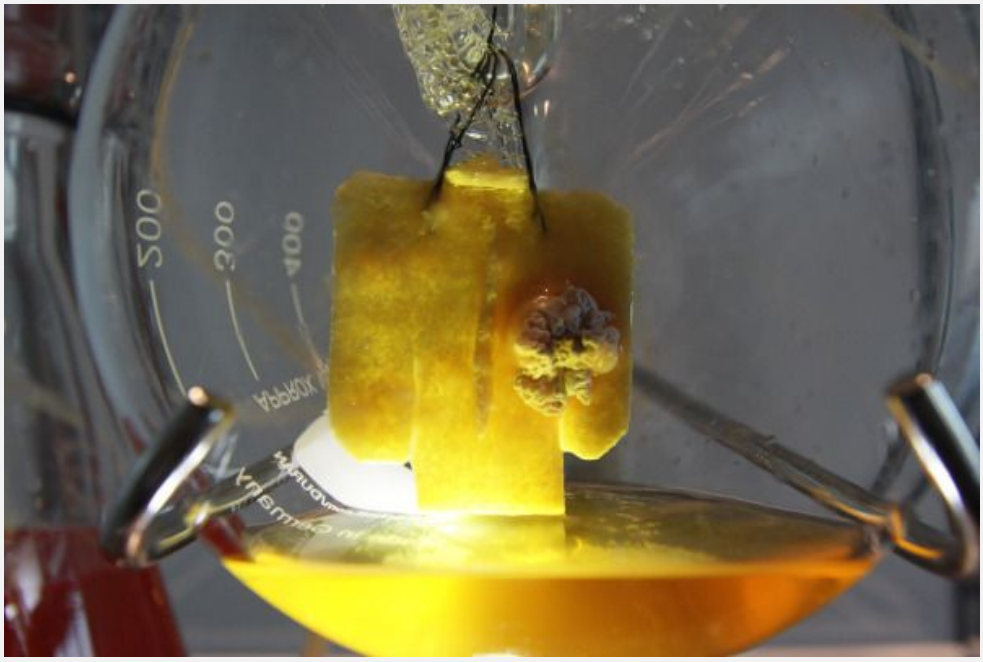
Catts and Ionat Zurr, his wife and fellow artist, have been experimenting in bioart for nearly two decades. They launched SymbioticA's progenitor, the Tissue Culture and Art Project, in 1996. That project's provocative works have included Pig Wings, three tiny sets of wings grown from pig-bone-marrow stem cells; experiments with lab-grown meat (see the chapter "Food: Ranch in a lab" for more about this project); semi-living "worry dolls," which were the first tissue-engineered sculptures to be exhibited live in a gallery context; and Victimless Leather (exhibited at the Museum of Modern Art), a miniature coat grown of cells inside a custom-made perfusion chamber. Living tissue is their medium — one that, given the right signals and nourishment, can grow into prescribed, fantastical forms.

This Semi-Living Worry Doll (left), seen alongside her model, is made from living cells and surgical sutures. The Pig Wings, seen here before painting, grew over nine months in a microgravity bioreactor, as bone tissue replaced the biodegradable polymer scaffolds that provided their structure. ***Image: Courtesy of the Tissue Culture & Art Project (Oron Catts and Ionat Zurr)***

Catts and Zurr are artists, but it was science that spurred them to this imaginative action. In 1997, a startling and unsettling image spread across the news. Researchers at the University of Massachusetts Medical School had grown cow cartilage cells into the shape of a human ear and implanted it onto a mouse's back. The mouse's blood vessels nourished the appendage, and the result looked like a horribly deformed mouse that had sprouted a human ear on its back. (The researchers later used similar techniques to grow replacement bones for patients' missing thumbs and a new chest plate for a boy born without cartilage or bone on his left side.)

“When we saw this image it was quite amazing for us,” Catts recalls. “One reason was because we’d reached that degree of treating life as a sculptural form, and also [because] it was ethically quite challenging.” Catts and Zurr decided that as artists they needed to participate in this radical redefinition of life, contribute to it, and subvert it.

SymbioticA — where resident artists and researchers collaborate within an academic biology department — was born in 2000. The lab/studio’s genre-bending identity blends the advantages of both art and science, freeing each from classic constraints. Here, artists use the trappings of biologists not only to reference and comment upon scientific ideas, but also to actively investigate their potentials. Researchers, for their part, pursue “curiosity-based explorations, free of the demands and constraints associated with the current culture of scientific research,” as the SymbioticA website explains.



This iteration of "Victimless Leather," a prototype of a stitch-less jacket grown from connective and bone cells, was exhibited at the Mori Art Museum in Tokyo in 2010. ***Image: Courtesy of the Tissue Culture & Art Project (Oron Catts and Ionat Zurr)***

So what does a creation such as Pig Wings do? It raises questions about the authorship and creation of life. At what point is art that has been created out of live mammalian tissue actually alive? Is it *any* portion of a person's complex living parts that define "life," or is it only a cohesive sentient body? Do humans have the moral certitude to deconstruct life-based organisms into disparate fragments for the sake of science? Or art?

Bioart itself raises ethical questions, which Catts and Zurr acknowledge. They endeavor to make the death of the artwork a public experience, and to

implicate the audience in the killing. We mess with life all the time, Catts suggests, but with art, we can take the time to think about what that really means.

Fundamentally, bioartists deliver an opportunity for the general public to approach the otherwise mysterious realm of genetic alterations and bioengineering. This invitation is essential, as many people have little comprehension of the intense bioethical disputes that happen chiefly in secluded meetings, in which private interests tend to win out over the needs of everyday people. Coaxing the public into an in-depth discussion of these issues is critical for the integrity and welfare of humanity — and for our prospects of using these dazzling technological developments well.

Terreform ONE's "Bio City Map of 11 Billion" visualizes the future of life on earth using an apt medium: life. ***Image: Courtesy of Terreform ONE***

According to many census sources, in the next 100 years we can expect the human population to reach 11 billion. Is this sustainable? At Terreform ONE, I started a data-visualization art project that directly confronts life and the human population's impact on the planet: the Bio City Map of 11 Billion. Highlighting the 25 densest cities on Earth, it displays the world population density in 2110 as a three-dimensional graph, on which the data are displayed in the form of bioluminescent E. coli bacteria, plotted and

grown inside petri dishes. We modified the bacteria with DNA that encodes fluorescent proteins found in sea anemones and jellyfish.

So, clustered across the map, glowing red E. coli under UV light represent future population projections, while green E. coli represent existing conditions in cities. We combined practices from biology (a dilution method to control the range of densities of E. coli populations in each petri dish) and architecture (stencils derived from CAD files that shaped the bacteria into specific geometries to display the current conditions), as well as cartography and urban planning. Meanwhile, on the back of the map, we used a photographic technique called bacteriography to underscore the zones of highest growth.

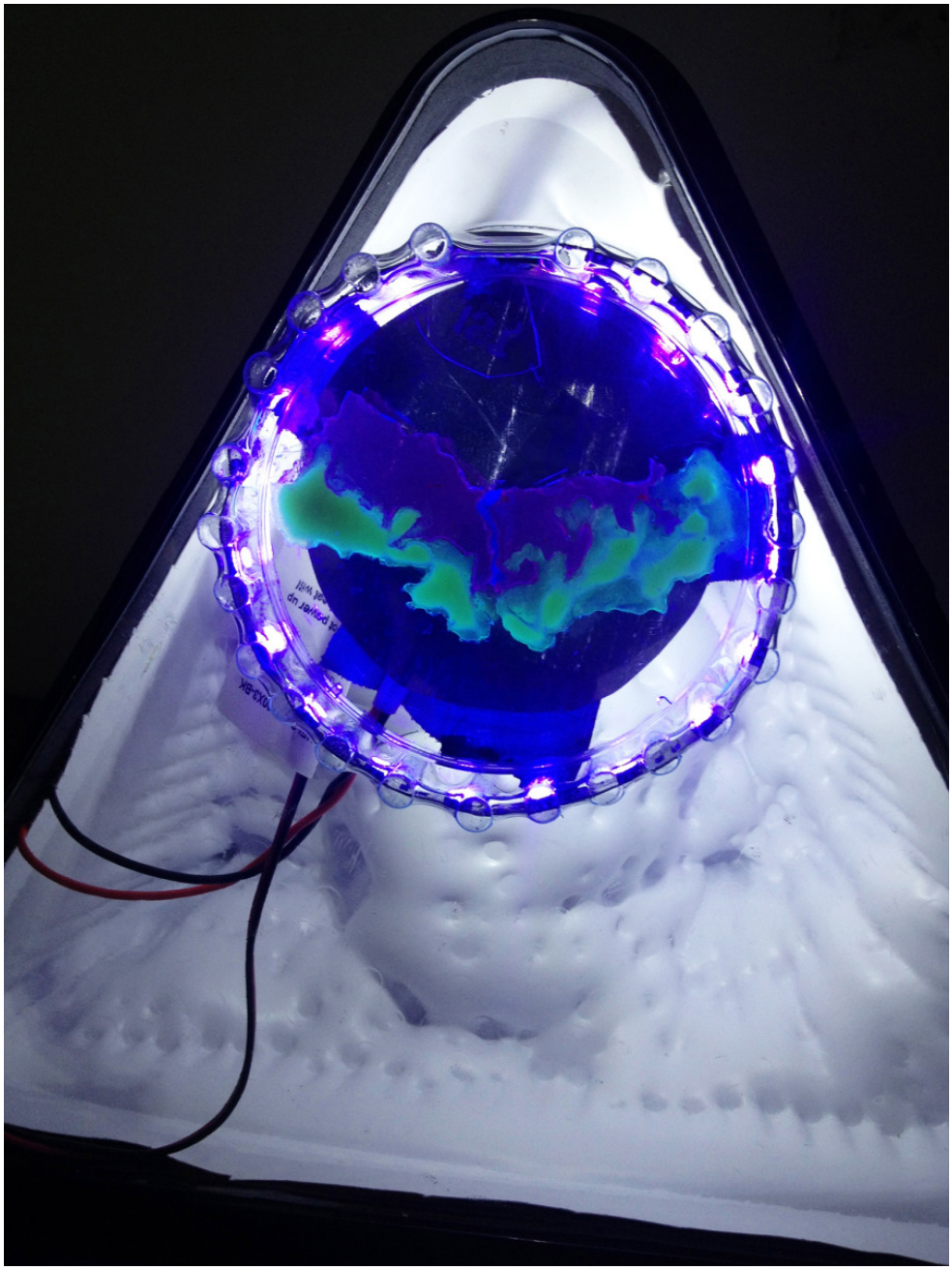
The map combines all the world's cities together as one continuous growth system. As human population expands, we see it as one single macro city spread across the continents. The project argues that most nations cannot view the effects of planetary population density through the lens of just one city or region; instead we aim to reveal the long-range effects of massive human population in areas of present and future urban intensity.

Rather than using computer code to mimic growth in nature, our method embodies the actual iterative vehicle of growth itself. Bacteria in this constrained form and under the right conditions behave almost identically to urban population patterns. In time, the mapping installation may illustrate patterns yet unobserved in typical digital computer models. It is this emergent and unfettered map of population that we wish to make into a spectacle. By using biolab-based materials, we expect to narrow the gap between idealized mathematical interpretations and observable events in nature.

While bioartists and designers undoubtedly aspire to bring the mostly inaccessible circles of science to the layman's conversation, I suspect that there's another factor that motivates their work: It is very satisfying to work

in the medium itself. After all, this is one of the first new mediums to become accessible in centuries, along with video and computational art. I can only suppose that numerous Northern Renaissance painters felt likewise when they were first exposed to innovative oil paint colors and textures.

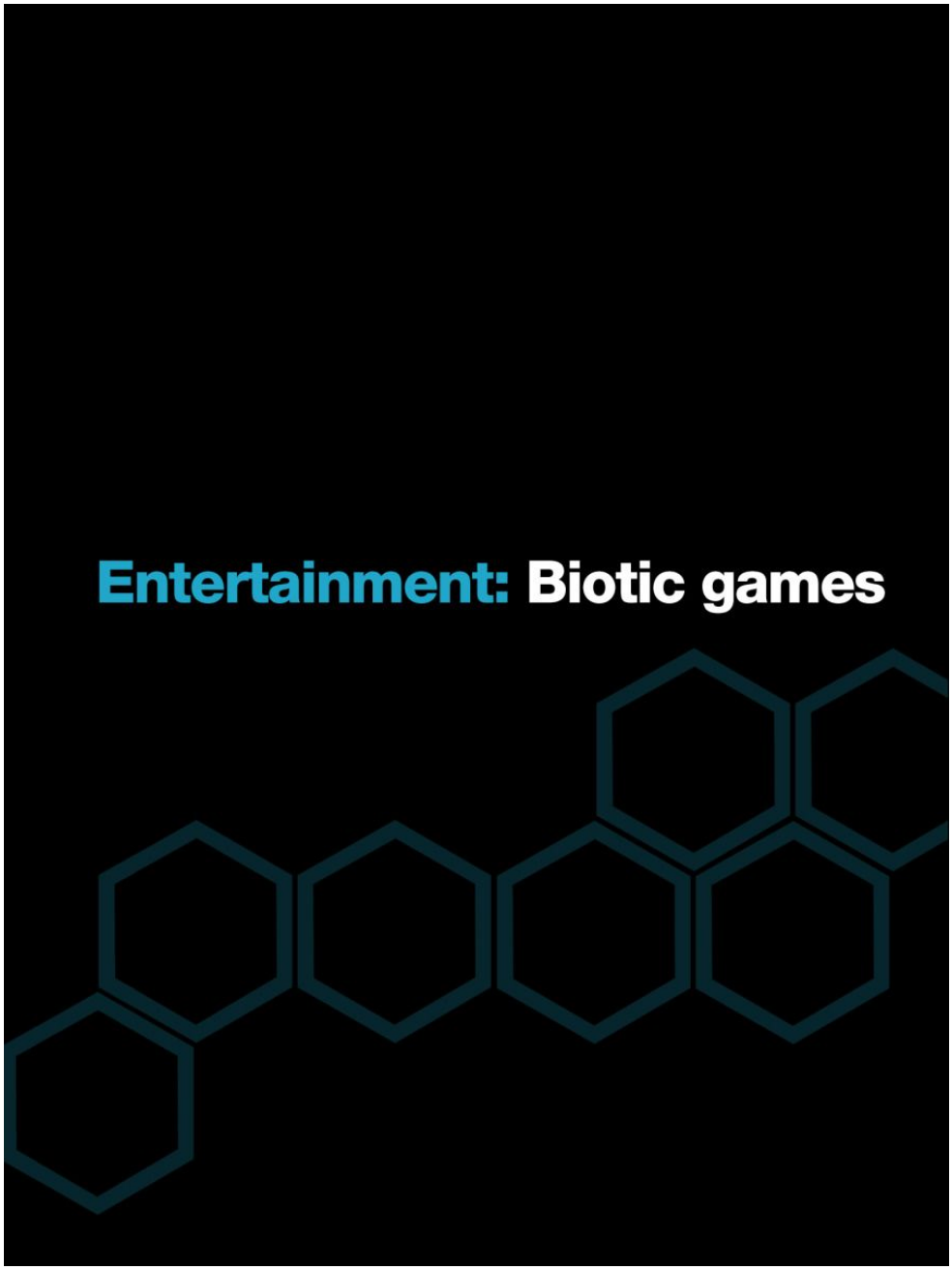
What will our successors do with the palette of life?



Bioluminescent green E. coli bacteria represent the human population density in a city of the future. This is the back side of an art piece, created by Terreform ONE and titled Bio City Map of 11 Billion, that highlights the 25 densest cities on earth a century from now. Image: Courtesy of Mitchell Joachim

Hamsa, made from found glass and the epithelial cells of a rabbit’s eye, Tissue Culture and Art Project, 1997. Image: Courtesy of the Tissue Culture & Art Project (Oron Catts and Ionat Zurr)

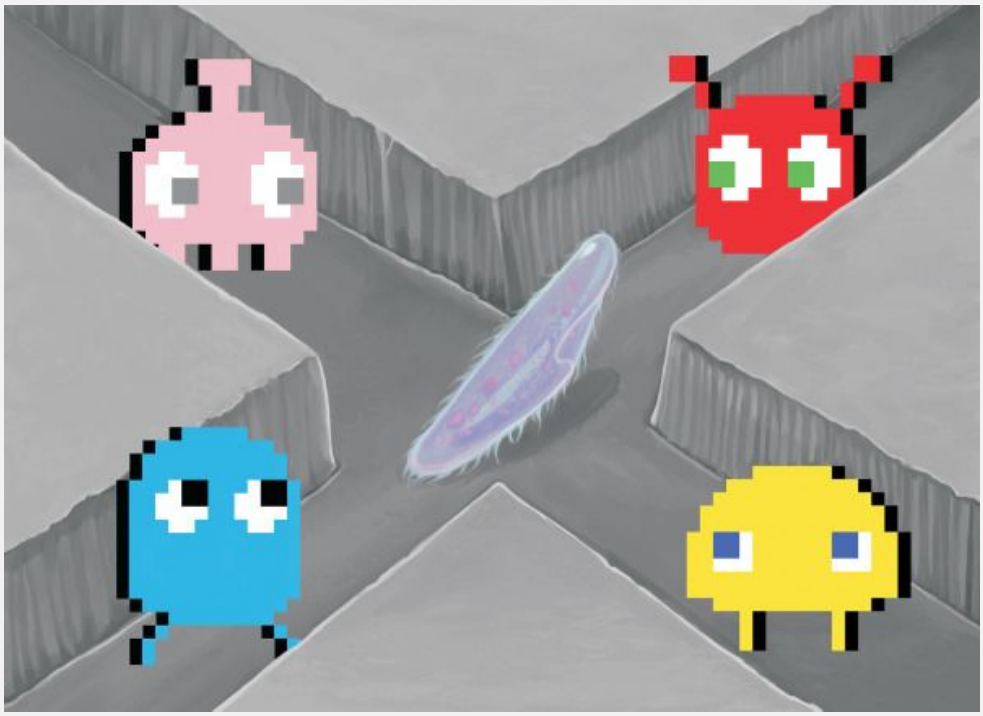
Visitors peer at In Potentia, created by bioartists Guy Ben-Ary, Kirsten Hudson, and Mark Lawson. The artists reprogrammed foreskin cells into induced pluripotent stem cells, then conditioned them to grow into neural tissue. The resulting “biological brain,” kept alive in its custom incubator, generates electrical pulses that are broadcast as an audible soundscape. Image: Courtesy of Guy Ben-Ary


Entertainment: Biotic games

Entertainment: Biotic games

By Nina Tandon

Console by console, level by level, computer-game designers have engaged in a decades-long quest to enrich the visuals and enhance the interactivity of games. From the multiplayer dynamism of *World of Warcraft* to the lush landscapes of *Flower* and *Skyrim*, we've come a long way from the days of Pac-Man. And now researchers in California have opened the door to a new world of gaming: Using microorganisms in the game design itself, they have made video games more life-like by making life part of the game.



This game mockup created by Ingmar Riedel-Kruse's team is inspired by Pac-Man. ***Image: Courtesy of Ingmar Riedel-Kruse***

The innovators are Ingmar Riedel-Kruse's bioengineering group at Stanford University. In traditional video games, players steer virtual characters on a screen. In these researchers' biotic game adaptation, the game pieces are instead living microbes contained inside a biotic game console, and the human player interacts with the microbes in real time, using a traditional game controller.

It works like this: The living characters are paramecia, unicellular microbes that are often abundant in stagnant basins and ponds. In the presence of physiological electric fields, a "galvanotactic response" is evoked — that is, the paramecia naturally swim toward the negative pole of the field. (I was very excited to discover that the fields they apply in their video game setup, 3 V/cm, are actually equivalent in strength to the fields I applied in my own research in cardiac tissue engineering!) In the game, the players' joysticks vary the spatial direction of the electric field applied to the microbes.

Riedel-Kruse's team has also explored using the process of chemotaxis, in which chemical gradients affect the direction in which the paramecia swim. The player's commands release chemicals into the console, causing the microorganisms to turn. The cells are imaged in real time with a microscope camera, the images are fed to a computer, and the paramecia's likenesses are then superimposed onto a virtual game board, where they interact with the game's characters and gamescapes.

Lovers of classic video games will find the virtual gamescapes that Riedel-Kruse has created familiar so far. In the soccer-like game *Ciliaball*, paramecia kick a ball into one of two goals; in *PAC-mecium*, paramecia forage for yeast while trying to escape a hunting zebrafish larva; in *Microbash*, the tiny organisms destroy bricks to free another cartoon

paramecium; and in *POND PONG*, inspired by the classic game *PONG*, each player uses chemicals to repel the paramecia toward the other player's side.

Riedel-Kruse's resume before developing biotic games almost presages the interaction between the "real" and "virtual" worlds that his games provide. After completing his university studies in solid-state physics in Germany, he worked as a business consultant at Accenture. Then he jumped into biophysics for his PhD at the Max Planck Institute, studying collective phenomena, molecular motors, and sperm cells. While a postdoc at CalTech, he got an offer for a faculty position at Stanford Bioengineering, and he began considering what he could engineer there using his particular expertise.

Then, one Sunday afternoon while still at CalTech, as he was reading a history of video games, Riedel-Kruse experienced what he describes as a "short circuit" in his brain. He was thinking about the parallels between game development and advances in science and technology, and in an *aha* moment, he asked himself: Why can't we make video games using modern biotechnology?

Ingmar Riedel-Kruse hopes biotic games will help raise awareness of the role microorganisms play in our daily lives. ***Image: Courtesy of Ingmar Riedel-Kruse***

So he started experimenting. Once he got to Stanford, Riedel-Kruse continued working on the problem with his students. They ran into a few dead ends, but then a student came up with the idea to use a galvanotactic response. They refined the electromechanics, tried several different species of microbe, and after a long, patient process of small successes, iterations, restarts, and tweaks — *eureka!* — they had a console that worked. Next they started integrating techniques of instrumentation, game design, and even education theory.

Riedel-Kruse explains that he hopes biotic games could pique players' interest in biology through the fun of "interacting with biological processes, without dealing with the rigor of conducting a formal experiment." As he writes in the *Royal Society of Chemistry Journal* in his 2011 paper "Lab on a Chip": "As playing pinball conveys a sense of physical concepts such as gravity, inertia, or spin, these paramecia games inform on micro-organismal behaviors."

In that educational spirit, Riedel-Kruse's team published their paper with open access (though they did file for a patent on their work). He wants others to explore and expand upon what they've begun.

And others already have. Biologist Ellen Jorgensen of Genspace, a community biology laboratory in Brooklyn, NY, featured a YouTube video of the biotic games in February 2011 and, as she says, "had it in the back of my mind for years to follow that up with a class." After software and hardware developer Geva Patz, who had taken Genspace's Intro to Synthetic Biology class, approached Jorgensen about teaching a class involving Arduino coding, the two joined forces to host a workshop in the spring of 2013 on how to build living video games. It was in this workshop that software engineer and mobile apps developer Keith Comito first heard the term "biotic games." He recalls being immediately captivated by the "beings in the machine, tiny organisms living their own lives, yet contributing to a grander process."

Just a week after the workshop, Comito joined forces with communications PhD student and Genspace member Sarah Choukah, as well as TED Fellow Oliver Medvedik, biologist and co-founder of Genspace, to build upon the Stanford technology using mobile phones. (Stanford's original model relied on a desktop-based Adobe Flash interface.) Comito recounted to me that after "a solid trifecta of all-nighters" fueled by "half-eaten boxes of pizza," they were ready to show their platform, "constructed of equal parts wood and rubber bands," at the

World Science Festival's Innovation Square. Comito describes the response as "incredible.… Adults and children alike were fascinated by the concept of playing with microorganisms" and "gave us myriad suggestions for improvements, such as a central electrode to gather paramecia together, illustrating how even children can contribute to fields such as biotechnology if given the chance."

In sum, he says, it felt like a magic trick. His trio has since made multiple improvements to their system, such as workarounds to prevent overheating and windproofing for exhibitions outdoors. They exhibited at NYC Resistor's 2013 Interactive show and at New York City's Maker Faire 2013. And, as Comito points out, "what has remained constant throughout every venue is the overwhelming interest and enthusiasm people have expressed."

The more Riedel-Kruse and others work with biotic games, the more their unique challenges become clear. Unlike the electronics in regular video games, microorganisms can't just be left alone; they must be cared for, otherwise they may not behave as well, or could even die. In addition, given the complexities of humanity's relationship with other life forms and the value we place on human education, research, and entertainment, it's not surprising that biotic games have already generated a vigorous bioethics debate. Are the organisms harmed? What kinds of interactions with organisms are considered positive, acceptable, or negative? And, of course, there's the question of free will: When the paramecia's direction is influenced by the applied electric field, do they lose their "freedom of choice"?

In a report on Mashable, for example, some commenters voiced concerns about the ethics of interfering with living things for entertainment, even on such a microscopic scale. Other readers pointed to the "obvious individual interests" of the microbes and expressed concerns with the games for nourishing "the idea that humans are not part of, nor do they

relate responsibly to the biological universe, but they master that universe." Still others, even if they find the games themselves not to be objectionable, raise the "growing question about the level of control that we humans have over the domain of life."

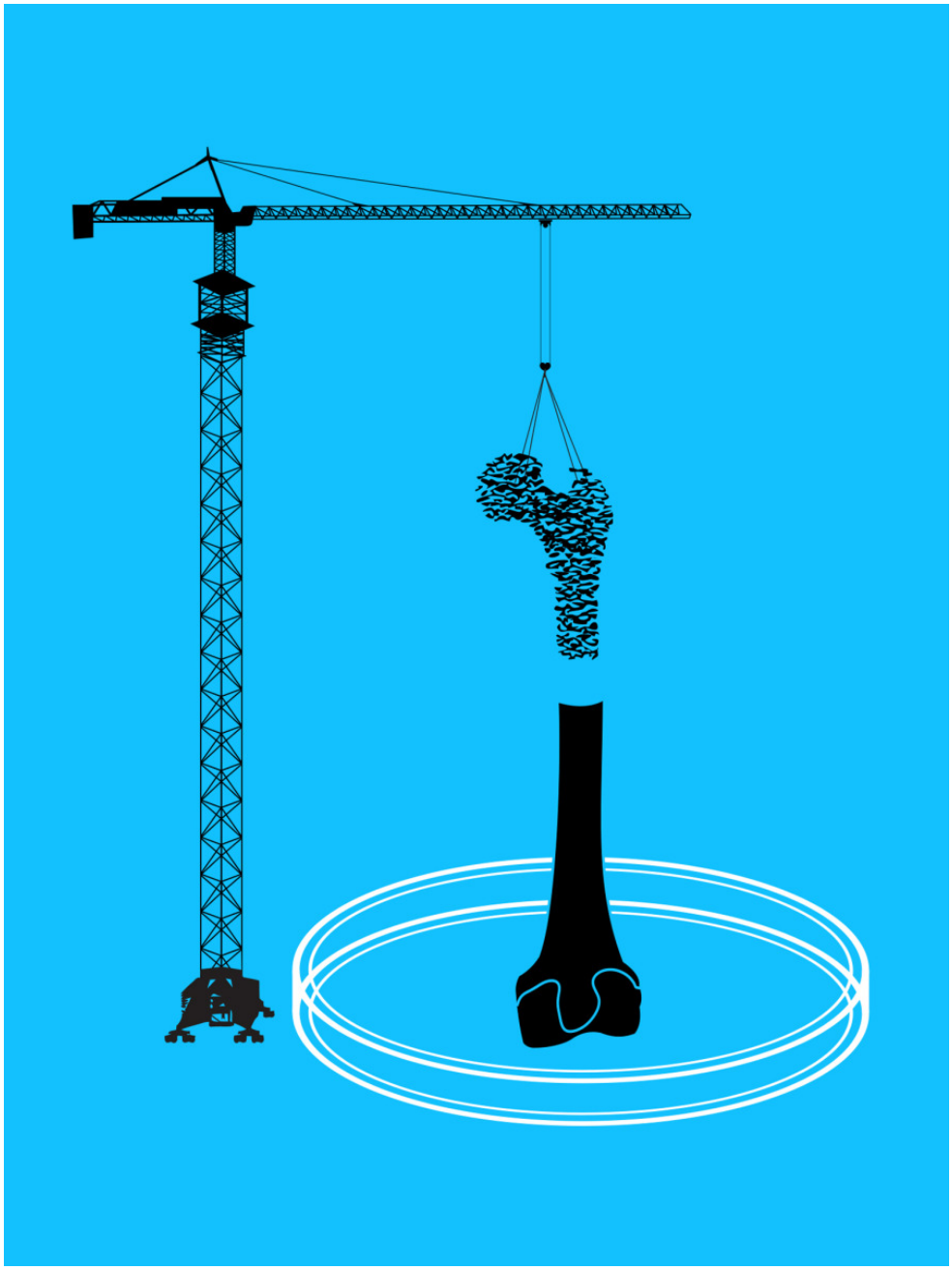
Along these lines, Comito admits to having been a bit stumped when a young girl asked him "if it hurt to control the paramecia, and if their movement was choice or compulsion." To her first question he was happy to answer no, telling her that paramecia do not have nervous systems. But in contemplating her second question, he wondered: "Even if a parameciumʼs galvanotaxis is naught but a consequence of ion channels reacting to voltage gradients, is this really that different, in terms of free will, than electrical impulses traveling throughout a brain?" He drew an analogy to human behaviors, such as traffic flows on city grids, which might "look like a compulsion too, from a suitable distance."

With these ethical ambiguities in mind, Riedel-Kruse says he favors game designs that are "pleasant, purposeful, and generating positive perspective versus scary scenarios." Itʼs important to him to educate the public about the microorganisms present in our everyday lives. We kill tens of thousands of bacteria, for example, when performing simple tasks such as cleaning our kitchens, bathrooms, or hands, or when we take antibiotics to cure diseases. Is this justified? How about for education, or for play? Like Oron Catts and the biosynthetic artists, Riedel-Kruse sees the debates around his work hinting at larger, more pervasive questions concerning societyʼs attitude toward life.

What will we encounter in the next level of biotic game design? Riedel-Kruse is excited to think of biotic games as a step toward a more generalized model of interactivity with biology, analogous to cloud computing. To get there, he aims to master interaction with a wider repertoire of different microorganisms, and engineer systems to keep them more stabile over the long-term, perhaps through automated temperature

control or feeding. Then he'd like to scale up the number of systems in parallel, and also allow for more versatility in the kinds of experiments that may be run with them, as a kind of "biology lab in the cloud." He imagines the capability to run experiments from your laptop, for purposes of real research or online learning.

As an apps developer, Comito (perhaps not surprisingly) is most excited about the possibilities of scaling up the technology to develop "massively multiplayer online games in which people communicate with each other via other living creatures, self-reflexive systems in which organisms control themselves in ways they never have before, or generative musical applications in which the composers are single cells." He is also keen on "provoking thoughtful dialogue regarding ethics, free will, and what it means to be human among the various forms of life that inhabit our world." It is his hope "that our game and others like it will go beyond even these questions, and invite people to consider a future where we find a way to cooperate with organisms of every scale. Such an approach, characterized by partnership with, rather than subjugation and destruction of, nature has the potential to foster the sustainable future all of us want, and can achieve."



Afterword

A world of possibilities opens up as we begin to consider cells as technological partners, collaborators in future technologies.

We'd like to imagine, going forward, even more combinations of the work we've explored here — Ingmar Riedel-Kruse's electrical fields controlling the direction in which Suzanne Lee's *Acetobacter* spin their threads as living looms, or SymbioticA engineering new tissue scaffoldings that inspire the architectural work of Terreform ONE, or Modern Meadow collaborating with EpiBone to grow genuine T-bone steaks.

But we also look forward to technologies further afield of our own imagination, because our work in tissue engineering and bio-architecture has taught us enormous respect for the power of nature. As much as we've learned as a species about biology, architecture, artificial intelligence, and systems engineering, we can only dream of coming close to nature's ability to do so much with so very little. Why? Because over billions of years of evolution, biology still knows more than a few tricks that scientists and engineers don't. While physicists create quantum effects by constructing experimental setups under vacuums and ultra-low temperatures, nature — warm and messy — is filled with marvels where quantum processes are likely at work, including bird navigation and the inner workings of photosynthesis. Gram for gram, the tiny mitochondria in cells convert energy 10,000 times more efficiently than the sun. And when living systems are injured, they show a remarkable ability to repair.

And so it seems that the paradigm shift that begins by asking "Can we do XX with cells?" is likely to be a powerful one. Nonetheless, scanning a list of industries, certain items, like administrative support services and air transportation, banking and broadcasting, insurance, leisure, postal service, and wholesaling, do nonetheless come to mind as examples of industries that might be immune. In these cases, the argument could be made that

machines or humans may continue to handle tasks so well that it would be hard to imagine cells doing them better.

And yet, given how cells are being engineered to produce novel biofuels, how bacteria may be employed to mine salt water for minerals, or how viruses or cells may be used to develop novel electronics (either inorganically or biologically based), it's hard to imagine any future industry that might be impervious to disruption.

Looking ahead, therefore, it will be increasingly important for us as citizens to be able to tackle the new questions that will undoubtedly arise when deploying and manipulating the technology of life.

For example: Are we playing God? This is a provocative and unavoidable question. Should we consider tinkering with the genetic material and/or behavior of viruses, bacteria, plants, and/or animals equally? And, if our human cells can be maintained outside the body, and our human bodies are actually housing more bacterial cells than human cells, what exactly does it mean to be human, anyhow? As with any powerful technology, there is as much ambiguity and potential danger as promise.

When thinking about how, as a population, we might better prepare ourselves for the unknowns ahead, many (this book's authors included) have advocated for increasing the familiarity of the general citizenry with science — our culture's collective "scientific literacy" — via DIY bio, citizen science, and increasing access to and interest in STEM education. The idea being that the better we as a population understand the technologies in question, the better we will be able to evaluate, debate, predict, and prepare for various scenarios.

However, when linking "What we can do?" with "What *should* we do?" we would be remiss not to note the important roles that the disciplines of philosophy, anthropology, linguistics, and especially history will likely also play in helping us develop moral frameworks to meet the challenges ahead.

Many of these situations aren't quite as new as we'd perhaps think; the first "bioreactors" date back to breweries, the first forays into genetics date back to captive breeding, the first online romances and internet banking frauds date back to the first telegraphs of the Victorian era (see the terrific piece "The Victorian Internet" for more about the parallels between the invention of the telegraph and the internet). Even our challenges around identity and ownership of cellular material echo past discourses around blood donation, which began in the 1600s, and, more recently, organ donation, surrogate parenthood, and in-vitro fertilization.

It's a human process to think about these challenges, but we've been up to the challenge so far. It just can't be outsourced; it's all hands on deck, and it's likely to be an adventure. If we can just learn to speak cells' language, we can coax them into doing so much — saving lives, conserving the planet, inspiring unprecedented works of art, providing joy, and, above all, continuing to command our wonder.

About the authors

Nina Tandon is CEO and co-founder of EpiBone, the world's first company growing living human bones for skeletal reconstruction. She obtained a Bachelor's in Electrical Engineering from the Cooper Union, a Master's in Bioelectrical Engineering at MIT, a PhD in Biomedical Engineering, and an MBA at Columbia University. She is a TED Senior Fellow, a Staff Associate Postdoctoral Researcher in the Laboratory for Stem Cells and Tissue Engineering, Columbia University, and Adjunct Professor of Electrical Engineering at the Cooper Union. Her PhD research focused on studying electrical signaling in the context of tissue engineering, and has worked with cardiac, skin, bone, and neural tissue. Nina spent her early career in telecom (Avaya Labs) and transitioned into biomedical engineering via her Fulbright Scholarship in Italy, where she worked on an electronic nose used to "smell" lung cancer. After completing her PhD, she consulted at McKinsey and Company, but since 2010

she has continued her work in tissue engineering. Nina has published 10 journal articles (cited >300 times, H=9) and six book chapters, and she has three patents. She's been published in *Nature Protocols* and *Lab on a Chip*, has spoken three times at TED, and in 2012 *Fast Company* Magazine named her one of their 100 most creative people in business. In her spare time, Nina enjoys practicing yoga, playing with puppies, running slowly, baking cookies, laughing with her niece, and avoiding folding the laundry.

Mitchell Joachim is a co-founder of the nonprofit Terreform ONE. He is an associate professor at NYU and EGS in Switzerland. He was formerly an architect at Gehry Partners and Pei Cobb Freed. He is a TED Senior Fellow and has been awarded fellowships with Moshe Safdie and Martin Society for Sustainability, MIT. He was chosen by *Wired* magazine for "The Smart List: 15 People the Next President Should Listen To," *Rolling Stone* magazine honored him in "The 100 People Who Are Changing America," and *Dwell* magazine featured him in "The NOW 99" in 2012. Mitchell has won many awards, including AIA New York Urban Design Merit Award, Victor Papanek Social Design Award, The Zumtobel Group Award for Sustainability and Humanity,

TED is a nonprofit devoted to “Ideas Worth Spreading.” It started out, in 1984, as a conference bringing together people from three worlds: Technology, Entertainment, Design. Since then its scope has become ever broader. Along with two annual conferences — the TED Conference in Long Beach and Palm Springs, Calif., each spring, and the TEDGlobal conference in Edinburgh, Scotland, each summer — TED includes the award-winning TED Talks video site, the Open Translation Project and Open TV