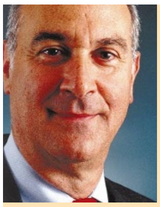
areas: nanotechnology and nano-science; tissue engineering (which includes biomaterials and, more specifically, biomimetics, biosensors, organ-culture systems and tissue regeneration); bioimaging; and bioinformatics and computer simulations, which is only now being used in medical teaching.

According to Swaja, BECON, or something like it, will continue to be the focus of activities at NIH for the near future. There is appropriations language that indicates that an Office of Bioengineer-ing/Bioimaging, reporting to the director of NIH, will assume responsibility and direction of BECON.

In the mid-1990s, Nerem believed that it was enough to integrate BME into the various institutes at NIH. Over the past five years, however, "I've become convinced that unless you are an institute at NIH, you're a second-class citizen — the power really resides with the institute directors". For Swaja, the current environment is one in which there are opportunities for engineers and physical scientists to show what they are capable of doing and to demonstrate that they can work with the biomedical and imaging community to foster this transdisciplinary field.



Creative fusion of many minds

Working mainly with synthetic biomaterials such as lipids and polymers, as well as functional derivatives that involve carbohydrates and other molecules, James Baker (left) and colleagues at the University of Michigan, Ann Arbor, on the Unconventional Innovations Program, are creating devices that will engineer cells on a nanoscale. Polymers, for example, can make 'smart delivery' systems for drugs and genes. They target a malignant cell, release the drug or gene and report any effects.

The participation of people from liberal arts and sciences, chemistry, physics, engineering and toxicology is crucial, says Baker, who is head of allergy and immunology in the medical school as well as leading the university's centre for biologic nanotechnology ."All of us have come to this, if I can put it politely, 'ad hoc', training ourselves," he says. "There is a lot of self-selection in this area because people who don't want to interact won't show up." He explains that his team can define something experimentally and then say to the synthesis people: "We see this structure–function relationship, how can we magnify that?" The toxicologist might then say the compound has a bad history *in vivo*, vetoing that line of thinking. "It's remarkable how you can overcome problems or prevent yourselves from going down blind alleys, if you have everyone together."

Baker and his colleagues would like to see a larger institute based on their current centre. "One of the really important things is that you get people who are cross-trained and understand the engineering side, the materials science side and the analytical side, as well as the biology and the toxicology," he says. **B.H.**

Unconventionally NIH

BME feeds into a better understanding of cancer, as well as better treatment and diagnosis, says Carol Dahl, one of the National Cancer Institute's (NCI's) two primary representatives to BECON and director of the Office of Technology and Industrial Relations at the NCI. To capitalize on this opportunity, the NCI has been an active participant in BECON and its initiatives, as well as developing NCI-specific programmes to nurture technology development and BE.

These have been created to smooth the problems technology and BME have encountered in gaining support from what is primarily a hypothesis-driven research focus at the NIH, says Dahl. The Phased Innovation Award, developed by the NCI, allows people to move rapidly from a feasibility stage to a development stage (see NCI in the 'Institutions' panel on page 466). There is also the Unconventional Innovations Program (UIP), an NCI programme that invests in long-term, high-risk and high-impact areas.

The NCI takes a more active scientific role in the UIP, which announced its first five awards last autumn (see 'Institutions' panel for new announcements). Investigators

Exploring the territory in tissue engineering

A disagreeable side effect of longer lifespans is the failure of one part of the body — the knees, for example — before the body as a whole is ready to surrender. For decades, bovine collagen and other materials have been used for repairs, but it is now possible to use human material to restore damaged or worn-out tissue.

Tissue engineering, which occupies the fertile area between materials science and biology, has its roots in cell biology, immunology, chemistry and bioengineering, but it's not uncommon to see apparently unrelated fields thrown together. Glenn Booma, a director of 'outcomes research' at Genzyme Tissue Repair, in Cambridge, Massachusetts, cites a laser-optics physicist joining a team of physiologists working on a process for solidifying an injected substance by photoactivation.

A working knowledge of more than one branch of science could be very helpful. A postgraduate education is necessary for most research jobs, although a bachelor's degree may suffice in technical support roles. Equally important is an ability to work and communicate with people from other fields, and to keep a global perspective even when concentrating on the details of a project. In a company environment the ability to shift gears rapidly is also a must. If a project turns out not to work, or if a competitor files a patent, says Booma, "then the company is going to want to rapidly reassign you to something new".

Your fate is out of your hands

Nancy Parenteau, chief scientific officer at Organogenesis, a company making wound-repair products in Canton, Massachusetts, says that the cross-fertilization between disciplines is part of the fun. "You should be able to pick up some of the other specialty's language, appreciate their issues and how they go about doing things." The hardest thing for scientists to come to grips with, she says, is that a project does not depend solely on any individual's work, even if it's an outstanding achievement. "In a way, your fate is no longer in your own hands. That can be difficult to become comfortable with."

Non-scientific factors can impinge on careers in a small company. Booma says that none who saw the seminal paper on cartilage defects in rabbits in 1984 would have dreamed it would take until 1997 to get approval from the Food and Drug Administration and commercialize their Carticel product. Now, however, investors do know, so even small companies with impressive technology platforms and good intellectual property may be bought up, as his company was in 1994 when, as Biosurface Technology, it joined Genzyme. "Genzyme and Organogenesis have shown that tissue-engineering products are effective and marketable, but now we have to show that they can be profitable," he says.

Those contemplating a career in tissue engineering should also be politically aware. Positive public attitudes translate into public support, whereas a negative impression can mean restrictive legislation, loss of funding and, in extreme cases, physical attacks on labs and personnel. Scientists should engage in discussion and clarify issues. Parenteau deplores the speculation that occasionally appears in the media as being harmful to the field and misleading and frightening to the public. Even preliminary or limited results can be misinterpreted, raising false expectations for many and confusing the few for whom a breakthrough will truly bring help. "The propose the work and the NCI then negotiates with them and engages them under contract for the next few years. The five most recent contracts amount to nearly $11.3 million over three years.

James Baker, principal investigator for a group receiving $4,427,711 at the University of Michigan at Ann Arbor, will use the grant to develop nano-scale devices for detecting and treating cancer. Although there was a lot of input from the NCI, says Baker, "I have to give them their due. They are setting their priorities, but are allowing us to direct towards those priorities in a way that makes the most sense given the specific technology."

One common aspect among the BE and BME groups that *Nature* has spoken to is that they have organized their departments and divisions in ways that are administratively more challenging in order to gain an intellectually richer environment.

At MIT's division of bioengineering and environmental health, most faculty members hold either 'dual' or 'joint' appointments. "We believe that joining the science of biology with engineering is so important that you do not want to do it in an isolated structure that departments often are," says Lauffenburger. Dual appointments are shared equally with the other department in terms of teaching and service duties, as well as hiring, promotion, tenure and salary review. Joint appointments are positions in which these areas are governed by another department. The departments sharing BEH faculty include chemical, mechanical and electrical engineering, as well as computer science, materials science, biology and chemistry. "Our strategic plan calls for adding another 10 to 12 faculty over the coming five to seven years, from a combination of internal transfers and external hiring," says Lauffenburger.

At the graduate level, BEH offers PhD degrees in bioengineering and toxicology. At the undergraduate level, there are minor bachelor degrees in both biomedical engineering and environmental health, and a mechanical engineering degree is in the planning stages. The goal of the graduate-level programmes is to define these disciplines, whereas the undergraduate programmes will connect traditional disciplines with problems and approaches in biotechnology and human health.

At the Georgia Institute of Technology (GT), a joint biomedical engineering department is being put together with the medical school at nearby Emory University. According to Nerem, the department will have space on both campuses, with two-thirds of faculty appointed through GT and one-third through Emory. Once appointed, they will act as a single department. A new PhD degree is going through the approval process, which will be a BME degree offered jointly by GT and Emory.

Over the next seven or eight years, Nerem estimates that GT will be hiring some 15 faculty. There are already seven faculty with primary appointments in the department, he says. They did not want simply to move the existing faculty into the new department. "I think it's important that mechanical engineering at GT is still strong in biomedical research," he says. A few of the faculty have moved into this new department, but most will be new faculty.

Generally speaking, Nerem thinks that "some of the best engineering students have an interest in biology and are excited about bioengineering". Getting biology students interested in engineering is not quite so easy, he says. The problem, he explains, is that many people who do biology as an undergraduate shy away from quantitative courses. Too often biology majors do not study calculus or ordinary differential equations.

According to Lauffenburger, bioengineering is in the very early stages of development in terms of both its definition and the identification of career opportunities for its students. "I think that it's a crucial challenge for us to help industry understand what we're trying to accomplish with this education, and how people like this will be useful to hire alongside the chemical, mechanical and electrical engineers they have traditionally hired," he says. **Brendan Horton**

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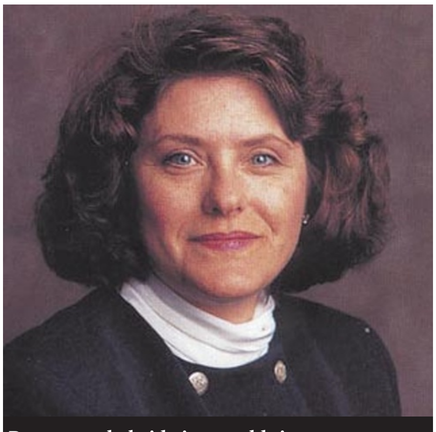
companies themselves, which have to go out and raise money in order to survive, have a need to play up the bright side and not dwell unduly on the limitations," Booma adds.

New university training programmes and faculty positions and public funding initiatives are good news for hiring trends. In the United States, the National Institute of Standards and Technology's Advanced Technology Program has funded product development in tissue engineering for the past two years with grants of $2–5 million. Last year the NIH set up a tissue-engineering working group, and may set up an institute. Says Gail Naughton, president of Advanced Tissue Sciences in La Jolla, California, "Tissue engineering used not to fit into any single category, but now the agencies are actually out there soliciting grant proposals. This is making a big difference." She foresees career opportunities at various levels.

With growing institutional support, the outlook for the next 10 to 15 years is rosy. Improvements in technique and understanding will speed up progress. For example, Naughton thinks that the question of embryonic stem cells will be obviated by improvements in separations and culturing.



Parenteau: hybrid vigour adds interest.

"Our growing understanding of how to keep cells functioning outside the body will allow us to manipulate them so that they can become almost any cell type," she predicts, citing recent publications (for example, see Jackson, K. A. *et al. Proc. Natl Acad. Sci. USA* 96, 14482; 1999) showing that human cells collected from bone marrow can be transformed into fat, bone or cartilage cells.

Parenteau worries about speculative media coverage, but agrees that what's true now for skin products will probably become reality for vascular, neurological, bone, tendon and corneal tissue. The immunological barrier is a major challenge, but inroads are being made. For example, the Boston company Diacrin has worked out how to mask animal cells so that they can be transplanted into humans; a product made from porcine neural cells to treat Parkinson's disease is in phase II trials. A decade ago neural regeneration at trauma sites was thought impossible. Today it is known that, if scarring is kept at bay, neural tissue has a great capacity to regenerate.

The role of genetics will also increase as tissue engineering is combined with gene therapy to enhance the growth of implanted tissue. The discoveries of genomics will affect the field, such as the as-yet unknown signals that differentiate between normal growth and healing. "Especially in a young field the opportunities are broad and abundant. It is exciting to participate in a field that is being born. Few of us get to do that," says Parenteau. **Potter Wickware**

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