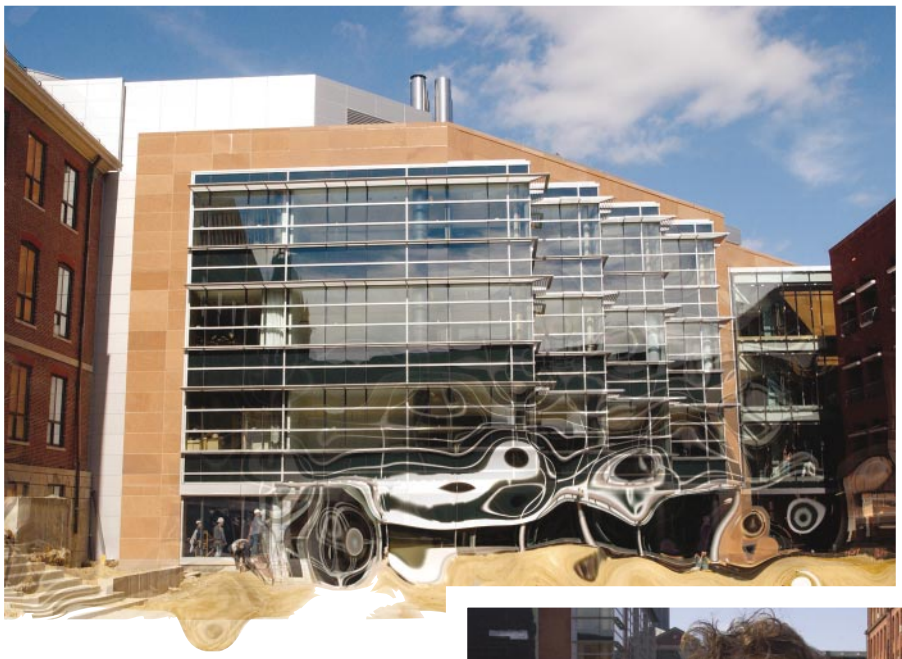
# Harvard's melting pot

At a new genomics centre, ethologists are rubbing shoulders with computer scientists, chemists and mathematicians. Peter Aldhous visits a bold experiment in multidisciplinarity.



BAUER: MARTHA STEWART/JON CHASE/HARVARD UNIVERSITY: MARCUS HALEVI

**Shape of things to come: Doug Melton (below) persuaded Andrew Murray (right) to take on the role of director at the new Bauer centre (above).**

Andrew Murray is used to standing out from the crowd. In the early 1990s, while rising though the academic ranks at the University of California, San Francisco (UCSF), his eye-catching array of facial piercings made him an instantly recognizable figure on campus.

More importantly, his elegant experiments into the checkpoints controlling cell division built his reputation as one of the leading biologists of his generation, and ensured that the brightest students beat a path to his door.

Now in his mid-40s, and having shed the facial metalwork, Murray is director of Harvard University's Bauer Center for Genomics Research, which celebrated its inauguration on 4 March. He is embarking on what could be his most ambitious experiment yet.

The Bauer centre aims to reap a post-genomic harvest by uniting physicists, mathematicians, chemists and computer scientists with a spectrum of biologists. They will work on collaborative projects dependent on high-throughput genomic analyses.

No one is quite sure what to expect yet, but there is a palpable sense of excitement among the centre's recruits. "This place, to me, looks like Disneyland," says mathematician Steve Altschuler.

As biologists struggle to make sense of reams of genomic data, many are wondering about enlisting the help of colleagues from other disciplines. But while most are still musing on the meaning of multidisciplinarity, the Bauer centre is pressing ahead. Its strategy: hire a diverse and talented group of young scientists with a yen for collaboration, and throw them together. "We'll put them in a box and we'll shake really hard and hope that some fun things happen," says Murray.

Murray didn't actually plan to become the centre's director. He has always urged biologists to think in an integrated way, rather than simply filling in the molecular details in particular systems. But as the new millennium dawned, his growing interest in evolution was constrained at UCSF, which as a medical school could not indulge such diversions. So, in the summer of 2000, he moved to Harvard, setting up a lab to investigate evolutionary questions, in addition to his existing research in cell biology. One of his current projects, for instance, aims to simulate the origin of new species by applying pressures mimicking natural selection to laboratory populations of yeast.

## Blazing a trail

As Murray arrived, the nascent Bauer centre was lacking a director. The original choice, Dari Shalon, a specialist in the production of DNA microarrays for analyses of gene expression, left when it became clear that his focus on technology development was at odds with the centre's wide-ranging mission. The centre's academic 'godfathers', developmental biologist Doug Melton and chemist Stuart Schreiber, who uses small molecules to disrupt gene function, set about convincing Murray to take over the reins. "After some trepidation, I said yes," says Murray.

Given the ambitions that Melton and Schreiber have for the Bauer centre, Murray's trepidation is understandable. Asked to explain the centre's mission, Melton leaps to his feet and scribbles the word '*Leptothorax*', a genus of ant, on his blackboard. Melton's own research may be focused on stem cells within the pancreas, but he evidently has more than a passing interest in the biology of social insects.

Melton starts explaining the difference in morphology between different castes in *Leptothorax* ants. He then draws a squiggly path, as might be taken by a foraging worker. When a worker finds a food source, others are recruited and soon begin taking a more direct route. Melton chalks a straight line back to the colony's nest.

To understand *Leptothorax* biology, Melton argues, you must study the mechanisms of genome regulation that differentiate workers from other castes. You need expertise in behavioural biology, and the analytical skills to determine how creatures with simple nervous systems can collectively arrive at the solution to a complex navigational problem. Melton turns round from the blackboard:

"That's why we need the genome centre!"

The Bauer centre doesn't yet have a multidisciplinary team working on the molecular mechanisms that underpin ant foraging, but in Hans Hofmann it has recruited a biologist interested in comparable conundrums.

Hofmann, a neuroethologist who joined the centre after completing a postdoc at Stanford University in California, studies cichlid fish from Lake Tanganyika in East Africa. These include a species called *Astatotilapia burtoni*, in which males can either defend nest sites to attract mates, or be non-territorial.

The two types of male look and behave very differently: territorial males are aggressive, have mature testes, and are yellow or blue with distinctive markings including dark stripes on their foreheads. Non-territorial males do not produce sperm, are sandy coloured, and school with groups of females.

Despite these profound differences, males switch readily between the two forms. At any one time, around a quarter of males are territorial, but there is a steady turnover — and any disturbance can overturn the *Astatotilapia* social order. For instance, if a hippopotamus churns up the lake bed, some territorial males will revert to the non-territorial form while previously non-territorial males seize their chance to reproduce.

## Fish and chips

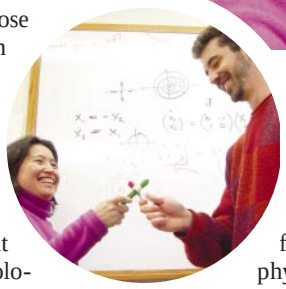
Hofmann wants to understand the shifts in gene expression that lie behind these changes, and how they are influenced by environmental and social cues. On each side of the *Astatotilapia* brain sit two populations of cells that secrete two hormones — gonadotropin-releasing hormone and somatostatin — known to be crucial to the shift to territoriality. Hofmann's studies involve dissecting out the tissue containing these cells, isolating messenger RNAs from the samples, and exposing them to DNA chips carrying the sequences of cichlid genes. By seeing where on the arrays the RNAs bind, he can tell which genes are active.

BAUER CENTER: MARTHA STEWART/C. RUSSELL FERNALD

**Hans Hofmann hopes to discover why these male cichlid fish look and behave differently.**

Working with the latest DNA microarray technology and expertise is crucial. But so, too, is the proximity of mathematicians such as Altschuler and his wife, Lani Wu. Hofmann suspects that making sense of his data will require a new conceptual framework that may only emerge from collaborations with people well versed in tough analytical problems. Altschuler and Wu's previous experience, for instance, includes working for Microsoft, developing algorithms for such tasks as separating background noise from audio signals — vital for the development of speech-recognition software.

Many former colleagues in behavioural biology remain flummoxed by Hofmann's residency at a genomics centre. But to him, this just shows that the gulfs between the various traditional disciplines within biology are greater than those dividing the diverse collection of scientists who have joined the Bauer centre. "Genomics, as I see it, will lead to a renaissance of organismal biology," says Hofmann. "There are still a lot of organismal biologists who do not see that and still a lot of molecular biologists who do not see that."



**Mathematicians Lani Wu and Steve Altschuler are adding a new dimension to the Bauer centre.**

CHRIS SANDER

Some recruits have faced a steep learning curve. Altschuler and Wu have spent much of the past few months sitting alongside undergraduates in molecular biology lectures, and learning basic lab skills. They say this is crucial if they are not simply to become a service department for colleagues who want to analyse the function of networks of genes and proteins. "It's not just analysing the data; it's influencing the experiment upstream," says Wu. "Having your own bench space helps."

## Battering ram

Altschuler says that a move into biology isn't for those who get their kicks by dazzling their peers with mathematical pyrotechnics. His and Wu's contribution may lie as much in introducing mathematical logic into the design and analysis of experiments as in devising sophisticated algorithms. "If we just contribute a couple of useful differential equations to a project, that's OK," says Altschuler.

Hofmann, Altschuler and Wu are just three of the centre's eight 'genome fellows', who were all selected for their willingness to collaborate and their multidisciplinary outlook. Laura Garwin, the centre's director of research affairs and formerly *Nature*'s North American editor, describes the fellowship programme as a "battering ram" that will assault the walls dividing scientific disciplines. The fellows will be appointed for three to five years, each running a research group of up to three people.

Murray is delighted with the first crop of fellows. But recruitment remains a high priority. Three vacancies remain, and Murray is especially keen to fill one of them with a theoretical physicist. "They have a relentless tendency to reduce problems to the fundamentals," he says.

Having got his cast of fellows together, Murray intends to take a hands-off approach to managing their work. He describes the Bauer centre as an "artists' colony", contrasting it with the "paramilitary organization" of explicitly goal-oriented genome centres. Nevertheless, there will be incentives to encourage fruitful interactions, including a pot of money specifically for collaborations between the fellows.

The Harvard authorities are betting on the Bauer centre spawning collaborations across the university more generally — and, in this spirit, the centre has opened its doors to Harvard scientists wanting to perform genomic analyses. The building into which the centre moved earlier this month was financed by a $25-million donation from investment manager and Harvard alumnus Charles 'Ted' Bauer, but its initial $6-million annual operating budget comes from the university's own reserves. It is part of a wider initiative to invest in new scientific developments, after concerns were raised about Harvard's future ability to compete at the very highest level.

Murray, who is aware that ambitious experiments can sometimes end in failure, has some reservations about the expectations being pinned on the centre. "There's a lot of hope being placed into what is still a fairly frail vessel," he says. But his new recruits are finding it hard to contain their enthusiasm. "It's the place of the future, we hope," says Hofmann. ■

**Peter Aldhous is *Nature*'s chief news and features editor.**

**www.cgr.harvard.edu**