The European Molecular Biology Laboratory Magazine

Issue 81 Autumn 2014

EMBL etc.

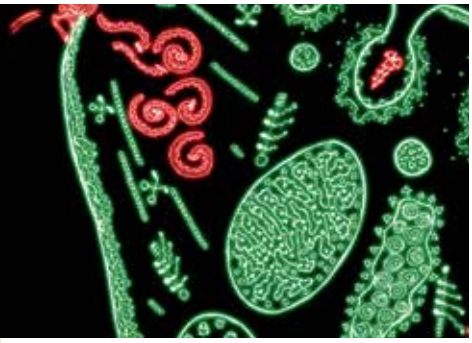
Music of the spheres

Contents

Nucleus

Synapse

Cultures



Regulars

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

Editorial

Greeting visitors at EMBL-EBI is a mesmerising artwork by Stephen John Wright, inspired by EBI-led research that makes possible the use of artificially constructed DNA as a data storage medium. Unveiled on 25 July, it features thousands of identical circles on a black field that Wright says is a visual simile for flows of information.

This notion also inspired the theme of this edition – flow in its many different facets. Our lead story reports on another unusual collaboration between art and science, one that researcher Nick Goldman and artist Charlotte Jarvis say has enabled them to think about their fields in new ways, realised through an intriguing project that combines bioinformatics, music and soap bubbles (page 10).

We have spent the past few months on the hunt for other such flows across the Lab. We found EMBL fellows teaching, dancing, mingling with Nobel Laureates (page 36), and even producing stunning artwork themselves (page 22). We visited EMBL's flow cytometry facilities, which are tasked with locating the cellular equivalent of needles in haystacks (page 20). And we peered inside the enclosures of starfish, urchins and anemones and discovered a flow of ideas inspiring innovative new research directions (page 15).

It's impossible to reflect all of the flows taking place across EMBL, but from artistic career paths to the Lab's 40th Anniversary celebrations, creativity, idea exchange, and smart thinking can be found in this edition from beginning to end.

Adam Gristwood
Editor

Word to remember

Axochord

Noun, Pronunciation: ˈaksə(ʊ)kɔːd

Zoology **– A muscle that runs along the midline of the marine worm *Platynereis dumerilii*.**

The location and genetic signature of the axochord imply that the origin of the first vertebrate skeleton is older than had been assumed (page 7).

Publisher
European Molecular Biology Laboratory, Heidelberg
Office of Information and Public Affairs

Editor-in-chief
Lena Raditsch
Head of Communications

Editors
Adam Gristwood, magazine editor
Chloë Cross, digital editor
Sonia Furtado Neves, science editor

Design
Edenspiekermann, Amsterdam

Printed by
ColorDruck Solutions, Leimen

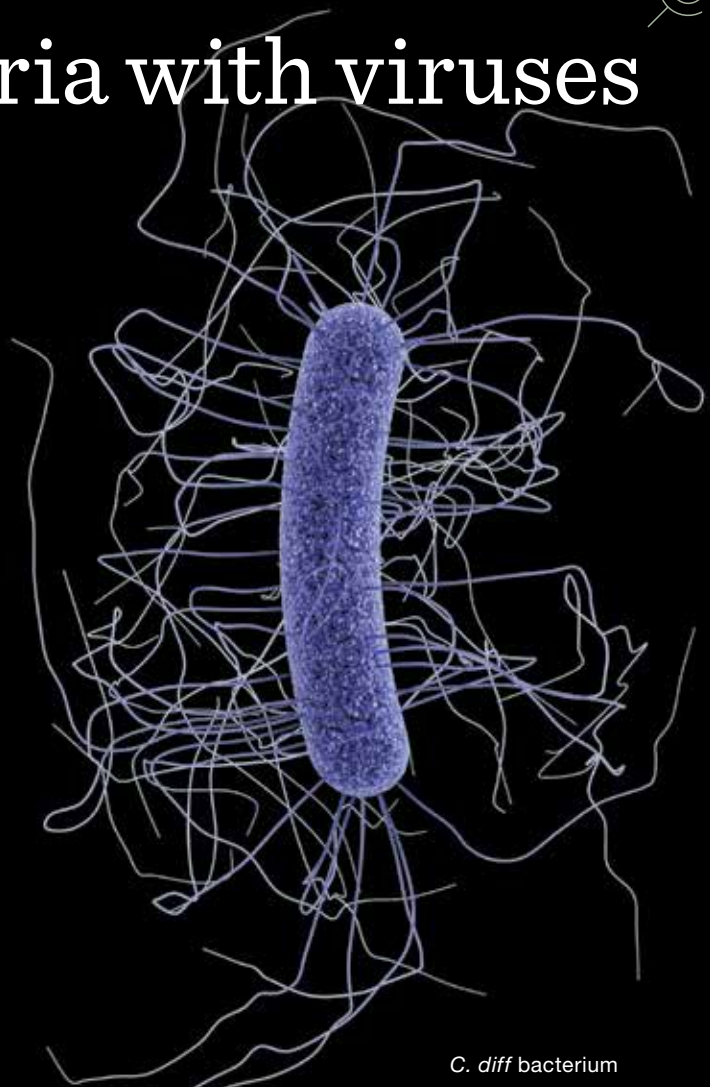
Contact
news@embl.de

Cover photo
Jon Mold

EMBLetc. ONLINE
NEWS.EMBL.DE

Fighting bacteria with viruses

Scientists show how bacteriophages destroy *Clostridium difficile* cells, opening up new possibilities for using viruses as an alternative to antibiotics. BY ROSEMARY WILSON



C. diff bacterium

IMAGE: JENNIFER HULSEY/CDC

Clostridium difficile (C. diff) **is becoming a serious problem in hospitals and healthcare institutes, where it can cause life-threatening cases of diarrhea. Such cases are very difficult to treat, because *C.diff* is unresponsive to many antibiotics. A potential alternative would be to use bacteriophages – viruses that infect and destroy bacteria, but do not affect other organisms.**

Bacteriophages enter a bacterial cell and hijack that cell's DNA replication machinery to reproduce. The cell then breaks up, releasing the newly formed bacteriophages. In order to develop and engineer effective bacteriophage therapies, a clear understanding of the viruses' life cycle is needed – in particular, how the bacterial cell wall is destroyed. While it is known that the enzymes involved, called endolysins, are produced directly before the break-up of the cell, just how these enzymes are activated remained a crucial missing part of the puzzle.

A common switch

In this study, Rob Meijers and his group at EMBL Hamburg, working in collaboration with Melinda Mayer and Arjan Narbad from the Institute of Food Research in Norwich, UK, compared two endolysins. One was retrieved from a bacteriophage that infects *C. diff*, and the other digests the cell wall of a *Clostridium* species that impairs cheese fermentation. At the German Electron Synchrotron (DESY) in Hamburg, the EMBL researchers used X-ray crystallography and small angle X-ray scattering – techniques which involve shining X-ray beams on a sample and measuring how that sample interferes with those rays – to deduce the enzymes' 3D structure.

"These enzymes seem to take on two different conformations," explains Matthew Dunne, a PhD student in Meijers' lab who carried out the research. "They appear to switch from a tense, elongated shape where a pair of endolysins are joined together, to a relaxed state where the two endolysins lie side-by-side." The switch from one state to the other triggers the release of the active enzyme, which then begins to degrade the cell wall.

"Remarkably, we found that the two endolysins have a common activation mechanism," explains Meijers. It therefore seems likely that this mechanism is not restricted to *Clostridia*-specific bacteriophages, but can be found in many others, too. "This knowledge could allow us to engineer effective, specific bacteriophages, not just for *C. diff* infections, but for a wide range of pathogenic bacteria related to human health, agriculture and the food industry."

Dunne, M., *et al. PLoS Pathogens,* 24 July 2014.
DOI: 10.1371/journal.ppat.1004228

FULL REPORT ONLINE
NEWS.EMBL.DE/?P=1186

Clarity in the cold

How fruit flies thrive in colder climes, revealed in a study by EMBL Heidelberg scientists.
BY SONIA FURTADO NEVES

Anne Ephrussi's lab at EMBL Heidelberg and colleagues at Rochester University in the USA have discovered one way in which the fruit fly *Drosophila melanogaster* manages to lay viable eggs not only at its preferred 25°C, but also at lower temperatures.

Their work focused on two particular molecules: *oskar* and Klar. *oskar* acts as a determinant in the egg cell, defining the region that will become the fly embryo's posterior. It is carried to the right place in the cell in the form of an RNA template, which is then translated into protein on the spot, where it is needed. However, at 18°C, in flies engineered to have no Klar, *oskar* RNA is carried to the egg cell's posterior pole, but not all that RNA stays there. The surplus *oskar* RNA is taken elsewhere, but is already primed for translating into protein, so the protein ends up accumulating in other parts of the egg cell – at the risk of rendering it unviable or causing major developmental defects.

This incoordination comes about, the scientists surmise, because the drop in temperature has a more dramatic effect on the machinery that anchors *oskar* in place than on the transport network. "If one process slows down more than the other, you may try to live with it – but you are probably going to fail," Gaspar explains. "The alternative is you have to find a dedicated regulator that brings down the other process; and that's what Klar does." In short, when a fruit fly egg cell is subjected to low temperatures, Klar cranks *oskar* transport down to almost nothing, to keep delivery of *oskar* at a rate that the anchoring machinery – which is considerably slowed by the temperature drop – is capable of handling.

At 18°C, embryos without Klar fail to develop normally. Bottom: normal embryo (with Klar) at 18°C

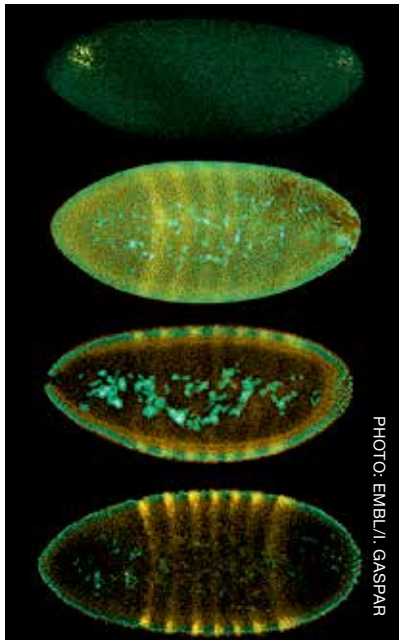


PHOTO: EMBL/I. GASPAR

Gaspar *et al. Journal of Cell Biology*, 21 July 2014. DOI: 10.1083/jcb.201310010

FULL REPORT ONLINE (WITH VIDEO): NEWS.EMBL.DE/?P=1323

IMAGE: EMBL

A fruit fly seen under an electron microscope

Surprisingly stable long-distance relationships

SFN Contrary to what was thought, sequences of DNA called enhancers – which control a gene's output – find their targets long before they are activated during embryonic development, Eileen Furlong's group at EMBL Heidelberg have found. The study also reveals that, surprisingly, the degree of complexity of enhancers' interactions in the 'simple' fruit fly *Drosophila* is comparable to what is seen in vertebrates.

Ghavi-Helm, Y. *et al. Nature*, 2 July 2014. DOI: 10.1038/nature13417

FULL REPORT ONLINE
NEWS.EMBL.DE/?P=937

New light on iron overload

LR Work carried out by the joint research team of Matthias Hentze, Director of EMBL, and Martina Muckenthaler, professor at the University of Heidelberg, has shed new light on the molecular background of a rare form of the iron overload disorder haemochromatosis. For the first time in living organisms, they demonstrated that in a form of the disease caused by a small mutation in the protein Ferroportin, which transports iron, the organ most affected by the disease's characteristic iron overload is the pancreas.

Altamura *et al. Cell Metabolism*, 5 August 2014. DOI: 10.1016/j.cmet.2014.07.007

FULL REPORT ONLINE
NEWS.EMBL.DE/?P=1344

From worm muscle to spinal discs

The origin of the first vertebrate skeleton is likely older than previously assumed. And surprisingly, it probably evolved from muscle. BY SONIA FURTADO NEVES

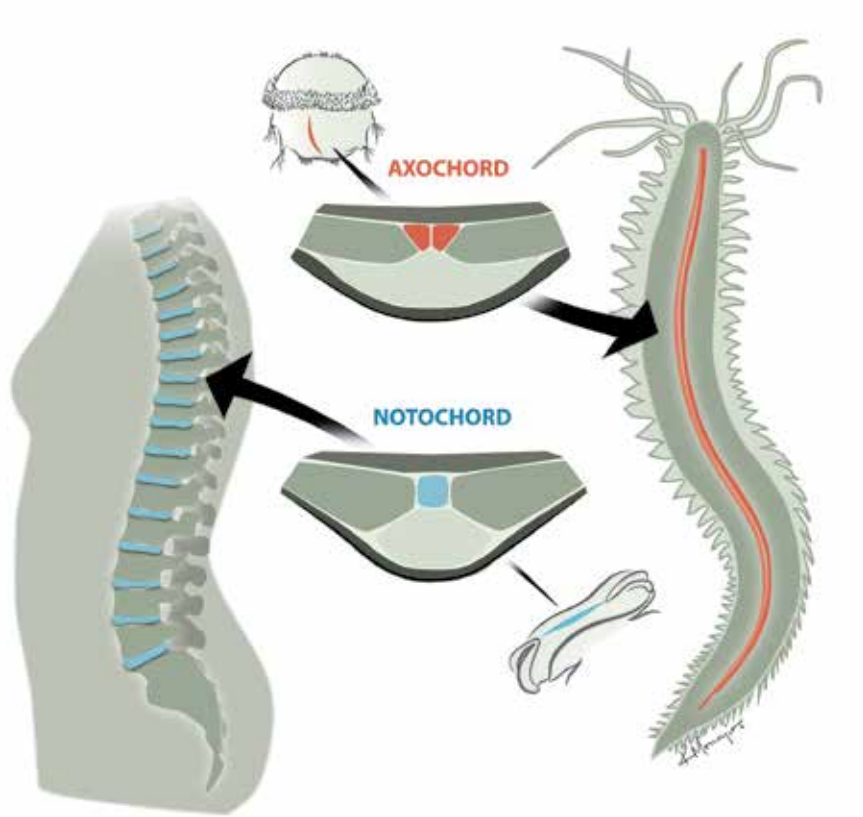
Thoughts of the family tree may not be uppermost in the mind of a person suffering from a slipped disc, but those spinal discs provide a window into our evolutionary past. Humans are part of a group of animals called chordates, whose defining feature is a rod of cartilage that runs lengthwise along the middle of their body, under their spinal chord. This structure, called the notochord, was the first vertebrate skeleton. It is present in human embryos, and is replaced with the backbone as we develop, with the cartilage reduced to those tell-tale discs. Since starfish, sea urchins and related animals have no such structure, scientists assumed the notochord had emerged in a relatively recent ancestor, after our branch of the evolutionary tree split away from the 'starfish branch'.

"People simply haven't been looking beyond our direct relatives, but that means you could be fooled, if the structure appeared earlier and that single group lost it," says Detlev Arendt from EMBL Heidelberg, who led the research. "And in fact, when we looked at a broader range of animals, this is what we found."

Antonella Lauri and Thibaut Brunet, both in Arendt's lab, identified the genetic signature of the notochord. When they found that the larva of the marine worm *Platynereis* has a group of cells with that same genetic signature, the scientists teamed up with alumnus Philipp Keller's group at the Howard Hughes Medical Institute in Janelia Farm, to use state-of-the-art microscopy to follow those cells as the larva developed. They found that the cells form a muscle, which they named the axochord, that runs along the animal's midline, precisely where the notochord would be if the worm were a chordate. A combination of experimental work and combing through the scientific literature revealed that most of the animal groups that sit between *Platynereis* and chordates on the evolutionary tree also have a similar, muscle-based structure in the same position. The scientists reason that such a structure probably first emerged in an ancient ancestor, before all these different animal groups branched out on their separate evolutionary paths.

Lauri, Brunet *et al*. *Science*, 12 September 2014. DOI: 10.1126/science.1253396

FULL REPORT ONLINE
NEWS.EMBL.DE/?P=1707



Platynereis has a muscle (red) which develops in the same place with the same genetic signature as the notochord (blue) that develops into our spinal discs

IMAGE: KALLIOPI MONOYIOS

Shedding light on chimeral twins

PHOTO: EMMANUEL KELLER

Study shows how the marmoset diverged from other primates, developing genes that give rise to unique reproductive features.

BY MARY TODD BERGMAN

The genome of the common marmoset, which was recently sequenced and analysed by an international research consortium, provides insights into both our own evolution and this tiny primate's reproductive system. "Unlike humans, marmosets consistently give birth to twins without the association of any medical issues," says Kim Worley, professor in the Human Genome Sequencing Center at Baylor College of Medicine in the US, who co-led the study. The researchers found that the gene WFIKKN1 may act as a critical switch between multiple and single pregnancies, though it is not the only gene involved.

Exploring the data

The marmoset team used the Ensembl genome resource, which provides reference information about different species and tools that align them with one another. "Once we got the annotated marmoset genome sequence into Ensembl, we could narrow our focus to the most potentially interesting regions of the genomes," says Magali Ruffier of the Ensembl team. "Using comparative genomics you can look at common ancestry among different primates or mammals, and ask questions like, which genes change faster over the course of evolution? Which genes lose their function? Can we find this in other species? Is it expressed in the same way?"

Having narrowed their question down from billions of DNA base pairs to thousands, the consortium researchers could test their questions experimentally. "One challenge in this kind of research is that we want to know what makes humans different from other species, and yet most of what we know about other primates on the genomic level is based on human data," adds Bronwen Aken, Primary Analysis Coordinator on the Ensembl team. "Once we have more information on other primate species' gene expression, protein sequences and interactions, we will start to get a clearer picture of how and why marmosets, humans and other apes evolved the way they did."

Worley, K.C. *et al. Nature Genetics*, 20 July 2014. DOI: 10.1038/ng.3042.

MARMOSET GENOME ONLINE: WWW.ENSEMBL.ORG

Major advance in stem cell technology

Researchers at EMBL-EBI have produced pristine stem cells, which can be precisely changed into clinically relevant cell types. Their work enables the development of more clinically effective cell therapies. BY MARY TODD BERGMAN

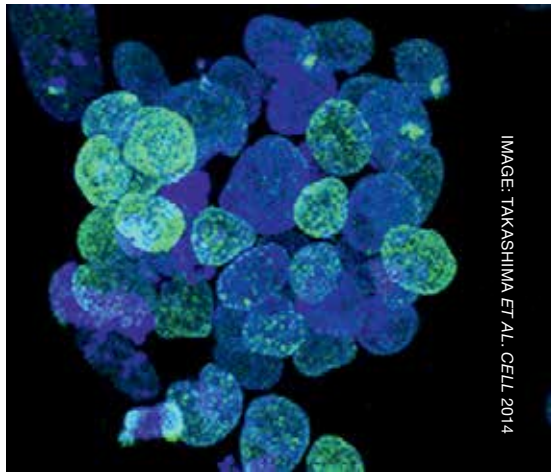


IMAGE: TAKASHIMA *ET AL. CELL* 2014

Experimental work was conducted hand-in-hand with computational analysis

In a study jointly led by EMBL-EBI and the University of Cambridge, scientists from the UK, Germany and Japan have resolved a long-standing challenge in stem cell biology by successfully 'resetting' human pluripotent stem cells to a fully pristine state, at the point of their greatest developmental potential.

Embryonic stem (ES) cells, which originate in early development, are capable of differentiating into any type of cell. Until now, scientists have only been able to revert 'adult' human cells into pluripotent stem cells with slightly different properties that predispose them to becoming cells of certain types. Authentic ES cells have only been derived from mice and rats. "Reverting mouse cells to a completely 'blank slate' has become routine, but generating equivalent naïve human cell lines has proven far more challenging," says EMBL-EBI group leader Paul Bertone, a corresponding author on the study.

Wiping cell memory

Taking a new approach, the scientists used reprogramming methods to express two different genes, NANOG and KLF2, which reset the cells. They then maintained the cells indefinitely by inhibiting specific biological pathways. The resulting cells are capable of differentiating into any adult cell type, and are genetically normal.

The experimental work was conducted hand-in-hand with computational analysis. "We needed to understand where these cells lie in the spectrum of the human and mouse pluripotent cells that have already been produced," explains Bertone. "We worked with the EMBL Genomics Core Facility to produce comprehensive transcriptional data for all the conditions we explored. We could then compare reset human cells to genuine mouse ES cells, and indeed we found they shared many similarities."

Unlocking the potential of stem cell therapies

The discovery paves the way for the production of superior patient material for translational medicine. Reset cells mark a significant advance for human stem cell applications, such as drug screening of patient-specific cells, and are expected to provide reliable sources of specialised cell types for regenerative tissue grafts.

Takashima *et al. Cell*, 11 September 2014. DOI: 10.1016/j.cell.2014.08.029

FULL REPORT ONLINE
NEWS.EMBL.DE/?P=1761

How the rabbit was tamed

BA Researchers from the Ensembl team at EMBL-EBI showed that rabbit domestication occurred due to small changes in many genes, rather than large changes in a few genes. Many of those altered genes are involved in the development of the brain and nervous system, which may explain the behavioural changes seen in domestic rabbits, such as a weaker flight response.

Carneiro, Rubin, Di Palma *et al. Science*, 29 August 2014. DOI: 10.1126/science.1253714

READ BRONWEN AKEN'S FULL BLOG POST:
NEWS.EMBL.DE/?P=1748

Music of the spheres

Science and art are often considered opposites – so what happens when practitioners in each field collaborate? The results can be spectacular…

BY LINDSAY BROWNELL

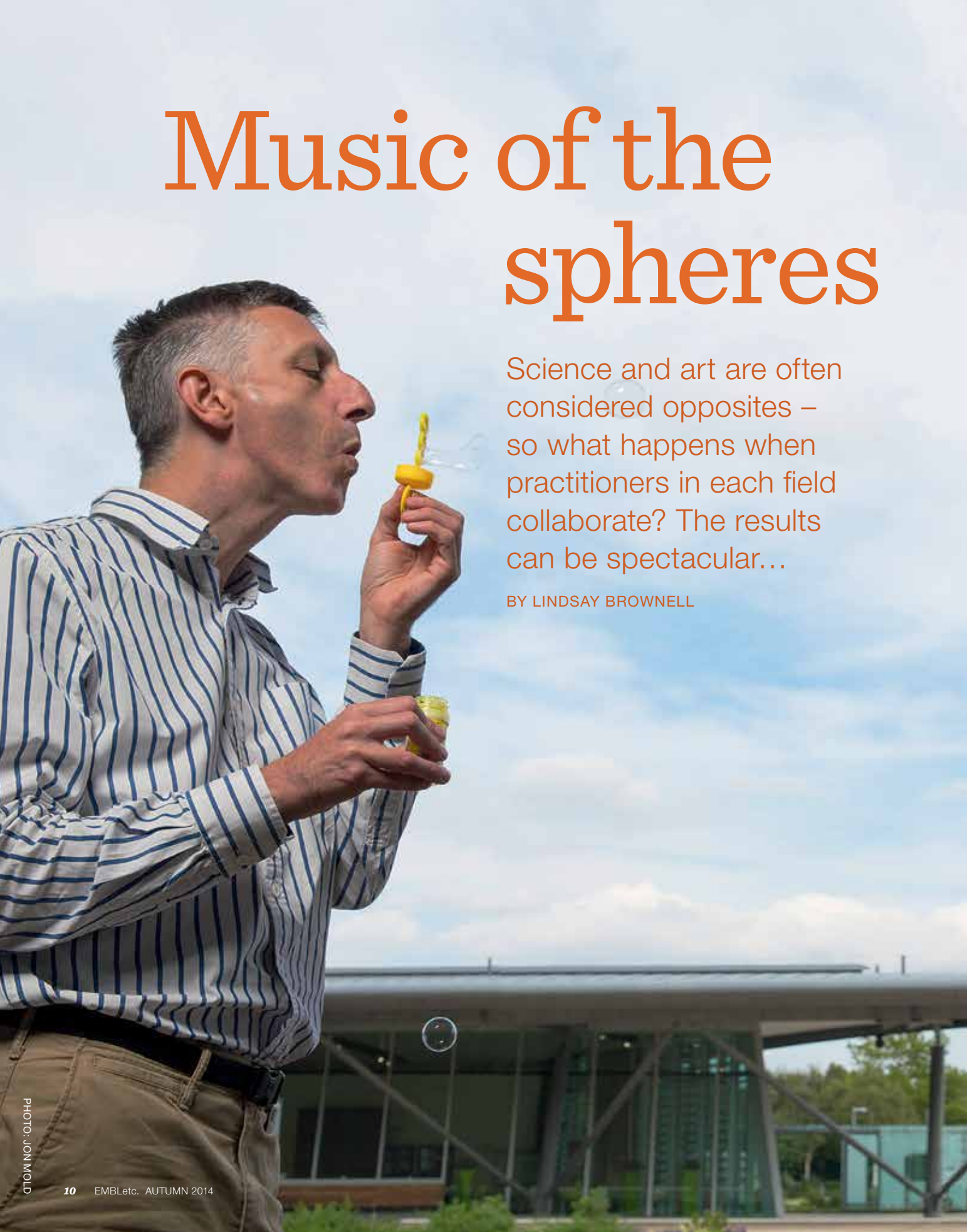


PHOTO: JON MOLD

They seem an unlikely pair: Charlotte Jarvis, adorned in the flowing black symbolic of artists, with boldly lined eyes and curly dark hair standing impossibly straight up from her head as if she had just emerged from a lightning storm; and Nick Goldman, a lanky bioinformatician, going gracefully grey, wearing chinos and a button-down shirt and sporting the perpetually rumpled look of a man whose mind moves much faster than his body. Despite their mismatched appearance, the artist and the scientist share a common passion for a very unusual type of storage medium – DNA – and are putting their heads together to create a unique art project involving bioinformatics, music and soap bubbles.

They met in 2012 when one of Goldman's colleagues at EMBL-EBI happened to see a flyer for an exhibition of Jarvis's previous art project, in which she collaborated with the Netherlands Proteomics Centre in Utrecht to encode the Universal Declaration of Human Rights into the DNA of a bioengineered bacterium. Goldman immediately spotted that Jarvis had done something very similar to a project he was working on: inventing a code to enable information to be stored in sequences of DNA. Goldman's method essentially uses synthetic DNA as a kind of hard drive, allowing diverse types of data like music recordings, images and documents to be saved and 'read' via DNA sequencing.

Goldman went to the opening and met Jarvis, and their mutual excitement about the implications of the technology created an instant connection. "Charlotte was very enthusiastic when I told her that it was possible to store any information, not just text, in DNA," says Goldman. "When I realised the scope of what you can do with that technology, it just completely blew my mind," Jarvis agrees. She asked Goldman to collaborate with her on a new initiative using his method of encoding data into DNA, and their interdisciplinary project was born.

Music in all things

When deciding what kind of information she wanted to store in DNA, Jarvis was inspired by a snippet of verse from Lord Byron's epic poem *Don Juan:*

> *There's music in the sighing of a reed;*
> *There's music in the gushing of a rill;*
> *There's music in all things, if men had ears;*
> *The earth is but the music of the spheres.*

"It really sums up my understanding of DNA: it's in all living things, it underpins life on our planet, it's kind of vibrating through everything," she says. "And I see some similarities between DNA and music: they're both quite fundamental, they're both quite abstract, they're invisible but they can be everywhere…so I decided that I wanted it to be musical."

Invigorated, Jarvis enlisted British composer Mira Calix to write an original piece of music that would be recorded and stored in DNA. Calix used the harmonic hum of the machines in the server room at EMBL-EBI – home to the world's most comprehensive collection of genetic databases – as inspiration. "It has the most incredible sound," says Jarvis, still awestruck by the recollection. "It's so loud that the people who work there have to wear ear protectors. It just hits you like a wall, the sound of all that genetic data being stored, all those ones and zeros that define life." But music is a living thing, not just fodder for the archives. Jarvis wanted to find a way to make the project more interactive, and to somehow convey the sense of wonder that she feels when considering just how much significance is contained within such a tiny molecule. Harking back to Byron's 'music of the spheres', she settled on the idea of infusing the DNA into bottles of soap bubbles, so that any bubbles blown will become spheres of musical DNA floating through the air.

The debut performance of Calix's musical composition is set for early 2015, and machines will fill the air with DNA bubbles at a specified point in the piece when the musicians fall silent, so that the music will only exist in the form of DNA. "We are going to fill the air with Mira's music, and then they can spread the composition on their skin, or later take a bottle home, mix it in their bath, do whatever they want with it," says Jarvis.

If some members of the audience want to actually listen to this section of the music, they can extract the DNA, sequence it, and then decode it using Goldman's method. The final piece of the project is a film of the musicians playing Calix's music in the EMBL-EBI server room. The film will be shown at exhibitions that Jarvis has planned for 2015. "It's definitely the most ambitious project I've ever been involved with," she says, "and there are still a lot of exciting things to come."

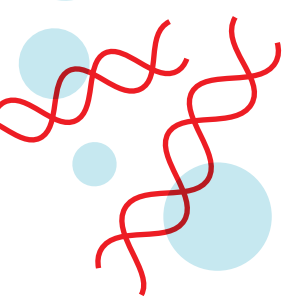
A two-way street

This is Goldman's first time embarking on a project that appeals to an audience with such a broad range of interests, and he is enjoying rubbing shoulders with the art world. "I find Charlotte really impressive," he says. "She's a bona fide artist, she's genuinely enthusiastic about science, and she wants to talk to people about it. That approach fits really well with my responsibilities as a scientist: not just doing science, but getting it out to the public."

Jarvis has been collaborating with scientists for five years, and has seen the 'science art' community expand a lot during that time. She finds it natural that artists ››

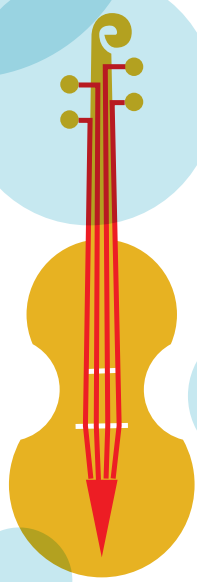
1

Jarvis enlists British composer Mira Calix to write an original piece of music – she does this, inspired by the hum of the huge data storage machines in the server room at EMBL-EBI.



2

The music is recorded and encoded in a form that could be represented by the letters of DNA. That DNA was then synthesised and infused into liquid soap.



3

Calix's music is performed on stage by an orchestra. Bubbles of the DNA-infused soap will be blown about during the performance, filling the air with miniscule copies of the original composition.

4

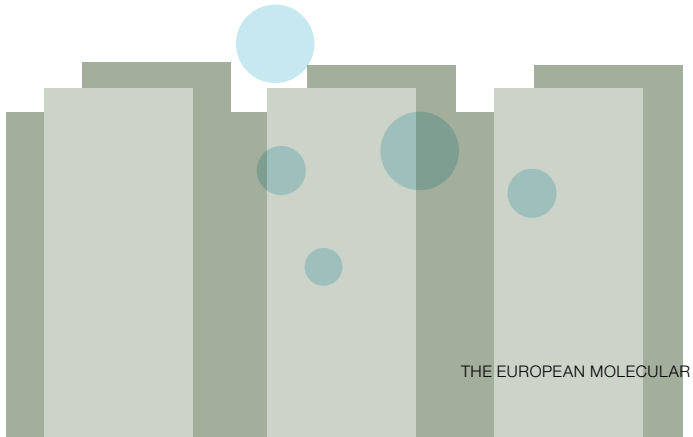
As the bubbles float through the air, the musicians fall silent. The bubbles become the only physical manifestation of the music.

5

After the performance, the soap mixture is offered to audience members as they leave. Theoretically, they could have the soap sequenced, whereupon a digital file detailing the sequence of the DNA fragments would be sent to them.

6

Then, using instructions online and some smart computer programming, they can decode the fragments to recreate the music file.



›› would want to work with scientists. "As an artist, you make art about the things that inspire you and the things that are changing the world," she says. "Science and technology are having the most incredible and important impact on our planet today, and not only in a physical sense; they're changing our own bodies, our own identities, and our perception of the world. I think it's completely natural that artists would want to engage with that."

The relationship goes both ways: scientists reach out to the arts both for inspiration and to get a more diverse mix of people interested in their work. For example, Sarah Teichmann, a group leader at EMBL-EBI and the Sanger Institute, recently collaborated with a composer on a musical project based on a 20-page printout of DNA sequences from the 1000 Genomes Project.

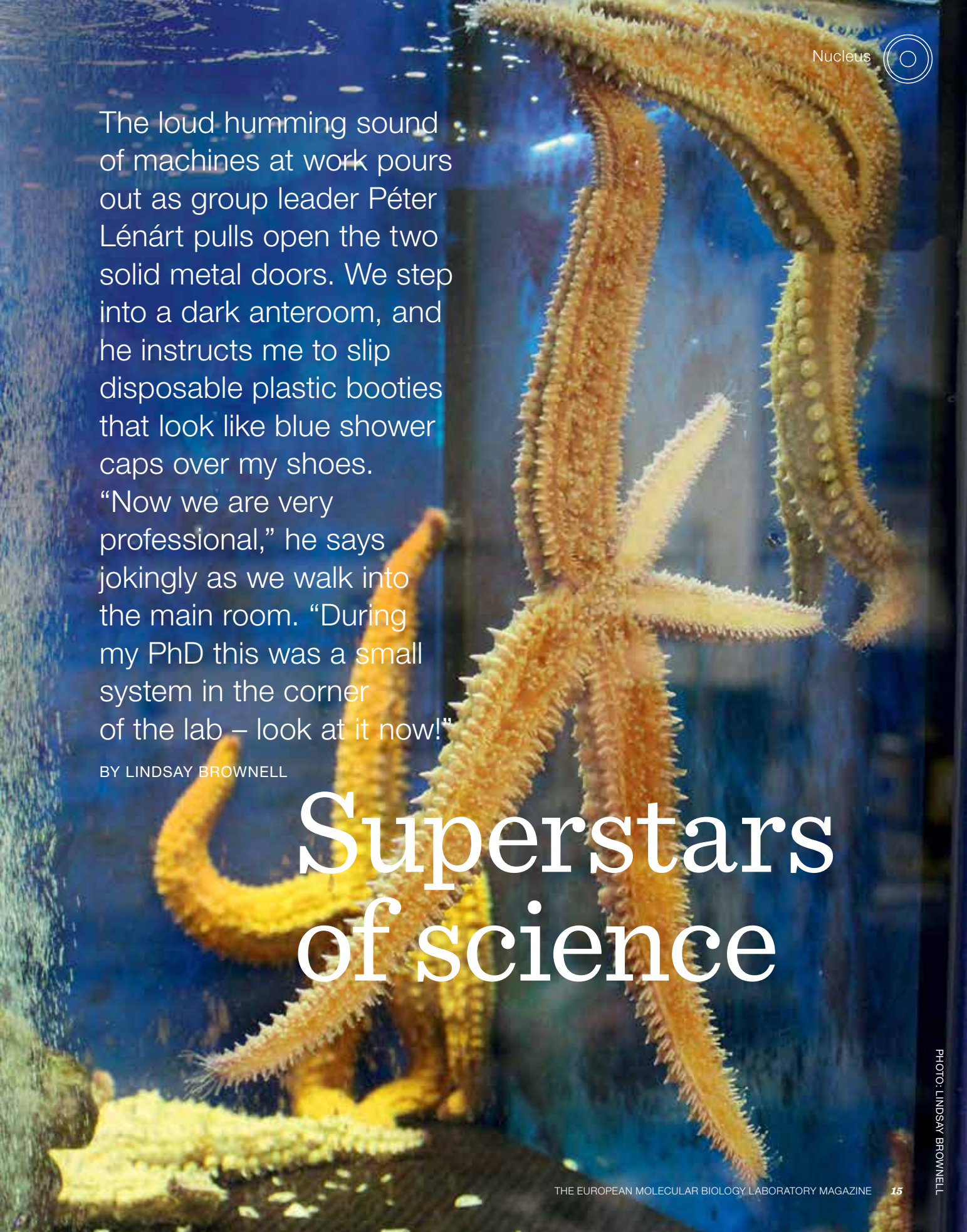
Jarvis thinks that this trend is driven in part by an increased emphasis on communication within the research world. Artists, she says, can help scientists reach a larger audience by translating their work into formats that are easier for the public to engage with and understand. "Rather than focusing on what exactly a technology does or what the end point will be, artists are quite good at looking at things tangentially. Their responses are more likely to be, 'Look at all these possibilities! Look at all the different ways we can interact with these results, question them, pick them apart and put them back together! Look how beautiful this can be!' So in that sense, artists can really offer something beyond what scientists are being forced to focus on."

"People experience lots of pressure to do just one area of science," Goldman agrees, adding that scientists need so much specialised knowledge to make progress that there is often little time to think about how to disseminate their work beyond the research community. But, he says, "There are lots of times when thinking through things in a different way gives you inspiration in your science. I could imagine sitting down with Charlotte and hearing her say 'Oh, it would be so much better if we could do this or that with DNA,' and then a minute or a day later I'd think, 'Actually, you could do that thing she wants with DNA,' and then we could both use that advancement in our own careers."

Arts and sciences: a natural fit

Goldman is taking full advantage of this chance to explore and promote science in different ways, because he knows it's a luxury few researchers have. "I'm lucky to have a job where I'm allowed to spend part of my time with an artist. Charlotte and I get on great – she drags me to some of the art events where she's pitching for funding or promoting the project, and I do the sciencey bit. I'm a bit of a pet scientist," he jokes, with a good-natured laugh. "And I would have no fear about her giving a talk at one of EMBL-EBI's events. I expect that there will be more of these kinds of collaborations across the sciences in the future. It's certainly been good for Charlotte and myself, and for EMBL."

"Science and technology are changing our own bodies, our own identities, and our perception of the world. I think it's completely natural that artists would want to engage with that."

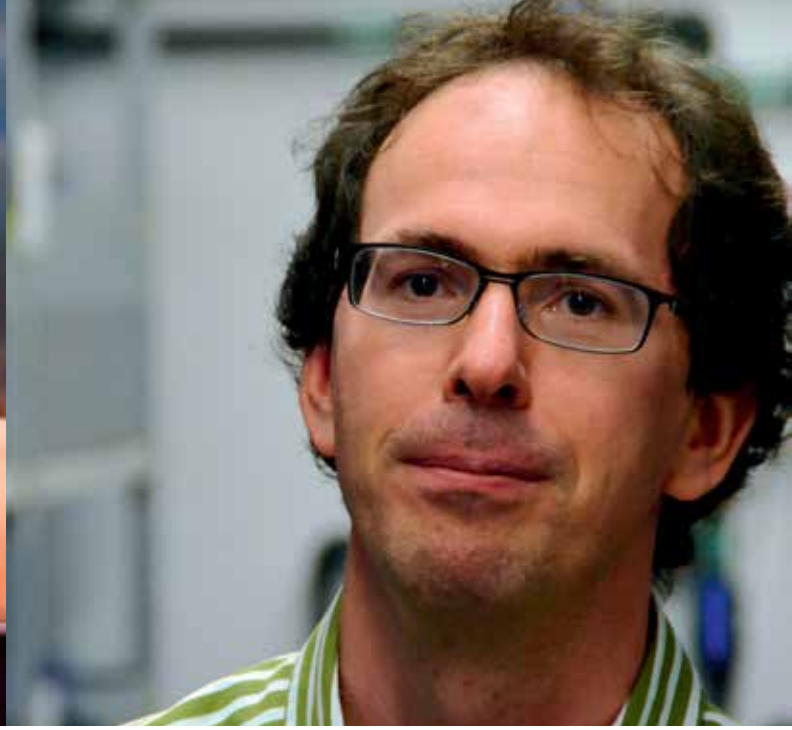


The loud humming sound of machines at work pours out as group leader Péter Lénárt pulls open the two solid metal doors. We step into a dark anteroom, and he instructs me to slip disposable plastic booties that look like blue shower caps over my shoes. "Now we are very professional," he says jokingly as we walk into the main room. "During my PhD this was a small system in the corner of the lab – look at it now!"

BY LINDSAY BROWNELL

Superstars of science

PHOTO: LINDSAY BROWNELL



The source of the noise is revealed to be not computer servers nor fume hoods but dozens of water tanks, filled with aquatic creatures that seem a bit out of place in the hills near Heidelberg, more than 400 km from the sea. Bright red starfish the size of my face adorn the ocean-blue walls of one tank; another holds spindly, ivory-coloured starfish with spines all over their arms; a third contains small, dark green ones with striking orange spots along their backs. Across the room are shallow, trough-like containers each holding more than a dozen bulbous African clawed frogs that periodically clamber over each other. A pale purple sea urchin clings to the glass of its enclosure, tiny tube feet holding it in place. The room resembles an aquarium or a pet store rather than a science lab.

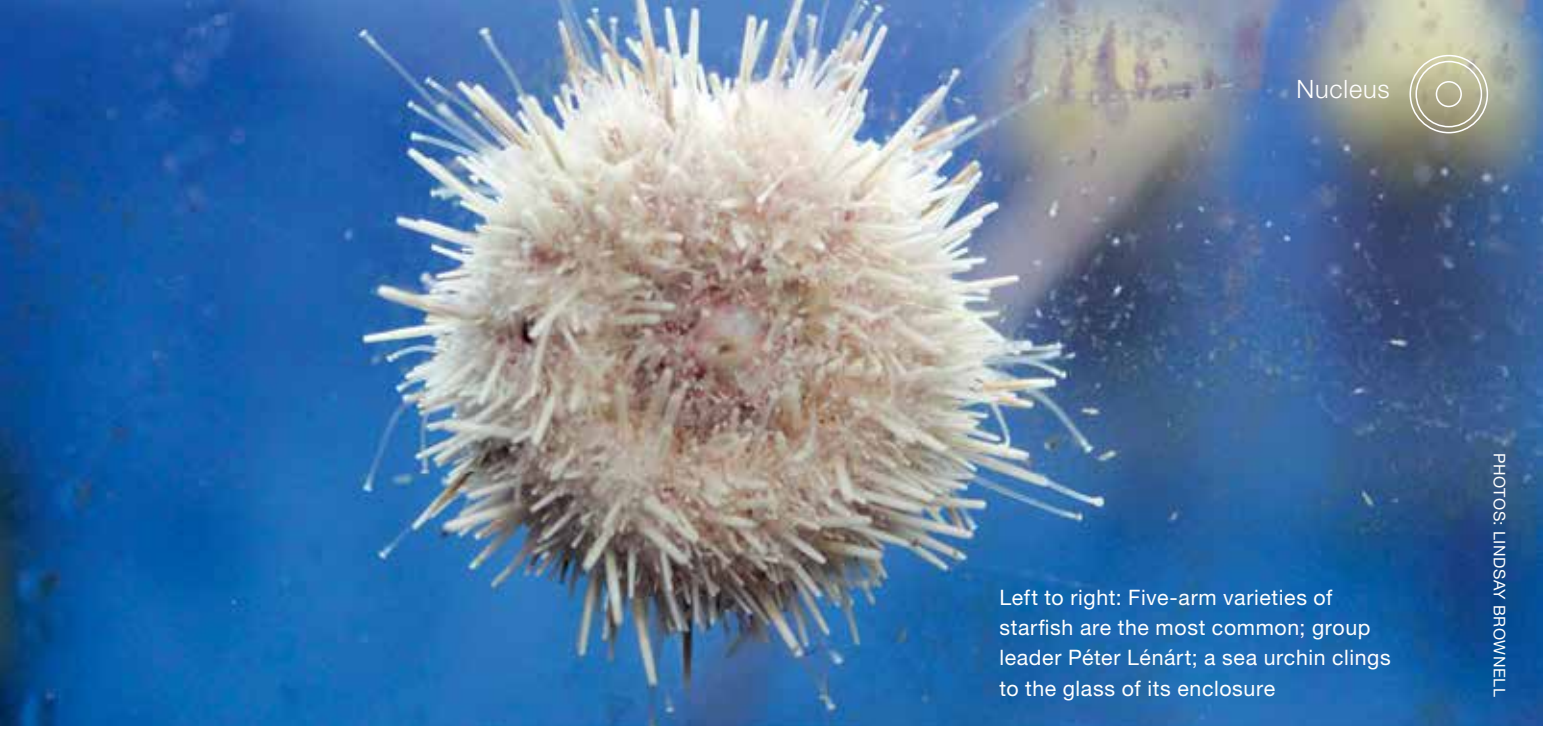
The right mix

Welcome to the marine facility of EMBL's Laboratory Animal Resources department. True to Lénárt's word, it is professional-grade: animal tanks are supplied with a 50/50 mixture of water from two 3000-litre containers that look like beer stills. One is filled with natural seawater that's shipped in from the North Sea every month, the other with artificial seawater that contains a defined mixture of salts to maintain crucial parameters such as salinity and pH. The facility is equipped with all the pumps, filters, lights and other elements required to properly care for its residents. Staff members monitor the animals throughout the day, and ensure each tank is kept at the right temperature and salinity.

The marine facility is the brainchild of Detlev Arendt, a senior scientist at EMBL Heidelberg who studies neural development and evolution in the marine worm *Platynereis dumerilii*. In 2003, frustrated with the limitations of keeping specimens in buckets of seawater in the lab, he spearheaded the construction of the current system, which provides everything needed to breed and maintain large numbers of his model organism in a controlled, consistent environment. "Our lab sort of jumped onto that project and connected our system to his," says Lénárt, gesturing to the starfish tanks. "The big red ones are called bat stars, and they are quite common along the west coast of the United States. We ship them here by FedEx." The green and orange starfish are similarly well travelled: Lénárt had these sent from Japan rather than the States, due to concerns over a recent decline in the starfish population in California that could threaten the health of the lab's supply.

Stars of the show

Lénárt's lab studies meiosis, the process by which a reproductive cell divides into gametes – spermatocytes in males or oocytes in females – that can then combine during fertilisation. Whereas meiosis in male starfish results in four equally sized spermatocytes, the female lineage produces one very large egg cell that is packed with nutrients to support a developing embryo. "One of the main things we are interested in is how division happens in these exceptionally large cells," says Lénárt. "It's extremely asymmetrical." With most of the cellular contents concentrated in one cell, the remaining three meiosis products become small 'polar bodies' whose only purpose is to serve as reservoirs for the extra DNA that needs to be jettisoned from the oocyte. "From an engineering point of view, it's like a scaling problem: how do you scale up cell division from a small cell to a large cell, and with such asymmetry?" Lénárt says.



Left to right: Five-arm varieties of starfish are the most common; group leader Péter Lénárt; a sea urchin clings to the glass of its enclosure

PHOTOS: LINDSAY BROWNELL

Meiosis is a difficult process to control and image in the lab, particularly in mammals. Mice, one of the most widely used model organisms, present many challenges: they must be ordered weeks in advance so that they are the right age to produce oocytes; the oocytes must be removed from the mouse's body and kept at 37˚C during their transformation into an egg cell; and the process takes about eight hours to complete, meaning that the imaging microscope must somehow be automated to keep track of the oocytes. Starfish, by contrast, are much easier to work with. They are one of the few animals whose maturation-inducing hormone has been identified, which allows researchers to control when the oocytes start to mature into eggs. "We just keep them at room temperature in sea water, we add the hormone, and the whole process takes one and a half hours. It's a system which allows you to do 'discovery' research and explore new things, because you can proceed quickly," says Lénárt.

Intriguingly, Lénárt and his team are discovering a large amount of diversity among oocytes of different species. "What is really exciting to me is that oocytes are single-celled in all animals," he says. "Normally adaptation to the environment happens at the organism level. But in the egg, it happens at the single-cell level." Different organisms' eggs are subjected to widely varying conditions: some float in the sea, some lay buried in desert sand, and some are contained within the mother's body until birth. Comparing different animals' cells at the same early developmental stage can offer insights into how they evolved into the fantastically varied pantheon of life that exists on the planet today.

Unexpected discoveries

Specifically, research on starfish oocytes has revealed diversity at the level of core cellular machineries that are highly conserved across very different organisms. "Now we are looking at how different cell types combine those common elements to achieve different cellular functions. It's like using the same set of Lego blocks to build either a castle or a pirate ship," says Lénárt. His group has found, for example, that an actin network used for cell migration in somatic cells has a different role in starfish oocytes: it's needed to break the nuclear envelope of the exceptionally large oocyte nucleus during cell division. This and other unexpected observations are what keep Lénárt and his group on their toes.

Starfish are rarely used to do this type of investigative research, which is often conducted in yeast or fruit fly cells. Lénárt is part of a growing community of scientists who are looking beyond established 'model organisms' and focusing their research on other creatures to explore nature's diversity. Detlev Arendt's lab was the first at EMBL to use *Platynereis* as its primary animal model, and has recently expanded its scope to include animals such as amphioxus lancelet fish and the starlet sea anemone *Nematostella vectensis*. These creatures are attractive for scientific study, not only because of their evolutionary significance – all of them have relatively simple neural networks – but because they lend themselves well to being grown and studied in the lab. "When you choose a new model organism, you have to consider not only the biological questions, but all the technical things as well," says Marzia Sidri, a project manager in Arendt's lab. "In general, it is much more difficult ››

›› to work with animals that grow too slowly or aren't easy to image."

Beneath the surface

Across the Heidelberg campus in the EMBL Advanced Training Centre, a computer monitor flickers to life in the training lab, displaying what look like tiny glass satellites floating above a black background. Switching between looking at the screen and through a microscope, Ina Arnone deftly manoeuvers two micropipetting needles into view using a series of six knobs and dials that she manipulates with practised ease. Three students in white lab coats peer over her shoulder, watching their instructor's every move. The needles converge on one of the delicate shapes and attempt to pin it in place. The first needle bumps the target so that it spins away in infuriatingly lazy circles, forcing Arnone to start all over again. She patiently begins readjusting the needles, one knob at a time, her calm determination evidence of her expertise. Finally, she moves one of the needles close enough to gently suction the satellite to it, which she does by sucking on a thin rubber tube attached to the needle. While that needle holds its prey in place, Arnone slowly moves the other one forward. The glassy shape resists slightly, and then the needle finally pokes its way through. The students let out an audible sigh of relief, while Arnone sits back from the microscope looking as relaxed as if she'd just sliced a tomato for lunch. "And that's how you microinject a sea urchin larva," she says.

Arnone has her own research group at the Stazione Zoologica Anton Dohrn in Naples, Italy, where she's investigating the evolutionary and developmental biology (evo-devo) of gene expression and neurology. Her primary model organism is the sea urchin, principally *Strongylocentrotus purpuratus*, the entire genome of which was sequenced in 2006, and *Paracentrotus lividus*, which is abundant in the waters near Naples. She has brought her purple, spiky specimens to EMBL Heidelberg for a week-long training course sponsored by the Neptune Consortium, a network created by the Marie Skłodowska-Curie Actions fund to train young scientists who are studying evo-devo in marine organisms. The fact that marine animals' eggs and larvae are easy to produce, largely transparent and develop relatively quickly has led many scientists like Arnone to look to the sea when choosing new model organisms to study. Her other Neptune partners have brought their own alternative model organisms as well, including the common jellyfish *Clytia hemisphaerica* and Arendt's *Platynereis* worms, turning the training lab into a temporary menagerie.

Students on the course practise injecting living, developing embryos with various substances that alter which genes are expressed, either by inserting new DNA or by blocking or enhancing specific genetic products (RNAs and proteins). Looking at how these modified embryos develop compared to normal embryos can help researchers understand the function of a given gene or pathway. Investigating these processes in primitive animals like sea urchins and jellyfish can also provide insight into how early body plans gave rise to the more complex features of 'higher' animals.

"Some changes that accrue in the embryo as it develops reflect the changes that have accumulated on the evolutionary scale," says Sidri, who helped organise the Neptune course. The embryos of many land animals, like chickens and humans, have primordial gill slits and neck arches that they lose as they develop, just as the ancestors of birds and mammals lost theirs when they evolved from fish-like ancestors millions of years ago. "That's the basis of the whole evo-devo field," says Sidri. Although evo-devo model techniques are commonly used on well-established model organisms such as *Drosophil*a,

Left to right: Project manager Marzia Sidri; the sea anemone *Nematostella*; sea urchin larva with red stained esophageal muscle fibres and green cilia, snapped during the Neptune course.

testing them on different species can reveal information that fruit flies might not be particularly well-suited to provide. "The reason why scientists are looking for new models is that you can't generalise the structure and function of all animals just by analysing one species. You need to analyse more animals so you can compare and understand more about them all," says Sidri.

Living organisms aren't the only source of insight: Giannis Kesidis, one of the students attending the Neptune course, is a paleontologist at Uppsala University in Sweden who studies arthropod fossils from the Cambrian period. Although his work doesn't directly involve microinjecting larvae, "it's very useful to know what the developmental biologists are working on, because their hypotheses often have evolutionary implications that lead them to collaborate with people like me, who work on the fossil record," he says.

Changing tides

Back in the marine facility, Lénárt shows me its newest addition: tiny jellyfish polyps donated by Evelyn Houliston, a researcher based at the Villefranche Oceanographic Laboratory in France who attended the Neptune course that week. Scarcely larger than a grain of rice, they're affixed to a clear plastic slide submerged in a small container of seawater hidden away in a makeshift cupboard. "We're still working on setting this up, so it's under construction," Lénárt says with a tinge of embarrassment, as if apologising for the polyps' juvenile state.

Establishing a new animal line for study takes some time, but Lénárt is excited about the insights another organism could offer for his research. "The jellyfish is very close to the bottom of the animal evolutionary tree, so we are hoping to see some of the very basic features of animal oocytes by studying it. Also, the polyp form reproduces by budding and grows on a glass plate just like plants, which offers great opportunities for genetic manipulation," he says.

Lénárt has watched the evo-devo field branch out to include animals beyond those typically used as model organisms over the past few years. "I think cell biology has been largely focusing on conserved features, and it is often argued that when we find a conserved mechanism in yeast or *Drosophila* or mice, we can apply whatever we learn about it directly to human cells," he says. "We are now at a stage where people are taking interest in the diversity of those mechanisms themselves."

Lénárt gazes at the squat, orange-spotted Japanese starfish sitting next to the large, spiky-armed ones. "While what happens in a starfish oocyte might not be exactly the same as what happens in a human egg, we are learning a lot about core cellular machineries by looking at their different functions in different places," he says. "It's a great way to learn about how those cellular mechanisms work which, at a basic level, seems to be pretty universal across cells in all species of life on Earth."

WEB EXTRA: THE FIRST OCEAN SAMPLING DAY TOOK PLACE AT MORE THAN 160 SITES AROUND THE WORLD IN JUNE. FIND OUT HOW EMBL-EBI IS INVOLVED AT NEWS.EMBL.DE/?P=1166

PHOTO: LINDSAY BROWNELL

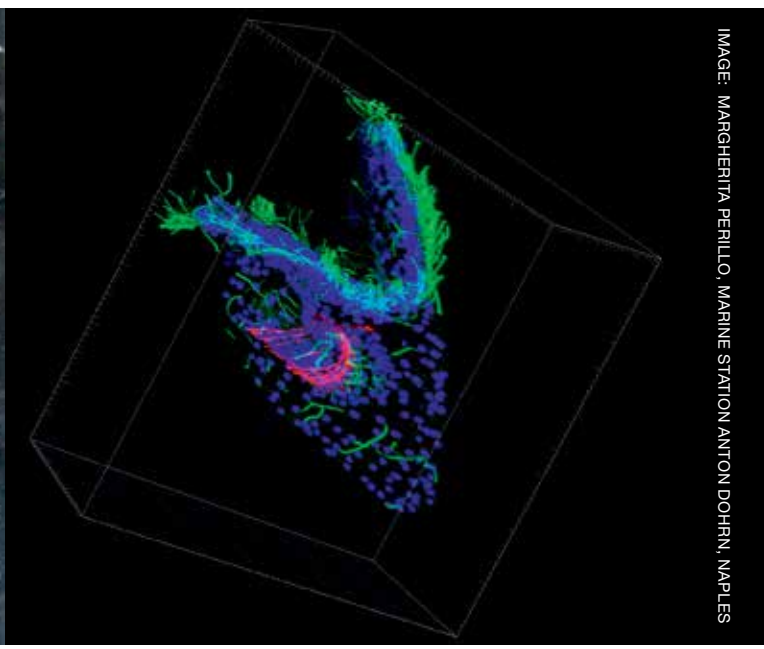


IMAGE: MARGHERITA PERILLO, MARINE STATION ANTON DOHRN, NAPLES

Go with

Looking for a needle in a haystack is hard enough. But now imagine that the haystack fills an entire room, it's dark and the pieces of straw and the needle are less than half the width of a human hair.

BY CLAIRE AINSWORTH

Worse, you have to sort through the whole lot before lunchtime armed only with a torch. Such are the challenges faced by Alexis Perez Gonzalez, manager of the EMBL Flow Cytometry Core Facility at EMBL Heidelberg, and his colleague Daniel Bilbao, of the EMBL Monterotondo facility.

The 'haystacks' in question are samples of cells, the trillions of tiny units that form our bodies and those of other creatures. The 'needles' are very rare cells – perhaps as scarce as one in a billion. Sometimes Perez Gonzalez and Bilbao also have to discriminate between varying kinds of needles, whose differences are barely detectable. Their expertise is helping EMBL researchers push back the boundaries of fields ranging from the molecular genetics of cancer to neurobiology. "With every researcher and almost every project, we have to come up with new solutions to address those challenging questions," says Bilbao. "Every day there is something new."

The secret of their success is a technique called flow cytometry, which allows them to sort through cell samples with extraordinary speed and accuracy. "You can easily go through millions of cells in seconds," says Perez Gonzalez. This allows the team to screen enough samples to find cells that would be too rare to detect using a microscope.

A glow in the flow

As their name suggests, flow cytometers analyse streams of liquid containing cells. These cells are grown in lab dishes or extracted from samples such as blood samples. They are mixed with liquid and loaded into the machine, which then streams a flow of cells past a beam of intense light in the form of a laser. To make the cells visible, researchers attach fluorescent dyes to them. The dye glows when it meets the laser light, allowing the machine to capture a snapshot of it.

the flow

Some dyes are attached to molecules called antibodies that home in on specific proteins in or on a cell; others rely on different biochemical tricks to tag particular molecules. Whatever the strategy, the dye allows researchers to identify cells that contain particular proteins of interest – perhaps one that marks out a cell as belonging to a specific cell type, such as a white blood cell. As well as finding their target cells, researchers can also use flow cytometry to look for changes in the kinds or amounts of proteins (or other molecules) present in those cells. Scientists can use several different-coloured dyes to tag several different proteins simultaneously. What's more, they can also measure other properties of cells: whether a cell is dead or about to die, stressed or happily proliferating, for example. "As long as we have a fluorescent dye that reflects the property that we want to measure, we can do it. And if we don't have a dye, we look for it," says Bilbao.

The cytometer can analyse the glow pattern of each sample to determine how many kinds of each cell it contains, or, in the case of a method known as fluorescence-activated cell sorting, pluck cells from the stream and sort them into different containers. The technique is constantly finding new applications in all fields of cell and molecular biology. "Essentially, the list is endless," says Perez Gonzalez.

Endless applications

Eileen Furlong's team at EMBL Heidelberg, for example, wanted to study how sections of DNA called enhancers control the early development of fruit fly embryos (see page 6). This involved finding rare cells in the fly embryos whose nuclei had the correct properties for study. "The issue with this project was the scale of it," says Perez Gonzalez. Furlong's team needed to find 40 million target nuclei per batch. Thanks to their close collaboration with Perez Gonzalez, they were eventually able to purify 100 million nuclei in half a day, adding up to several billion nuclei found so far.

Furlong's project was an example of needle-finding. Jan Ellenberg's team, which studies cell division, presents Perez Gonzalez with an additional problem: identifying different needles even though they are hard to see. As well as being rare, the cells Ellenberg is looking for glow only very faintly. But the machines at EMBL Heidelberg contain unusually powerful lasers, meaning that even though each snapshot lasts only 2 millionths of a second, there is enough light for the detector to capture the glow.

The ability to quickly and precisely measure up to 20 different properties in a single cell has allowed the Monterotondo facility to uncover hitherto hidden diversity in the samples they test. For example, it is helping Paul Heppenstall's group look for populations of neurons responsible for sensing pain and touch, and aiding Martin Jechlinger's team's search for stem cells involved in breast tumours.

"We have the ability to quickly and precisely measure up to 20 different properties in a single cell"

These strong lasers, together with the ability to modify the cytometers, mean that Perez Gonzalez and Bilbao have the flexibility to adapt the instruments and propose new ways of using them to meet the ever-more demanding challenges their users bring. "Someone may come with a crazy idea that will end up in a *Nature* paper and you need to give full support to this idea," says Perez Gonzalez. "This normally means challenging the instrument to its limits."

Inspired by nature

The poster image for this year's EMBL PhD symposium, created by Mariia Burdyniuk, a PhD student in the Lénárt group at EMBL Heidelberg, beautifully encompasses the event's theme: 'Inspired by biology – exploring nature's toolbox.'

BY SONIA FURTADO NEVES

Shedding light on life: viruses can be used to insert fluorescent markers and other genes into cells.

THE 16TH EMBL PHD SYMPOSIUM TAKES PLACE 23–25 OCTOBER AT EMBL HEIDELBERG.
FOR MORE INFORMATION VISIT:
PHDSYMPOSIUM.EMBL.ORG

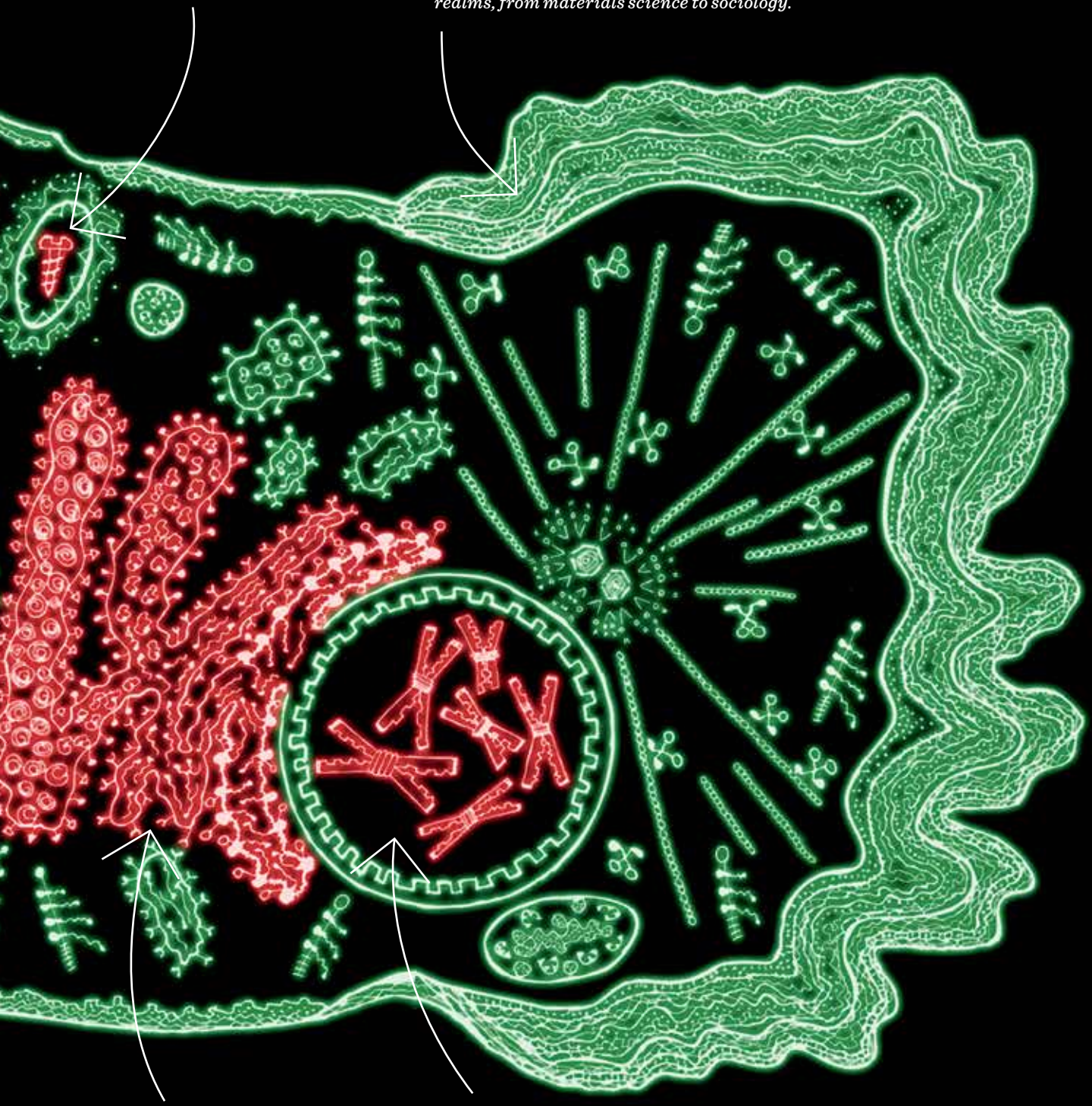


IMAGE: MARIIA BURDYNIUK. EDITED BY PETRA RIEDINGER

International connections

During the development of the human brain, hundreds of billions of nerve cells in the nervous system are making new connections. Despite this unimaginable amount of wiring, the main component of our nervous system, the neuron, always seems to know exactly where to go, and extends nerve fibres – or axons – towards their final target with precision and determination.

BY ROSEMARY WILSON

How is it possible that, in this seemingly random network of connections, nothing goes wrong? What invisible hand steers the neurons safely to their destination? Through a collaboration spanning several years, three continents and several close calls with airport security, Rob Meijers, group leader from EMBL Hamburg, and collaborators have determined the structure of an unusual protein complex that plays an important role in guiding neurons.

Triggered attractions

At the tip of growing axons sits a 'growth cone', a fan-shaped structure with finger-like extensions. Receptors expressed on the cone recognise signals from the cell's surroundings, which they interpret into path-finding instructions, like a dog following a scent trail. These signals, or guidance cues, trigger an 'attract' or 'repel' response. One of the four major families of guidance cue proteins is netrin – from the Sanskrit word "Netr" meaning "one who guides" – a small but unique family of proteins that can trigger attraction and repulsion. How one molecule performs these contradictory push-and-pull functions has long been a mystery.

Netrins have undergone very few changes during evolution and are conserved across the entire animal kingdom. Meijers and colleagues studied netrin-1 in complex with one of its receptors, DCC, which together trigger an attraction. The structural data, published in *Neuron*, show that a single netrin-1 molecule can bind with two molecules of DCC simultaneously. "One binding site is specific to DCC," explains Meijers, "but the second is not. It is a generic binding site that can ››

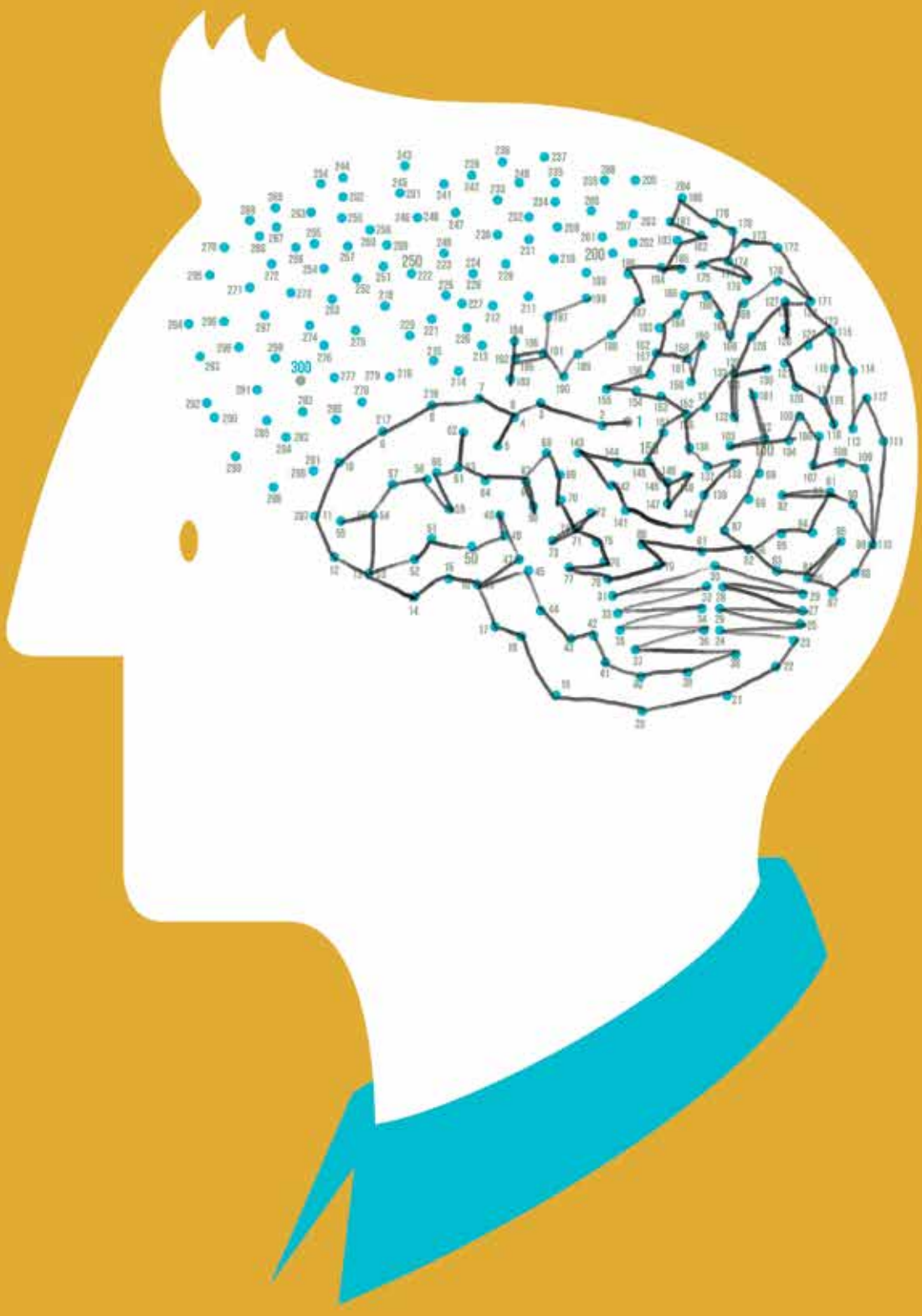


ILLUSTRATION: AAD GOUDAPPEL

"Normally, you sacrifice a few crystals before finding the ideal conditions, but those crystals went straight to the beamline and the first one diffracted successfully."

›› also accept other receptors." Exchanging DCC for another receptor in the non-specific site switches the neuron's response from attraction to repulsion, changing the protruding axon's direction of growth.

Boston–Hamburg–Beijing

The finding is the result of an ambitious research project that accrued many thousands of frequent-flyer miles for the scientists and their samples. "It has been an extraordinary journey," says Lorenzo Finci, the postdoc who worked on the project with Meijers, and who globe-trotted between three of the world's top science institutes – and into several nerve-wracking situations.

Finci was recruited by Jia-huai Wang from the Dana Farber Cancer Institute in Boston, to work in a newly established lab at Peking University. After receiving a short-term EMBO fellowship to fund a three-month stay in Germany, he arrived in Hamburg in November: "My first Thanksgiving outside of the US," he says. "I didn't know where to find a traditional Thanksgiving turkey, so instead I celebrated with a burger, which I'd heard were famous in Hamburg!" During a cold winter, Lorenzo worked together with Nina Krüger from Rob's group to work out how to purify netrin and, crucially, how to put it together with DCC.

Straight to the beam

Once Finci's fellowship ended and he returned to China, the project became even more international, which proved as stimulating as it was stressful. "Everything works on a 24 hour cycle," says Meijers, "When I wake up, China has already been working for six hours. By the time I go to bed, Boston has another six hours worth of data to hand back to Beijing." Transporting samples was also problematic: "Getting liquid samples in and out of China is impossible by mail." Finci took advantage of a family trip to Turkey, enlisting his cousins to race him through Istanbul traffic so that he could ship samples to Hamburg overnight.

Meijers and his group got to work, and within a week crystals had formed – but was it the sought after DCC-netrin complex? "I received an excited email that it was," Finci recalls. "I called my supervisor, Jia-huai Wang, maybe 50 times before he finally called me back and I shared the good news!" Meijers stresses the advantage of having immediate access to the beamlines and sample characterisation facilities at the PETRA III synchrotron ring on the Deutsches Elektronen-Synchrotron (DESY) campus. "We crystallised the protein complex using our on-site facility the same day," he says. "Normally, you sacrifice a few crystals before finding the ideal conditions, but those crystals went straight to the beamline and the first one diffracted successfully."

Binding site negotiations

Later that week, the group noticed there were actually two binding sites on netrin, and decided to have a friendly bet on which site was more physiologically relevant. "Site one would be celebrated with Dutch-brewed Heineken, site two with Tsingtao," says Finci.

Characterising the two binding sites meant more trips for Finci. "He acted as a 'mule', travelling back and forth between Beijing and Hamburg 10 times," says Meijers. "After one 13-hour trip from Beijing to Hamburg, the customs agent called me over," says Finci. "I declared the bag's contents, and showed them the paperwork. Two hours later, I had an audience and was being investigated by five agents and two dogs!" EMBL Hamburg's administrators came to the rescue, rushing over new

PHOTO: MARTA MAYER

Nina Krüger (front), with Rob Meijers and PhD student Magda Chegkazi

paperwork with official EMBL seals. On returning to Beijing, this time with netrin in hand, the same thing happened. "I learned two important lessons: to carry documentation with impressive seals, and a box of chocolates for my friends the customs agents."

It turned out that both binding sites are important, so rather than beer, the teams celebrated with wine and a Peking Duck dinner when Meijers visited Beijing. "Most protein binding sites have a 'lock and key' mechanism," he explains. "This second non-specific binding site is unusual: it is positively charged, as are the receptors, so normally they would repel each other, like equivalent magnet poles." Instead, it seems that sulphate ions sit in the binding site and negotiate which receptor is received. "These negatively charged ions are organised in such a way that they can also be replaced by certain sugar-like molecules, called heparan sulphates," he adds. "We know that deactivating sugar molecules confuses neuronal wiring – to make a link that suggests sugars and small molecules are important in selecting receptors could be relevant for rational drug design."

Beyond neurobiology

Although their work has concentrated on the field of neurobiology, the results have possible applications in the field of cancer biology. Many cancer cells produce netrin to attract blood vessels that nourish them and help them grow. Interrupting this netrin supply could starve the tumour, or at least prevent it from growing. DCC stands for 'Deleted in Colorectal Cancer' and its absence seems to result in uncontrolled cell growth and tumour metastasis. "Maybe now that we know more about how DCC and netrin-1 work, we can attempt to influence cell growth and stop tumour metastasis in its tracks," says Meijers.

Finci, L.I., Krüger, N., Sun, X. *et al. Neuron*, 7 August 2014. DOI: 10.1016/j.neuron.2014.07.010

Embracing cellular complexity

'A Million Peptide Motifs for the Molecular Biologist,' a paper from Toby Gibson and like-minded colleagues in *Molecular Cell* boldly claims.

BY LINDSAY BROWNELL

Those not steeped in structural and computational biology will likely miss the joke; the review completes a trilogy of papers published over the last two decades, each one upping the numerical ante on its predecessor ('One thousand families for the molecular biologist' by Chothia in 1992 and 'Ten thousand interactions for the molecular biologist' by EMBL alumni Aloy and Russell in 2004). The upward trend in the literature parallels recent discoveries that cellular systems are much more complex than earlier generations of scientists had predicted.

As a molecular biologist, "you've got to be reductionist. You've got to tease apart the systems and then rebuild them" to understand them, says Gibson, a team leader at EMBL Heidelberg. "What happens is that you can then easily underestimate the complexity in the system." He hopes to bring that complexity to the fore and reestablish it as a primary concern for the field going forward.

Myriad Motifs

Gibson and colleagues focus their review on segments of proteins called peptide motifs - short molecular interaction sites within larger 'intrinsically disordered' protein regions. Being disordered doesn't mean those regions misbehave; they simply don't fold into a specified shape on their own. They need to be bound by another molecule to become more rigidly shaped, whereas the natively ordered regions, called 'globular domains,' are always folded and therefore more amenable to analysis using techniques like X-ray crystallography.

Peptide motifs far outnumber globular domains in the human proteome, and not only can they bind to other proteins, many of them can also be modified by a variety of enzymes at post-translational modification (PTM) sites.

Phosphorylation, the most common type of protein modification, is predicted to occur at about 400,000 PTMs. But there are more than 300 different kinds of PTMs that most likely interact with a variety of molecules, making one million peptide motifs an appropriate estimate.

"You could knock out a single phosphorylation site in a mouse and never be able to see any effects."

Some scientists argue that not all PTMs are functional because they vary between species and accumulate changes quickly, traits that might imply that they aren't vital for survival. In addition, a single PTM might have so small an effect that mutating it wouldn't change the observable cell function. But, says Gibson, the sheer number of possible protein interactions means that a PTM might be active only under a set of very specific conditions. "You could knock out a single phosphorylation site in a mouse and never be able to see any effects. But that site might only work when an animal experiences starvation plus dehydration or some other combination of stressful conditions, which are unethical to do in experiments," he says.

Deceptively simple

Some peptide motifs have turned out to be important potential targets for drugs, such as two that are hijacked by HIV to get out of infected cells and attack healthy cells. When those motifs are mutated, new viruses get to the cell membrane but can't exit properly. The prospect of halting the spread of HIV by interfering with just those two motifs is a compelling reason to keep studying peptide motifs, because there might just be other potentially lifesaving insights waiting to be discovered.

Gibson is keenly aware that cautioning scientists to account for the complexity presented by PTMs is in direct conflict with the assertive language that garners press coverage and accolades. "A paper might say, 'We found out how [the protein] P53 works', but if you change the experimental conditions or the cell type, P53 works very differently. All these dogmatic titles that you see in prominent articles about how the cell works are never true, except in a very limited sense," he says. "There's a kind of unholy alliance of editors and big signalling labs who want to keep on making these easy-to-sell statements." It's not a field-specific problem, either – many scientists whose work depends on models tend to eschew complexity, because modelling requires stripping the object or process being studied down to its simplest form so that the computations are feasible. Gibson thinks this is a fundamental problem because it ignores all the potential outcomes that could happen under different circumstances – outcomes that could, for example, cause a drug to help some patients while inadvertently harming others.

Complexity in context

How would Gibson and his colleagues recommend a molecular biologist proceed when facing the daunting prospect of a million peptide motifs? The answer is best summarised by the conclusion of their paper itself: "A careful choice of experimental design to test motifs is crucial...because an important challenge for the community is to not only identify binding motifs and PTM sites, but also functionally characterise these peptide motifs by investigating them in the right biological context."

Tompa *et al. Molecular Cell,* 17 July 2014. DOI:10.1016/ j.molcel.2014.05.032

40 years young

PHOTOS: ROBERT SLOWLEY

Above: Science comedian Robin Ince captivates the audience at EMBL-EBI's 20th anniversary in June

Reunions, conferences, gatherings, public lectures, outreach activities, and more have brought hundreds of staff, alumni, special guests, and visitors together across EMBL sites and beyond to mark the Lab's 40th birthday. While EMBL has long shaken off its newcomer badge, it is clear its spirit, attitude and people remain very young at heart. Here is a just a glimpse of what's been going on.

Below: Nobel Laureates and EMBL alumni Christiane Nüsslein-Volhard and Eric Wieschaus in conversation at the Festakt event at EMBL Heidelberg in September

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

"I am always surprised by how many leading scientists have passed through EMBL at some point."

EWAN BIRNEY, JOINT ASSOCIATE DIRECTOR, EMBL-EBI

Clockwise from left: Guests at all events were very well catered for; members of the public were expertly guided through experiments during a Forschercamp at EMBL Heidelberg in July; a range of different acts kept participants entertained until the early hours

"I really enjoyed the opportunity to see so many friendly faces again. I think the large number of people who attended is a great testament to what EMBL means to all of us."

MARTIN JINEK, ASSISTANT PROFESSOR, UNIVERSITY OF ZURICH

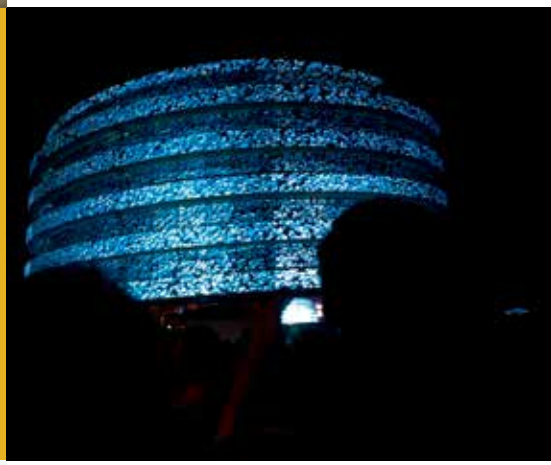
PHOTOS ON THIS PAGE: EMBL PHOTOLAB/MARIETTA SCHUPP

"I find EMBL like its own planet, similar to New York – everybody has a story to tell and comes from all walks of life."

HORST HAMANN, PHOTOGRAPHER

"An unforgettable and magnificent occasion. I felt somehow I had come 'home' and it is amazing that you all managed to make ancient alumni feel so very welcome and significant."

MELANIE PRICE, SENIOR RESEARCHER, LAUSANNE, SWITZERLAND



PHOTOS ON THIS PAGE: EMBL PHOTOLAB/HUGO NEVES

Clockwise from top left: Staff and alumni fill the Klaus Tschira Auditorium at EMBL Heidelberg during the EMBL 40th Anniversary Reunion in July; the event featured a spectacular light show by media artist Markos Aristides Kern; the celebrations were combined with EMBL's annual Lab Day, with fun and scientific work from staff across EMBL sites on display

PHOTO: RALF OFFERMANNS

Clockwise from left: Photographer Horst Hamann installing D_N_A | Portraits by Horst Hamann, an exhibition of photos of staff and alumni; current staff join alumni and special guests for a buffet lunch at a celebration at EMBL Monterotondo, which also marked the outstation's 15th birthday; Nadia Rosenthal, former head of outstation, was one of many special guests at the celebration; young researchers presented their work to the public during a series of matinees taking place throughout EMBL's anniversary year

PHOTO: MEHRNOOSH RAYNER

"EMBL is run by people who continuously come up with new ideas, and this has allowed Monterotondo to grow and flourish in the context of the European scientific environment."

NADIA ROSENTHAL, HEAD OF EMBL AUSTRALIA

PHOTO: MEHRNOOSH RAYNER

PHOTO: CEMM

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

"EMBO and EMBL have shown that when Europe combines its forces by bringing together its best talents, it can lead the world in science and innovation."

ROBERT-JAN SMITS, DIRECTOR GENERAL OF THE DG FOR RESEARCH AND INNOVATION, EUROPEAN COMMISSION

PHOTO: CEMM

Clockwise from top left: Alumna Louise Barlow at EMBanniversary, Austria; a 'Science Tree' symbolising unity in the life sciences in Europe was planted during the joint EMBO|EMBL Anniversary Science and Policy Meeting in July; Giulio Superti-Furga captures a picture-perfect moment at the EMBanniversary, Austria celebration

Cultures

PHOTO: F. HOFFMANN-LA ROCHE LTD

Adventure science

EMBL fellows went on some refreshing, rewarding and remarkable expeditions across Europe this summer. Here are some of the highlights…

Source of inspiration

BY CHARLES BREEZE, PHD STUDENT, EMBL-EBI AND UNIVERSITY COLLEGE LONDON

A global encounter, covered by broadcast and print media from every corner of the world, the Lindau Nobel Laureate meeting represents an annual highlight of the scientific calendar. Some of the most prominent and influential scientists in the world meet hundreds of talented young scientists and this year, I was one of four EMBL fellows who were amongst them.

One of the most inspiring people I met at the meeting was Oliver Smithies, a Nobel Laureate best known for his contributions to gel electrophoresis and gene targeting. He gave us some useful advice: most notably, to share our science openly. For one of every hundred people who might copy us, he said, we would miss a chance to influence or motivate 99 who share our passion for science.

I will never forget the yacht trip delegates took to Mainau, known as the flower island. We set off from the port at Lindau, crossing Lake Constance under the clear morning skies, with the snow-capped Alps in the backdrop. Upon arrival we were greeted with a view of the island's stunning 18th century castle, looming over the cliffs above. The experience was unforgettable and has reinforced my passion and motivation for science.

Nobel Laureate Tim Hunt shares his expertise and experience with the group

PHOTO: JELENA TICA

From students to mentors

BY MICHELE CRISTOVAO

"We had the coolest project, the best mentors and the best team – it was a really, really nice experience!" These were the words that Sara from Belgrade, a big fan of theoretical physicist Richard Feynman, used to describe her experience at the Summer School of Science (or S3++) in Pozega, Croatia. S3++ took place in July – an annual event organised jointly by Croatia's Society for Out-of-Frame Education and the Science and Education Centre.

Over 10 days, high-school students from all over the world dived into the exciting world of scientific discovery, guided by a group of young scientists. This year, S3++ had a special EMBL flavour: the mentors Sara praised so highly were PhD students Jelena Tica and Matilda Males from EMBL Heidelberg, who took on the role of project leaders and, together with five students, undertook to 'Explore the Genome with Next-Generation Sequencing'.

"The aim of our experiments was to explore variations in different genomes in order to understand how changes in the genome architecture may lead to phenotypic variation," Tica explains. "Our group looked into three different primate genomes and explored structural similarities and differences within and in between species. I gained friends and colleagues, with whom I hope to stay in touch. But most of all, this experience made me fall in love with science all over again!"

Duygu Sari is back row, second from left. Participants at Roche Continents came from all over the world

PHOTO: F. HOFFMANN-LA ROCHE LTD

100 different stories

BY DUYGU SARI, PHD STUDENT, EMBL GRENOBLE

Day 1: In Salzburg, it's raining like crazy. I think back to all the work I have to do in the lab: experiments to run, papers to read and write... Then we arrive and my concerns melt away. 100 young science, music and arts students from all over the world are here for Roche Continents, an exciting programme of seminars, concerts and workshops taking place during the city's world-famous festival. Our goal is to explore common grounds of creativity – like syllables with different sounds in the same song.

Day 2: We learn how Roche evolved into a cornerstone of big pharma, and the important role of art in its history. Then, we drum! It might sound weird, but I learn how to breathe: we smile, we beat; we breathe, we beat; we hug; we beat. The performance brings home feelings of freedom and open-mindedness.

Day 3: Tonight we see a poignant opera and afterwards we have the privilege of meeting the conductor, the main actress and the Salzburg festival president Helga Rabl-Stadler. I learn how organised and disciplined an artist's life must be. They, too, must overcome difficulties and solve challenges: "Fail, fail and fail better!" says Rabl-Stadler.

Day 4: We return from a free afternoon to attend a lecture, listed in the schedule as 'The Art of Quantum Molecular Dynamics'. It sounds a little tedious, but we're in for another surprise: it's our chance to get up on stage and create 'Danceroom Spectroscopy', a project that allows dancers to influence graphics and sound through their movements.

Day 5: Tonight, contemporary music in a beautiful church. It reminds me of a horror movie soundtrack: strange noises come from many different angles. I feign enjoyment, but afterwards we meet the composer, and his explanation and efforts to define new music tastes help to persuade me of its merits.

Day 6: When we arrived, we were told we'd see the change in ourselves in just one week. I see in myself that I am not afraid to fail any more. It's difficult to say goodbye, but having the opportunity to be part of Roche Continents and meet all these great people makes me smile all the way back to Grenoble.

Nordic networks

From scratch six years ago to more than 40 research groups today, there was much to look back on, and forward to, when researchers of the Nordic EMBL Partnership for Molecular Medicine convened in Umeå, Sweden at the end of August for their annual network meeting. Speaker of the Partnership Kjetil Taskén explains more. BY ADAM GRISTWOOD

PHOTO: EMBL PHOTOLAB/MARIETTA SCHUPP

The Partnership brings together the Danish Institute for Translational Neuroscience (DANDRITE), the Institute for Molecular Medicine Finland (FIMM), the Laboratory for Molecular Infection Medicine Sweden (MIMS), the Centre for Molecular Medicine Norway (NCMM) and EMBL. Kjetil Taskén is Speaker of the Partnership and Director of NCMM.

What are the key objectives?

The central goal is translational medicine – taking discoveries from the lab to the clinic to health benefits. There have already been significant improvements in healthcare as a result of translational research, but there is also huge potential to push forward and to do this better. Flagship projects increasingly incorporate large data sets from genomics, proteomics, biobanks, health registries, as well as information on communities. Since the partnership agreement was signed we have become a powerful force and have created excellent infrastructures, networks and training programmes geared towards tackling these research challenges. Collectively, we are focussed on enhancing the research enterprise so that patients can benefit quicker from advances, while at the same time facilitating highly ambitious blue-skies research that is crucial in making translational medicine happen.

What kind of creative flows do you see?

The partnership spans almost the entire research spectrum: human genomics and systems medicine (FIMM); infection and microbiome (MIMS); brain circuitry and neuronal disease (DANDRITE); and disease mechanisms (NCMM) – there are almost too many examples to choose from! One exciting area is the increasing use of tools, algorithms and other platforms to integrate genetic and molecular information with traditional clinical knowledge and tailor treatment to individual patients. Another is the development of elegant structural biology methods to better understand tricky elements such as membrane proteins and molecular transport. But there are many more. Our connections with EMBL are very important in this respect – we have adopted the EMBL model in terms of international recruitment and scientific reviews, which really increases quality at all levels, and we initiate valuable scientific exchanges, joint appointments, and symposia like the one here at Umeå.

How about the main challenges?

The partnership is spread across four different countries, which can create logistical challenges, as well as being quite young. But there have been ways to turn this to our advantage, especially with the addition of DANDRITE as the partnership's fourth node in 2013 and the extension of the partnership agreement for another 10 years. We are focused on enhancing the cohesion that we have established thus far and further increasing our interactions with EMBL to improve our knowledge exchange and use of available infrastructures – as we grow we will see this happening more and more. Other priorities include enhancing connections with local research communities, as well as gaining more recognition beyond the world of science.

Pathways Science meets arts

Playwright, author, and art director: skills not often associated with the trade of a scientist.

BY MICHELE CRISTOVAO AND ADAM GRISTWOOD

But since completing his PhD at EMBL, neuroscientist Giovanni Frazzetto has put on each of these hats, driven by an infectious passion to connect his research with society and culture at large. Now, as an academic coordinator of the College for Life Sciences at the Institute for Advanced Study in Berlin, he helps early career researchers pursue daring and unusual research projects that cross boundaries – in much the same way his own work has.

"My role here is to coordinate an initiative that helps life science researchers think about how far their research can go in its explanations, and explore how different disciplines might help to fill in the gaps – be it history, linguistics, psychology, economics, law, or other," he explains. "My role involves responsibilities such as screening and selection, facilitating collaborations and providing mentorship. The most important aspect is that fellows are free from any administrative constraints and this delivers an environment that is intellectual, creative and collaborative. Studies are highly varied and range from the reasons underlying the diversity of life, to the evolution of human reproduction, to the neuroscience of memory forgetting."

Frazzetto learned first-hand the benefits of a multidisciplinary approach whilst studying the neuroscience of anxiety-related behaviour during a joint-fellowship at EMBL and the London School of Economics. "While we are learning a great deal about anxiety, when trying to understand something as complex as emotions it is important to reflect and ask: can the brain tell us how we feel?" says Frazzetto, who last year published a popular science book exploring this question in the context of emotions such as love, joy, grief and anger. "Emotions are something very personal and subjective, and one looks for the explanation that is most apt – regardless if this is an experiment, a work of art, or a philosophical text."

As a researcher, Frazzetto often found himself thinking about how he could grab hold of such questions and turn them inside out. He started with small steps – helping with EMBL's Science and Society programme, taking a creative writing course and submitting articles to magazines. From here, he scaled up, co-directing an art exhibition examining how modern brain science has penetrated popular culture, scribing plays exploring neuropsychological disorders, and setting up a network to connect neuro- and social scientists across Europe. "The skills learned here might apply equally well to jobs in areas as diverse as science policy, technology transfer or science communication," he explains. "Think about what motivates you – I have always followed a philosophy of looking beyond the obvious: take risks, follow your instincts, and see where it leads."

FOR MORE ON FRAZZETTO'S WORK VISIT: GIOVANNIFRAZZETTO.COM AND WIKO-BERLIN.DE/CFLS

PHOTO: EMBL PHOTOLAB/UDO RINGEISEN

Branches The perfect meal

Grab some dark chocolate, put on some headphones, close your eyes, and relax. Comfortable?

BY ADAM GRISTWOOD

A simple experiment designed by Oxford University psychologist Charles Spence encourages users to flick between high- and low-pitched sounds as they enjoy a delicious bittersweet snack. And if you happen to experience sweetness flooding over your taste buds as you listen to the high notes, or bitterness as the pitch gets lower, you are not imagining things.

This tasty exercise, which Spence describes as "sonic seasoning" illustrates one of many approaches that his team, in collaboration with neuroscientists, marketers, musicologists, designers and chefs, are using to better understand our experience of food and drink. "Flavour is shaped not only by taste and smell, but by the environment, the context of the meal, and visual cues," he explains. "Food is the one place where all the senses come together. The room, the music played, even the shape and colour of your plate – they all matter."

Sensory science

Spence's publication list reads like an experimental tasting menu. In one study, designed with top Spanish chef Ferran Adria, diners rated an identical strawberry mousse as 10% less sweet if served on a black plate rather than a white one. Another illustrated how perceptions of whisky can be influenced to be more grassy, woody or sweet, depending on lighting, background noise, or surrounding scents. He has looked into why tomato juice is a drink of choice on an airplane but not on the ground, and found that potato chips that sound crunchier, taste better. "Even before we put food into our mouths our brains have made a judgement about it," explains Spence. "People buy a wine that tasted great while on holiday in the sun, open it on a cold winter's

night and it tastes horrible – everyone has had a version of this experience."

The work has attracted the attention of academia and industry alike. Coffee giant Starbucks has developed playlists for customers to listen to, to get that 'coffee-shop experience' at home. While chocolate company Cadbury was dealt a harsh lesson when it gave its Dairy Milk bar a more rounded shape, only to receive complaints from consumers who believed the recipe had been modified (it hadn't). The reason? Round tastes sweeter. "Surprisingly, these perceptions are common across groups of people," Spence explains. "By taking our understanding of how the brain works, we can learn which shapes, instruments and notes go with particular tastes, and present them together to make food healthier and taste better."

New ideas on the menu

Amongst many other projects, Spence is currently working with a philosopher and a chef to identify ways of making insects more attractive as a substitute for meat – and the work is opening up the tantalising prospect of nudging people into making healthier food choices. "Before the focus has been on technology in the kitchen – you do not see it, but taste the results," he says. "Going forward I think we will increasingly see more things like directional soundscapes and harnessing mobile technologies at the table. Restaurants are a fantastic test bed of innovation – and if you can convince chefs that the colour of their plate matters, then it could be on the menu the following day, just like that."

Charles Spence is speaking at the EMBL|EMBO Science and Society conference Foods are us! On eating and becoming, which takes place at EMBL Heidelberg on 6–7 November.

WWW.EMBL.ORG/SCISOC2014

PHOTO: UNIVERSITY OF CAMBRIDGE

Awards & Honours

Sarah Teichmann, research group leader at EMBL-EBI and the Wellcome Trust Sanger Institute, has been recognised by the Biophysical Society for her outstanding contributions to biophysics. The Michael and Kate Bárány Award for Young Investigators recognises an outstanding contribution by a person who has not yet achieved the rank of full professor. Teichmann's nomination listed her as "one of *the* leading structural computational biologists of the younger generation."

Stephen Singer, a fellow within the framework of the Molecular Medicine Partnership Unit, is a co-recipient of the 2014 Hella Bühler Prize. Awarded by the University of Heidelberg, the 150 000 euro prize recognises outstanding work by young scientists in the field of cancer research. Singer is currently working between the Medical Faculty of the University of Heidelberg and the Beck group at EMBL Heidelberg as part of a career development fellowship aimed at intensifying and broadening connections between the two institutes.

Q&A Where is computational biology heading?

QUESTION SUBMITTED BY SCOTT SCHORR OF PITTSBURGH, USA

Ask EMBL anything!

What inspired the EMBL logo? How do you pronounce *drozdowiczii* in "*Streptomyces drozdowiczii*?" Will we ever grow an artificial brain in the lab? On the occasion of EMBL's 40th Anniversary we are exploring 40 questions people have asked about the Lab.

STAY TUNED OVER THE COMING MONTHS ON NEWS.EMBL.DE

Unravelling DNA riddles

The structure of DNA was discovered more than 60 years ago, but many questions remain unanswered. Most fascinating is how the DNA molecule can function while being compressed so tightly inside the cell's nucleus. If a strand of DNA were as thick as a fine thread, it would be like packing 20 km of thread into a chicken egg. All the functions in the human body depend on various processes to unfold, duplicate, segregate, couple and decouple this bundle of DNA correctly, so that the right genes are expressed at the right time. Many of these mechanisms have been studied, but we still don't fully understand how they work – like watching a game of sport without knowing the rules. New computational developments are needed in order to learn about all the 'players' involved and fully unravel this enigma.

Single cell sequencing

Progress lies not only in advances in computational methods, but in the experimental techniques that develop alongside them. One of the most promising is single-cell sequencing – studying the genomes and transcriptomes of individual cells, rather than averaged data from across millions of cells. Single-cell techniques will allow us to investigate the heterogeneity within a population, which in turn helps us model accurate networks that describe cell behaviours. Such approaches will likely improve data acquisition as well, greatly increasing the amount of data available to construct models of complex cellular networks. Understanding these networks will enable us to make predictions about the behaviour of cells in health and disease, opening up new avenues for treatment and prevention.

A bigger picture

Rather than look at the evolution of one particular gene or molecule, advances in computing will allow us to effectively look at all of evolution at once. We can in principle do this today, but the problems scale so rapidly that it's not currently possible to evaluate evolution across large numbers of organisms. Even ambitious evolutionary analysis projects need to restrict themselves to just some of the available genomes and/or filter out the weaker conflicting signals, because to do the same algorithms for everything available might take a hundred years or more based on today's computing power. Progress in the coming years and decades will transform this landscape.

PHOTO: EMBL PHOTOLAB

Erica Valentini, PhD Student, EMBL Hamburg

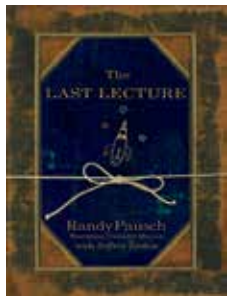
Mike Stubbington, postdoc, EMBL-EBI

PHOTO: EMBL PHOTOLAB

Kristoffer Forslund, postdoc, EMBL Heidelberg

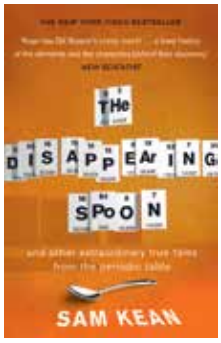
Reviews

Which book best gets your creative ideas flowing? A team of bibliophiles from the Lab has picked out the stories that have inspired them at work, or elsewhere.



The Last Lecture, **Randy Pausch**

When Carnegie Mellon professor Randy Pausch was asked to give a talk under the title *The Last Lecture,* no one imagined that it would actually be his last one. Diagnosed with terminal pancreatic cancer, Pausch makes the decision to give a talk that could be his final legacy. The lecture, called *Really Achieving Your Childhood Dreams,* is about making the best out of the time we have, fighting for our dreams, overcoming obstacles, and above all, living rather than dying. The narrative leads the reader to consider how they might make their own childhood dreams come true. One of the most inspirational and powerful books I have ever read. VASILIKI KARYOTI, DESKTOP SUPPORT ENGINEER, EMBL HEIDELBERG

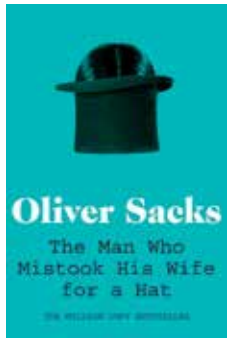


The Disappearing Spoon, and Other True Tales of Madness, Love, and the History of the World from the Periodic Table of the Elements, **Sam Kean**

I picked up *The Disappearing Spoon* at a train station by chance and was immediately hooked by this collection of bite-sized, fascinating, and sometimes quirky anecdotes about the chemical elements. Rather than explain how the periodic table works, the book presents a fantastic array of science stories that cover history, personalities and even global politics. Having studied chemistry, I have always been interested in the periodic table – however, over time the magic of the elements got smothered with technical terms and industrial production pathways. This book managed to rejuvenate my fundamental fascination for this topic and it will probably convince even hardcore biologists that there is a world beyond C, H, O, N, S and P worth investigating. MARIE KIRSTEN, POSTDOC, EMBL HEIDELBERG

Stranger in a Strange Land, **Robert A. Heinlein**

It inspired Iron Maiden, is a headline event in Billy Joel's *We didn't start the fire* and is one of my all time favourites. The story presents a new world that questions our status quo: our society, beliefs, politics ... everything. A young man is brought to Earth after being raised from infancy by Martians and this pretext is used to shake the reader loose from prejudice in its many manifestations and explore why we should question everything, including our scientific research. Robert A. Heinlein was a visionary of his time – many of his hypotheses are still valid and some of his science fiction is now reality. A must read. DANIEL PASSON, POSTDOC, EMBL HAMBURG



The man who mistook his wife for a hat, **Oliver Sacks**

Neurologist Oliver Sacks describes some exceptional cases of patients who have experienced problems with perception, emotion, language or memory in some insightful and compassionate short stories. Imagine after a brain injury, you can no longer speak in your mother tongue but keep speaking a second language. Or you can no longer learn anything new, remaining imprisoned in that very moment for the rest of your life. Or that you cannot recognise everyday things such as a plate of food or even your spouse. I was inspired by the author's fascination with how mental functions map onto specific brain areas – the brain really is a striking machine. JOSE VIOSCA, POSTDOC, EMBL MONTEROTONDO

Alumni

A year to remember – 40 to celebrate

EMBL's anniversary year has seen tremendous alumni engagement. More than 700 alumni spanning EMBL's four decades and five sites joined us at celebrations in Hinxton, Monterotondo, Heidelberg, and Vienna (page 30). More than 100 alumni contributed as organisers, speakers or sponsors at these events, as interviewers, writers or material contributors to the magazine *40 Years EMBL* (page 46), and as donors or contributors to the EMBL archive (page 45). More than 500 have put on the anniversary sports shirts worldwide, spreading the EMBL message "Vom Leben lernen" (learning from life). We thank you for your enthusiastic support and feedback, and look forward to meeting more of you at the remaining anniversary events in Hamburg and Grenoble.

Mehrnoosh Rayner
Head of Alumni Relations

Nominate board members!

MR In 2015, we will be saying goodbye to Alumni Association board members Giulio Superti-Furga (Chair), Maria del Mar Vivanco (Vice Chair), Anastasia Politou and Maj Britt Vorgrimmler as their final term in office ends, while they continue to work with EMBL on projects dear to their hearts.

Remaining board members, Marja Makarow (Vice-Chair), Annabel Goulding (Treasurer), Gareth Griffiths, Des Higgins, Jacqueline Mermoud, Preben Morth, Joep Muijrers and Sarah Sherwood will stand for re-election in a bid to continue their second and final term in office. We would like to encourage members of the alumni community to cast their vote in the elections in Spring 2015, and to nominate themselves or others to stand for board positions. Board members can serve up to two terms in office (one term is four years), and are expected to attend the two annual meetings held in Heidelberg and an EMBL outstation in rotation.

Please contact alumni@embl.org by 14 November for nominations or more information.

Mark your diaries

19 October
Application deadline: John Kendrew Award 2015 & Lennart Philipson Award 2015

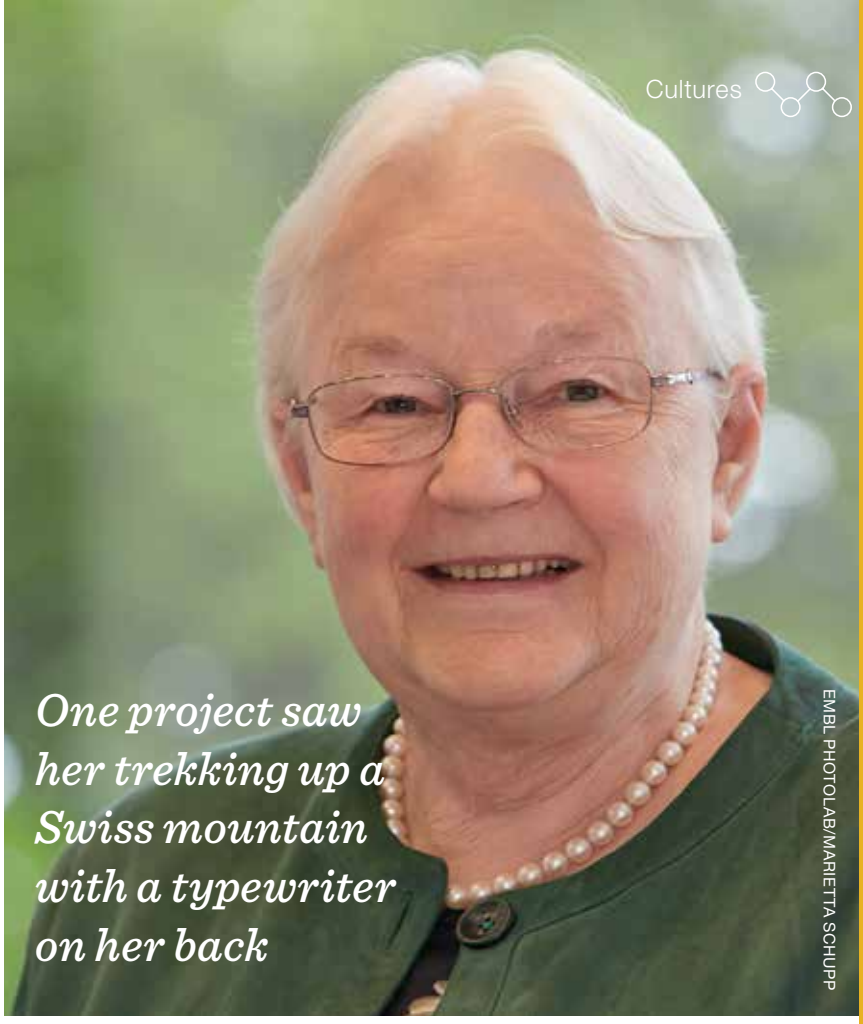
24 October
EMBL-VIB Alumni event, VIB, Ghent

14 November
Nomination deadline for EMBL Alumni Association Board elections 2015

27-29 November
EMBL Hamburg 40th Anniversary Symposium and Celebrations and Alumni Association board meeting, EMBL Hamburg

Witness to history

Forty-five years ago, alumna Frieda Glöckner made a phone call that changed her life. Whilst working as a secretary at the Medical Biology Laboratory in Rijswijk, in the Netherlands, her manager J.A. Cohen died unexpectedly. Cohen was vice-chair of EMBO's Council, and part of a team of ambitious scientists who were sowing the first seeds of a joint European venture in molecular biology. Eager to find another job in the field, she contacted EMBO's executive secretary Ray Appleyard – soon she was on the train to Brussels, where she was hired on the spot just as project EMBL was beginning to take off. BY ADAM GRISTWOOD



EMBL PHOTOLAB/MARIETTA SCHUPP

Front-row seat

It was the beginning of an adventure that provided Glöckner with a front-row seat to EMBL's history. She was involved in drawing up the Lab's first indicative scheme, organised initial steering committee meetings, and later served under four directors general as the institute grew from a mishmash of container rooms to the sophisticated multi-site operation it is today. "In the beginning, it was difficult to imagine what the Lab might become," she says. "There was no bus service, infrastructure, or electricity – all of that had to be put in place."

She was also present at perhaps the most significant meeting in EMBL's history – the official signing ceremony at CERN, Geneva in May 1973. "It was attended by a who's who of biology," she says. "Beforehand, many questions were being asked: How much money would be needed? How much were governments prepared to pay? Who would sign? But the team of scientists driving the project, led by Sir John Kendrew, had strong belief and were very effective at communicating its potential benefits. It ended up a marvellous occasion."

Above and beyond

Ahead of the signing, Glöckner recalls hastily stitching together a makeshift flag to replace a missing one – a steadfast approach that characterised her early years in the Lab where she was administrator, recruiter, event organiser, and diplomat all at once. One project saw her trekking up a Swiss mountain with a typewriter on her back for a meeting with Jeffries Wyman, then Secretary General of EMBO. In another, she travelled to China where she spent four months studying mandarin in order to liaise with Chinese visitors. "I had to rush back for the winter council meeting, where they needed me to take minutes!" she smiles.

As the scope of the Lab's programmes grew, Glöckner's role evolved into heading up EMBL Council's meeting secretariat where, before retirement in 2007, she organised and meticulously recorded further events that have shaped EMBL's history. "People can learn a lot from how the EMBL model has been achieved and it is crucial we preserve as much of this history as we can," she adds. "I was always surrounded by people with great ideas, skill and passion, and looking back it makes me very proud to say that I was there at the start of something really big."

WEB EXTRA:
EMBL.ORG/ARCHIVE

PHOTO: EMBL PHOTOLAB

Successes, challenges and the future

As a birthday gift to EMBL, the Alumni Association initiated an anniversary magazine documenting EMBL's path from a newly established laboratory in the hills of Heidelberg to a multi-site, global leader in modern molecular biology. The 40-page magazine, produced by the Alumni Relations office, includes voices of staff and alumni, an EMBL timeline, scientific highlights, and photos spanning back to 1973 – when CERN announced a "birth in the family". Here, in an exclusive extract, Giulio Superti-Furga, Chair of the Alumni Association, interviews Iain Mattaj, EMBL Director General. BY GIULIO SUPERTI-FURGA

Iain Mattaj, EMBL Director General, 2005-present. At EMBL since 1985.
Giulio Superti-Furga, Scientific Director and CEO, CeMM, Vienna. EMBL Team Leader, 1991–2004, Developmental Biology

What are the most important ingredients of EMBL's success?

I don't think there is a single ingredient. The turnover system is a critical aspect of how EMBL functions, because people need to be able to succeed in a short time. I think one of the secrets of EMBL is that the Unit heads are always looking for people with the potential to open new scientific directions.

What is the biggest challenge for the future?

One reality of life as a leading research institute is that it's expensive. And another is that we need the ongoing support of our member countries. They have always been extremely supportive and very generous with EMBL. In a period of recession like now, these countries need to be brave to continue to invest in education and research.

We as alumni admire that no matter how high the bar gets EMBL seems to be capable of jumping over it.

We are intergovernmental rather than national and therefore both want and need to serve our member states. In the context of molecular biology this means we have to try to do things in ways or in combinations that national labs do not or cannot do. The fact that we have major activities in providing scientific services, in technology development and transfer, in advanced training and in international collaboration in addition to research is a powerful motor and motivation.

What do you think could be themes in the next 10-15 years? Where is EMBL going?

Biology will continue to become more relevant to human health and this will change EMBL. The development in imaging technologies will continue, as will the ability to 'do biochemistry' using imaging. We need to be flexible. People have asked whether EMBL should do more immunology, plant biology or neuroscience. The answer is maybe 'yes', but we need to have the right people with the right ideas to do so.

FULL INTERVIEW, MAGAZINE AND MORE AT EMBL.ORG/ALUMNI/NEWS

Divali, or the festival of lights, is a big celebration on the island. It commemorates the triumph of light over darkness, and signifies new beginnings for Hindus.

Mauritian people have a strong culture of giving and at each festival we very much look forward to sharing bowls of sweets with our neighbours.

Locus Mauritius

Noorie Karimbocus, a PhD student at EMBL Heidelberg, takes us to her favourite spots near her hometown of Vacoas-Phoenix, Mauritius.

Slavery is an integral part of Mauritian history and the rugged landscape of Le Morne Brabant peninsula was used as a shelter for runaways. In 1835, according to legend, police travelled there to report that slavery had been abolished, but many slaves believed they were being chased and leapt to their deaths. Today, Le Morne is a symbol of the slaves' fight for freedom and their sacrifice. It is also a UNESCO World Heritage site.

Mauritius is characterised by multiculturalism and a plethora of colourful festivals fill our calendars.

PHOTOS: KESHAV RAMREKHA

Events

October
14

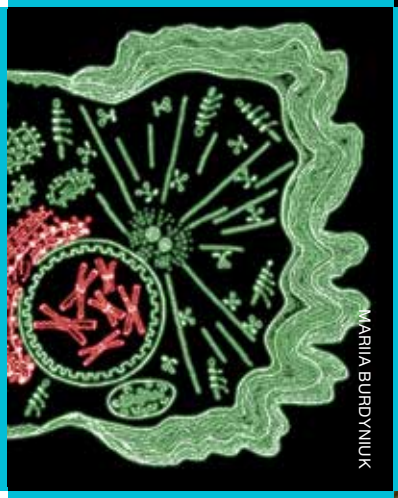
Print Media Academy, Heidelberg
Heidelberg Forum: Das Human Brain Project: Simulation und Realität – Karlheinz Meier, Universität Heidelberg

October
16

EMBL-EBI
Careers Day 2014

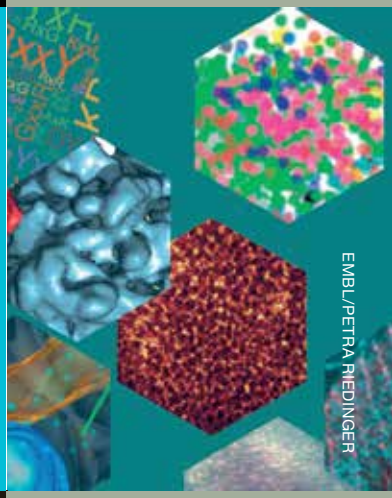
October
23-25

EMBL Heidelberg
The 16th EMBL PhD Symposium: Inspired by Biology – Exploring Nature's Toolbox



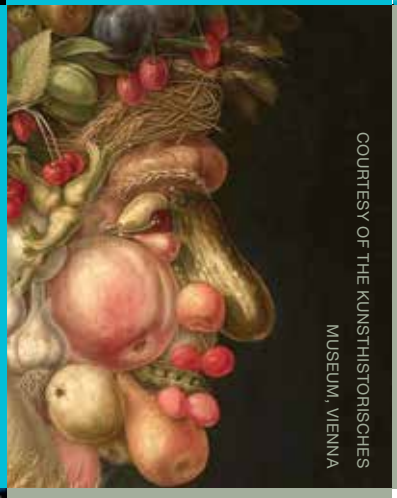
October
26

EMBL Heidelberg
Sunday matinee: Der Sonne entgegen; wie unseren Vorfahren aus dem Meer ein Licht aufging – Silvia Rohr, EMBL Heidelberg



November
6-7

EMBL Heidelberg
15th EMBL|EMBO Science and Society Conference: Foods are us! On eating and becoming



November
17-20

EMBL Heidelberg
EMBO|EMBL Symposium: Frontiers in Metabolism: From Molecular Physiology to Systems Medicine

November
21

EMBL Grenoble
Science and Society seminar: The new big science of the human brain: Social and ethical implications – Nikolas Rose, King's College London

November
24-26

EMBL Heidelberg
Winter Council Meeting 2014

VIEW THE COMPLETE LIST OF EVENTS ONLINE
EMBL.ORG/EVENTS