

July 2009

# Paul Sabatier University

Scientific magazine issue n° 5



Headlines

**Nano-machines**

**Evolution**



[www.ups-tlse.fr](http://www.ups-tlse.fr)

with the participation of

Délégation  
Midi-Pyrénées du CNRS



Administration déléguée  
Midi-Pyrénées, Limousin de l'Inserm

Instituts  
thématiques



**Inserm**

Institut national  
de la santé et de la recherche médicale

## Five years already!

The first issue of Paul Sabatier University magazine appeared in June 2004.

Since this time, our objective has always been to keep you informed of everyday life at our university through periodical scientific reports on current research highlights from our laboratories as well as interviews with the scientists involved in this research. We have always chosen articles of a high standard explained in a simple way so that they can be understood by non-specialists.

The first topic in the present issue is about **nanomachines**. This is a specific domain in nanoscience where close collaboration between specialists in physics, chemistry and biology is required, and for which the local research teams in Toulouse are recognized as being among the best in the world. Here, you will discover how researchers are designing wheels, bearings, rotors and engines at the nanometre scale, just like real mechanics would do, but using the most advanced technologies. Really fascinating!

Since we are commemorating Charles Darwin this year, we thought it would be timely to have a look at the present state of knowledge on the theory of **evolution**. Even though genetics has now become a valuable tool, we will see that it still does not give us all the answers when it comes to biological evolution. While being at the heart of a number of scientific investigations in life sciences, the theme of evolution plays a structural role in relevant research studies at our University.

I hope you enjoy reading this issue of our magazine.



**Gilles FOURTANIER**

President of Paul Sabatier University

### Currently used abbreviations

UPS: Paul Sabatier University (Toulouse, France)  
 CNRS: French National Center for Scientific Research  
 INSERM: French National Institute for Health and Medical Research  
 INSA: National Institute of Applied Science  
 INRA: National Institute for Agricultural Research  
 INPT: National Polytechnic Institute of Toulouse  
 ANR: National Research Agency

SCIENTIFIC MAGAZINE UPS  
 N° 5 — JULY 2009

**Cover illustration:**

The golden-crowned sifaka (*Popithecus tattersalli*) is an endangered forest lemur from north Madagascar.

**Publisher:**

Gilles Fourtanier

**Editor-in-chief:**

Daniel Guedalia

**Managing editor**

English version:

Frédéric Momprou

**Editorial Board:**

Isabelle Berry

Patrick Calvas

Carine Desautly

Gaël Esteve

Daniel Guedalia

Guy Lavigne

Frédéric Momprou

Aude Olivier

**Editorial advisor**

English version:

Belle Dumé

**Mailing:**

Joëlle Dulon

**Guest editors:**

**Nanomachines:**

Frédéric Momprou

**Evolution:**

Etienne Danchin

**Graphic design and print:**

Ogham-Delort

05 62 71 35 35 n°9158

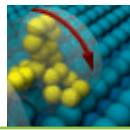
**Copyright:**

July 2009

ISSN: 1779-5478

Print: 500

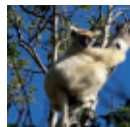
# contents



4

Headline:

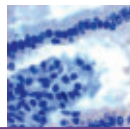
**Nanomachines**



12

Headline:

**Evolution**



19

**News**

Your comments and suggestions are welcome:  
**[revue-paulsabatier@adm.ups-tlse.fr](mailto:revue-paulsabatier@adm.ups-tlse.fr)**

On-line Scientific Magazine UPS:

[http://www.ups-tlse.fr/27503789/1/fiche\\_\\_pagelibre/&RH=rubrech03](http://www.ups-tlse.fr/27503789/1/fiche__pagelibre/&RH=rubrech03)

## Mechanical nanomachines

Made of a single molecule or of a complex assembly of well assembled molecules at the molecular scale, nanomachines mimic the functions of macroscopic scale mechanical machines. Understanding and mastering these machines is the goal of a group of researchers from Toulouse in disciplines like chemistry, biology and physics.



>>> Christian JOACHIM, CNRS senior scientist at CEMES, (CNRS lab associated to UPS), Laurence SALOMÉ, CNRS senior scientist directrice at the IPBS (joint UPS/CNRS lab) and Christophe VIEU, professor at INSA and researcher at LAAS (CNRS lab associated to UPS). © Cyril Frésillon/CNRS.

Miniaturization is everywhere today: in cars, helicopters, satellites, calculators, memories and phones. We are now starting to construct real nanomachines for applications in biology, mechanics and electronics.

Craftsmen and engineers began developing their technical knowledge in the field of miniaturization a long time ago. We are still amazed by Anticythere's astronomical clock that represented a miniature version of the solar system in the house of the Greek philosopher Hipparchus. It was made of a few tens of gears in bronze and measured several centimeters in diameter. From Arab scientists to the clock craftsmen at the end of the middle ages and revisited by Blaise Pascal for his calculating machine, these miniature machines remained the same for centuries without reducing further in size. First invented for microelectronics, monolithic technology gave a new direction to miniaturizing mechanical and electronic devices. It is now possible to fabricate solid state material gears with a diameter smaller than 100 nm. Then, a new question appeared at the beginning of this century: starting from this scale, can we continue to fabricate and make rotating wheels, to assemble trains of gears or to construct mechanical machineries that are tinier still?

### Smaller and smaller

This question is of interest for machine technology because it is generally taken for granted that reducing the overall size of a machine will improve its response time or its energy efficiency compared to the non-miniaturized version of the machine. This question also sheds new light on old physical principles, like the quantum superposition

principle or the second law of thermodynamics. Since the middle of the 1970s, and thanks to the pioneering research of P. Boyer (1997 Nobel Prize in Chemistry), we now know that Mother Nature is already an expert in this field. Certain very basic life processes use complex macromolecular machinery, relying on protein assembly, for example, to create motion.

A new word thus appeared in the scientific world: "nanomachine". For some, a nanomachine is a machine that is just a few nanometers across. For others, it is a miniature machine whose elementary parts are fabricated with a precision on the order of a few nanometers. The six articles in this special issue describe nanomachines that are very representative of both these definitions and which are being investigated at Toulouse Laboratories.

### Systems and approaches

At UPS, several biology teams have dissected nanomachines found in living matter using in vitro experimental approaches. For example, at IPBS, two teams are working on DNA machinery responsible for DNA replication and recombination, two processes very essential to maintaining and controlling genome evolution. To study DNA replication, researchers are analyzing the work performed in a cell by protein nanomachines, mapping the synthesized DNA molecules one-by-one. The method used is called molecular combing, but a potentially more efficient approach is being developed at LAAS. The mechanics of recombination are also being studied by a second group working in collaboration with colleagues from LMGM. Their approach is based



>>> An artist's view of nanomachines. Background: photo of Anticythere's astronomical clock (2nd century BC, Athens National museum).

on the observation of work performed by nanomachines by detecting changes induced in DNA molecules over time. This is accomplished by a molecular “jokari”, or the technique of “tethered particle motion”. A different version of this tool, the magnetic clamp, allows researchers to study the behavior of biological nanomachines when force is applied. It is used by a team from LMBE to solve migration mechanisms in a Holliday junction that exists between two DNA molecules exchanging their threads.

At LAAS, we are studying an even more complex protein machine, made of hundreds of proteins assembled in a flagella engine, 45 nm in diameter. This natural engine is the base of the bacteria thread and allows propulsion at impressive speeds (60 times a bacterium length per second). We aim to understand how this nanoengine works and set up technology able to reproduce this natural nanomachine in an artificial environment. We are also studying why such mechanisms are so efficient and are trying to discover how this nanomachine assembles itself. To understand its mechanics and its assembly, nothing beats trying to re-assemble it from its basic elements, proteins!

At CEMES, the Nanosciences group is approaching the nanomachines question from the bottom up. Instead of using standard miniaturization tools and fabricating smaller and smaller machinery, the scientists are starting from the atoms themselves. They are increasing the number of atoms in the machine to find the

exact number of atoms required to construct a gear, a rack and pinion machinery, and even a car. This approach was born in Toulouse. For a molecular machine to work, the GNS researchers are using a scanning tunneling microscope, invented in 1981. It is able to map the surface of a metal (or a semiconductor) with a precision better than 0.01 nm. After having fabricated a very sharp tip, we can manipulate a single atom or a single molecule one at a time and then “feed” the molecular machine with the energy needed for it to function.

Contact: [joachim@cemes.fr](mailto:joachim@cemes.fr),  
[Laurence.Salome@ipbs.fr](mailto:Laurence.Salome@ipbs.fr), [cvieu@laas.fr](mailto:cvieu@laas.fr)

CEMES: Centre d'Elaboration de Matériaux et d'Etudes Structurales/ Center for Material Elaboration and Structural Studies

IPBS : Institut de Pharmacologie et Biologie Structurale/ Institute of Pharmacology and Structural Biology

LAAS : Laboratoire d'Analyse et d'Architecture des Systèmes/ Laboratory for Analysis and Architecture of Systems

LBME : Laboratoire de Biologie Moléculaire Eukaryote/ Laboratory of Eukaryotic Molecular Biology

LMGM : Laboratoire de Microbiologie et Génétique Moléculaires/ Laboratory of Microbiology and Molecular Biology

# The nanomachines of genetic recombination

During the life of a cell, DNA, which stores hereditary information, is rearranged either spontaneously or in response to damage such as chemical attack or radiation. The recombination consists of successive breaks and ligation reactions performed by proteic complexes, true living nanomachines. By exchanging DNA strands, these machines are responsible for genetic variation, the first step towards evolution.

On the Paul Sabatier University campus, three research groups investigate, using single molecule approaches, different types of genetic recombination: transposition, specific-site recombination and homologous recombination, each catalyzed by its proper enzymatic machinery.

**Transposases** catalyze the displacement of DNA sequences from one position to another in the genome (transposition). Such sequences are abundant in all genomes (they make up 40% of the human genome), so understanding how these machines function is the objective of the LMGM research team and a major challenge. Moreover, the ability to control the transposition process in vitro has important applications in healthcare (such as in gene therapy, for example).

motors driving strand-exchange between a pair of similar DNA molecules. This process of homologous recombination, which takes place in response to breaks in the DNA double helix, is essential for DNA repair and maintaining genome integrity.

## Watching the recombination machines at work

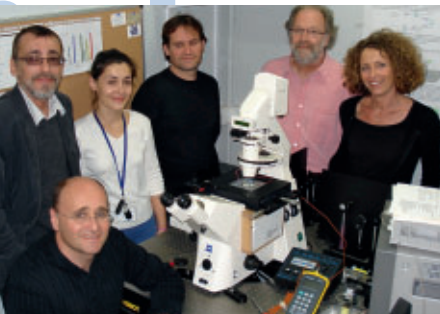
First attempts to characterize these biological machines made use of conventional biochemical methods. These experiments revealed that recombination involves successive, cleverly orchestrated steps and that self-assembly of the machineries is crucial for efficient function and regulation. To unravel the structural details and dynamics of the processes, our teams have recently introduced single molecule methods. The Tethered Particle Motion technique, developed at IPBS, tracks the displacement of a nanoparticle attached to the free end of a DNA molecule anchored on a glass slide at the other end. The dynamics of the DNA molecule and consequently changes in its length, rigidity or curvature, can thus be monitored. This technique is highly sensitive and allows us to detect the binding of a single protein onto the DNA molecule. Important results have been obtained in these experiments. For example, we have demonstrated the formation of a loop as the first step in the transposition mechanism and measured the migration velocity of a Holliday junction (site of cross-strand exchange). Using a micron-sized magnetic particle, a force can be applied to the DNA molecule. Introducing torsion in the DNA molecule using this method, known as "magnetic tweezers", is employed by the LBME team to improve our understanding of helicase as well as other enzymes. Researchers in the LMGM and IPBS teams complete these studies of the recombinases and transposases with direct visualization of their action on DNA molecules by means of atomic force microscopy (ITAV platform).

## Recombinases

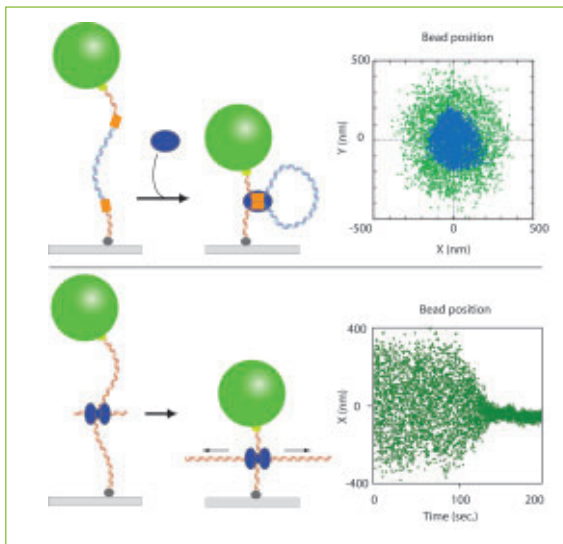
operate recombination between chromosomes at specific locations of identified sequences. For example, the recombinases XerC and XerD, studied by another team at LMGM, separate the chromosomes in dimers formed accidentally during the replication in *E. coli*. By restoring the integrity of the genome, this machine assures the survival of bacteria affected by this genetic anomaly.

**Helicases**, studied by a team at LBME, assemble to form the

Contact: [laurence.salome@ipbs.fr](mailto:laurence.salome@ipbs.fr)



>>> from left to right : Philippe ROUSSEAU, assistant professor at UPS and researcher at LMGM (joint CNRS/UPS lab), Mikhaïl GRIGORIEV, INSERM senior scientist at LBME (joint CNRS/UPS lab), Catherine TARDIN, assistant professor at UPS, researcher at IPBS, François Cornet, CNRS senior scientist at LMGM, Michael CHANDLER CNRS senior scientist at LMGM and Laurence SALOMÉ, CNRS senior scientist at IPBS.



>>> The movement of a bead attached to the free end of a DNA molecule allows to monitor the action of biological nanomachines. Top: assembly of two specific sites along a molecule by a transposase or a recombinase form a loop accompanied by a decrease in the amplitude of bead movement. Bottom: a helicase catalyzes the migration of the junction between two DNA molecules exchanging their strands, which is revealed by a continuous decrease in the amplitude of bead movement.

# Nano techniques to study DNA Replication



>>> Aurélien BANCAUD, CNRS research scientist at LAAS.

Recent advances in techniques that allow the nanomachinery behind replication of individual DNA fibers to be observed open up new perspectives. Goal: to better understand the links between replication defects and genetic instability.

DNA replication machinery is a crucial nanobiological complex that efficiently duplicates the entire human genome before chromosomal partition. This process begins in multiple specific domains called "origins of replication" and progresses via replication forks, multicomponent protein complexes, including DNA polymerases, which ensure the accurate duplication of genomic DNA. DNA replication represents a dangerous moment in the life of the cell as endogenous (structured chromosomal domains) and exogenous events (environmental genotoxic agents) challenge genome stability by interfering with the progression of replication forks. Failure to protect stalled forks or inappropriate replication processing results in the accumulation of genomic aberrations, leading to different human pathologies. This is particularly true in cancer lesions where chronic replication stress occurs, causing high-level genetic instability and, in turn, to increased malignant progression and chemotherapy resistance. However, the molecular mechanisms involved in this replication stress in cancer cells have remained elusive as the replication profiles vary considerably from one cell to another and biochemical approaches failed to give a clear picture of the deficiencies involved.

## Analysis of DNA replication by DNA Combing

Single-molecule nano techniques have proven to be powerful approaches to monitoring DNA replication in a variety of organisms, including human cells. Unlike other replication assays, these techniques allow the direct visualization of individual replication forks progressing along single chromosomes. The recent development of these approaches provides a unique opportunity to understand the links between DNA replication defects and genetic instability, which play a central role in cancer, by identifying the origin of endogenous replication stress at early stages of cancer development and opening new windows for the development of original anticancer treatments that target DNA replication.

The more advanced version of these

techniques, which is called DNA combing (CNRS-Pasteur Institute joint patent), has been developed in France by Dr. Aaron Bensimon and is used by a limited number of laboratories, including our Genetic Instability and Cancer laboratory at IPBS (joint UPS/CNRS lab).

DNA combing is a powerful single-molecule technique that allows the direct visualization of individual replication forks progressing along single chromosomes following incorporation of fluorescent nucleotides. This procedure, with a 0.005 Mb resolution, allows parallel and long DNA fibers (up to several megabases) to be stretched on silanized coverslips with a uniform extension of 2 kb/ $\mu\text{m}$ . The sites of DNA synthesis are detected along individual DNA fibers with monoclonal antibodies against nucleotide analogs. This technology, which can provide information regarding critical parameters of the replication process, such as origin density and fork speed, allowed us to identify one potential source for replicative stress in human tumors<sup>(1)</sup>.

## Nanochannels, an alternative and innovative approach

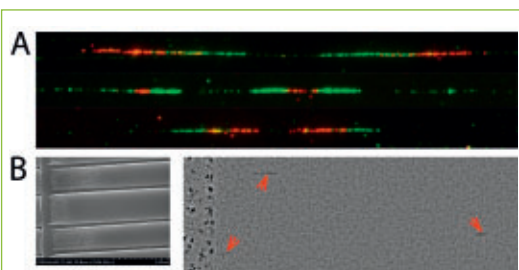
The Nano-Ingénierie et Intégration des Systèmes group at the CNRS Laboratory LAAS has developed new methodological procedures based on nanomanufacturing as an alternative to combing. Thanks to the tools resulting from microelectronics, which make it possible to structure matter down to the nanoscale, it is now possible to design nanocapillaries of approximately 100 nm diameter. The DNA molecules inserted in these nanochannels are stretched longitudinally in a way that is comparable with combing. This alternative combing is dynamic since it does not require immobilization of molecules on surfaces, thus paving the way towards medical high-throughput applications.

(1) (Pillaire et al., *Cell Cycle* 2007, recommended article in Faculty of 1000 Biology).

Contact: [Jean-Sebastien.Hoffmann@ipbs.fr](mailto:Jean-Sebastien.Hoffmann@ipbs.fr)



>>> Marie-Jeanne PILLAIRE, INSEERM research scientist at IPBS and Jean-Sébastien HOFFMANN, INSEERM senior scientist at IPBS.



>>> (A) DNA fibers with incorporated fluorescent nucleotides combed on coverslips. (B) Electronic microscopy of nanochannels engraved in silicon. The parallel structures measure ~150 nm width and height. The insert represents a fluorescent microscopy of DNA inside the nanochannels (red arrows) and other circular DNA molecules in macroscopic channels (left).



>>> Christian JOACHIM, CNRS senior scientist; Henri-Pierre JACQUOT, PhD student; Gwénaél RAPENNE, associate professor at UPS, researchers at the Centre d'Elaboration de Matériaux et d'Etudes Structurales (CEMES, CNRS lab associated to UPS).  
© Cyril Frésillon/CNRS .

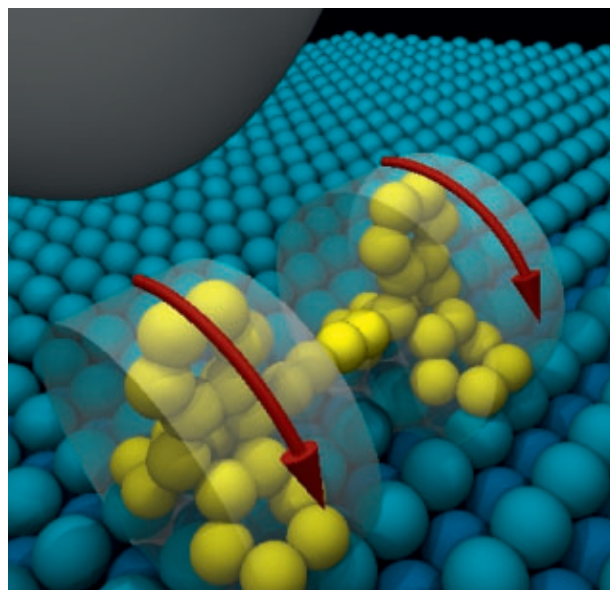
## From nanometer-sized wheels to molecular vehicles

In the history of inventions, the wheel is at the heart of considerable scientific and technological development. Researchers at the CEMES have been among the first to design nanomachines equipped with wheels, thereby opening the way to a nanocar made of a single molecule.

The use of wheel rotational motion around an axle led to mechanical machinery with multiple gears, followed by engines and ultimately the industrial revolution. Reaching the nanometer size, which is the smallest possible dimension for a wheel, represents a great challenge for chemists and physicists. In the past few years, chemists at the CEMES have been working on the design and synthesis of molecular machines equipped with wheels. Step by step, they have been pioneers in this field, together with colleagues at the Free University in Berlin (Dr Leonhard Grill's group). The originality of their approach lies in confining the studies to one molecule only, chosen among a number of possible candidates, deposited on a metallic surface. With its ultrafine tip, which is stabilized 1 nm above the surface by an electric current induced by the tunnel effect, the scanning tunneling microscope (STM) produces a map of the molecules present on the surface. This tip also enables researchers to manipulate the molecules one by one in order to study their mechanical properties.

### A wheelbarrow molecule

After the synthesis and observation of a wheelbarrow molecule in 2005 (a molecule composed of a rigid board, two legs and two wheels), researchers showed in 2007 that when two wheels are mounted on an axle, one of them is able to rotate under the push of the STM tip. They succeeded in controlling the direction of the rotation, which opens the way to the synthesis of functional nanovehicles. Experimentally speaking, the molecules were carefully deposited onto a very clean copper surface, and observed by the means of an STM. The STM tip is used both as a probe to capture an "image" and as a nanosized finger to trigger the rotation of the wheel, being placed in the perfect position for that purpose (see figure).



>>> The two wheels-and-axle molecule is pushed by the tip apex (in gray) of the scanning tunneling microscope on a copper surface.

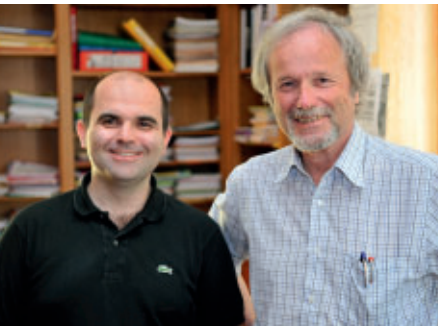
### Towards a nanocar

Such wheels have an intrinsic drawback, they have three sharp blades instead of a smooth "tire". Researchers at the CEMES are currently developing a new family of rigid wheels, circular in shape and slightly curved, so as to minimize the mechanical interactions with the surface while increasing the rigidity of the architecture. These results open the way to the creation of mechanical molecular machines, with the long-term objective of placing all the machinery required to achieve a nanocar (wheels, chassis and engine) on a single molecule, to transport matter in the nanoworld.

Contact: [rapenne@cemes.fr](mailto:rapenne@cemes.fr)



# A family of molecular motors



>>> Gwénaél RAPENNE, associate professor at UPS, Jean-Pierre LAUNAY, professor at UPS and head of the CEMES, researchers at the Centre d'Elaboration de Matériaux et d'Etudes Structurales (CEMES, CNRS lab associated to UPS). © Cyril Fréssillon/CNRS.

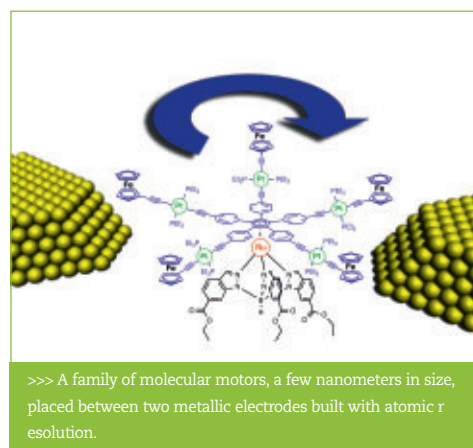
Despite the simplicity of motor operation, it is still a tremendous challenge to transform energy into motion and to conceive a nanomotor composed of a single molecule. Researchers at the CEMES have succeeded in doing just this, using the original electrostatic motor as a model.

In the field of nanoscience in general and molecular nanomechanics in particular, one current challenge is the conception and construction of nanometer-sized molecular motors, that is, machines that transform energy into work in a continuous fashion, through controlled unidirectional rotation. This motion should be reversible and big enough to observe and exploit.

## Electrostatic motor

Motors synthesized at the CEMES were designed to be addressed individually. Their operating principle means connecting the molecule using two nanoelectrodes acting as electron tanks, as shown in the figure. The molecule is composed of a fixed part (stator) anchored onto the surface, and a mobile part (rotor) carrying oxidizable groups. Under external polarization, the positive electrode injects charges of identical sign into the mobile part of the motor, which then repulses the electrode and therefore induces rotation. This constitutes an electrostatic motor, whose operating principle was described as early as 1748 by Benjamin Franklin! The motor rotates by consuming the energy that results from the transport of electrons from a low electric potential zone to a high potential one. The asymmetry of the system allows the direction of rotation to be controlled.

Such motors have a piano stool structure. The fixed part (in black in the figure) is covalently bound to the surface. The mobile part is a platform (in blue) terminated by five electroactive groups. Successive electron transfer processes take place on the electroactive groups and induce rotation of the mobile part of the molecule in a certain direction. A ruthenium atom between these two parts acts as a joint, giving the motor an organometallic character. We have synthesized several molecules of different sizes and structures, illustrating the various criteria



>>> A family of molecular motors, a few nanometers in size, placed between two metallic electrodes built with atomic resolution.

that should be met. First of all, the system should be as rigid as possible so as to avoid useless rotations that would waste energy in unwanted movements. Then, the rotation should be easy around the vertical axis but not at the expense of the integrity of the molecule, that is, the fixed and mobile parts should not be dissociated. Finally, the redox potentials of the various parts of the system should be compatible with the electron transfer processes required.

Several international collaborations have been established with complementary research groups in physics (Max Planck Institute, Stuttgart, and University of Ohio) in order to anchor the motor on specific surfaces and to study this electron-induced rotation. In the longer term these motors could incorporate nanometric robots able to accomplish various tasks, in medicine to everyday life, or to power the nanovehicles we are developing.

Contact: [rapenne@cemes.fr](mailto:rapenne@cemes.fr)

# A molecular rack-and-pinion

To develop complex molecular machines, researchers need to master mechanics at the molecular scale. Experiments along these lines have been done with a view to controlling the rotation of a pinion on its molecular racks



>>> Christian JOACHIM and André GOURDON, CNRS senior scientists, members of the NanoSciences Group (CEMES, CNRS lab associated to UPS).

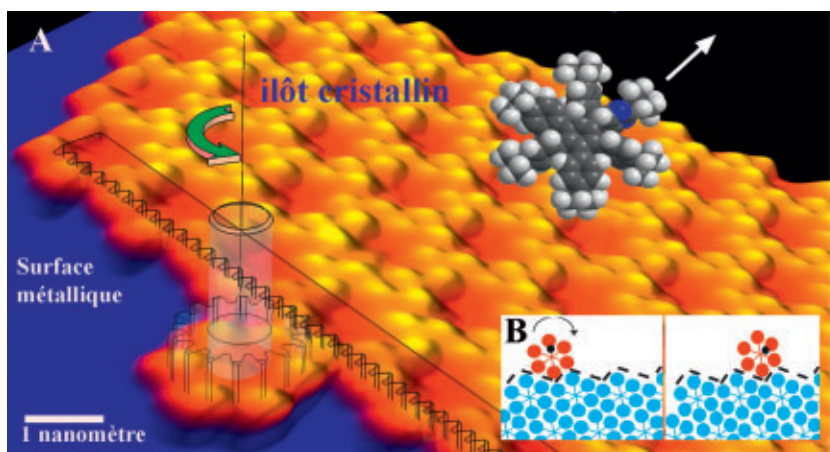
Designing and synthesizing molecules able to perform precise mechanical actions are key to developing future complex molecular machines made from nanometer-sized building blocks. To demonstrate this, researchers first needed to show that a mechanism as simple as a pinion able to roll on a rack could be made at the molecular scale.

First, a six branch star-shaped molecule was designed and synthesized. In order to be able to follow the rotation of the molecule, one of the branches is chemically different from the five others with two nitrogen atoms in blue as shown in the molecular model (see figure). When a scanning tunneling microscope (STM) image of the molecule is recorded, this branch shows a large tunnel current contrast.

It is therefore possible to determine the orientation of the molecule in each tunnel image. These molecules are also able to self-assemble on an ultra-clean metallic surface. The molecules spontaneously form crystalline 2D islands made of a monolayer of perfectly organized molecules, 2D crystals of pinions. The step-edges of these crystalline islands keep the tooth-shape of the molecules and so can be used as a rack.

## A tip to move the molecule

The mechanics experiment is carried out the following way: 1) An isolated pinion molecule is manipulated, using the STM tip, towards the rack so that at least one of the branches engage in the teeth of the molecular rack. 2) The STM tip is then placed vertically at the centre of the pinion. 3) The tip is brought close to the molecule to become its axis of



>>> A – STM image of a 2D crystal of hexa-tert-butylpyrimidypentaphenylbenzene; one of the molecules has been displaced using the microscope tip to engage it in the monolayer step-edge, which acts as a rack. B – The rack and pinion concept. C – The presence of nitrogen atoms, shown as white spots, allows to show the rotation of the pinion when moving along the step edge.

rotation. 4) The tip is then displaced, step by step, parallel to the rack. The pinion molecule then starts turning around its axis as a function of the rack teeth it encounters during movement. This rotation can be observed either from the tunnel current or by imaging the pinion at each sixth of a rotation step. In this way, we have demonstrated that the concept of rack and pinion can be applied at the molecular scale. The mechanical movements of the molecule are classical in appearance. The rotation direction is controlled by the displacement of the tip along the rack. The next step will be to replace the STM tip by an atomic scale axis adsorbed onto the surface, to be able to build a gearing box and continue constructing complex molecular machineries.

Contact: [gourdon@cemes.fr](mailto:gourdon@cemes.fr)

## The flagellar nanomotor of bacteria

Bacteria have developed a complex yet highly efficient nanomachine to move: a rotary motor coupled to long flexible filaments, or flagella, acting as a helix. Today, a research team at LAAS is studying and rebuilding this machinery piece by piece with the help of nanobiotechnologies.

Microorganisms, like bacteria, have developed specific organs that perform all sorts of functions linked to survival. These organelles are amazing, complex molecular constructions that still cannot be imitated by man. Among them is the bacterial flagellar nanomotor, which allows the bacterium to move at high speeds. The motor is 2000 times smaller than the diameter of a human hair and 45 times smaller than the bacterium itself.

The flagellum can be compared to the helix of a boat. Its rapid rotation, on the order of 10000 revolutions per minute for some species, enables the bacterium to run 60 times its length per second. Nature, through evolution, has thus selected efficient and robust molecular architectures that are rotary motors.

The project of the LAAS team is twofold: first, the goal is to understand how these machines work. Second, to set up a technology that allows the machine to be assembled from its elementary components, proteins. However, the exact

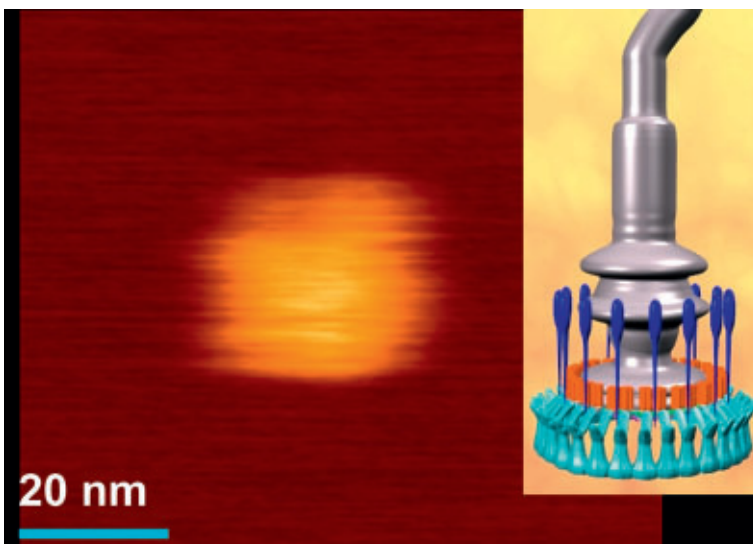
mechanisms behind this nanomotor are still a matter of controversy. In order to understand its behavior, we use tools from the emerging domain of nanobiotechnology to assemble this nanomachine brick by brick on an engineered surface and integrate it inside artificial devices.

### Assembling the bionanomachine

This approach, which involves fabricating the object itself, raises a major scientific question: is it possible to monitor the assembly of proteins on a surface and assemble natural nanomachines? The image shows a possible arrangement for the different parts of the flagellar nanomotor (stator and rotor), together with an experimental Atomic Force Microscopy (AFM) image in liquid of one of the rings of the motor (M-ring) reassembled on a biomimetic surface obtained by soft nanolithography. These first encouraging results open the way for developing techniques capable of rebuilding natural bionanomachines and integrating them inside artificial devices such as biosensors or nano-cargos. The artificial assembly of such biological motors is an ambitious technological challenge that couples different state-of-the-art techniques: production and purification of membrane proteins, surface chemistry and self-assembly, nanolithography and dynamic imaging at the nanoscale in native conditions using AFM. This work is the fruit of a collaboration between LISBP (INSA Toulouse) and IPBS (UPS/CNRS).



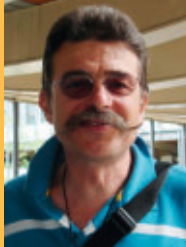
>>> Jérôme CHALMEAU, PhD and Christophe VIEU, professor at INSA, researchers in the NanoBioSystem group of LAAS (CNRS lab associate to UPS).



>>> On the right, a schematic view of a bacterial flagellar nanomotor. Flagellum base and rotor is in gray, stator in dark blue and orange, C-ring (in light blue) is responsible for the rapid change of rotation direction. On the left, an AFM image in liquid of the self-assembly of proteins making up the M-ring (FlhG proteins) on a mimetic surface prepared by soft nanolithography on a glass slide.

Contact: [cvieu@laas.fr](mailto:cvieu@laas.fr)

## Evolution: a broad framework for biology



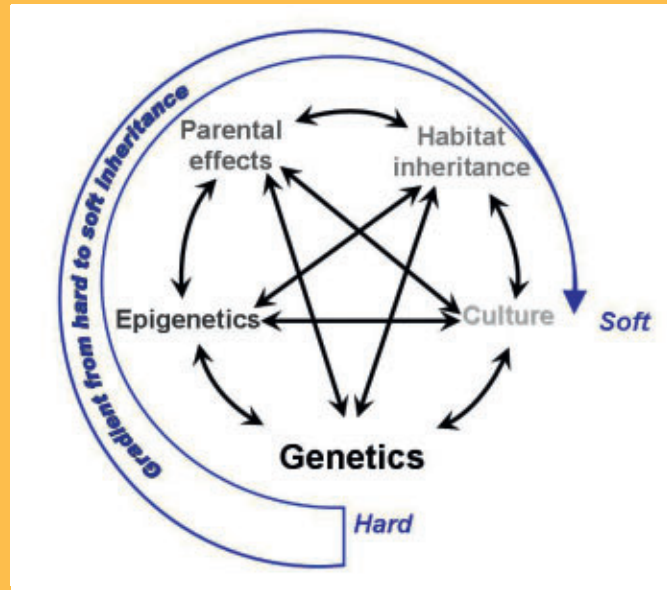
As Dobzhansky so rightly said in 1973<sup>(1)</sup> “nothing in biology makes sense except in the light of evolution”. In other words, evolution constitutes the most comprehensive and general framework for the study of life on earth. Evolution thus plays a major theme in many biological research projects at Paul Sabatier University.



Evolutionary approaches are currently undergoing profound change, and it is not unlikely that historians of science in the future will use strong words such as ‘revolution’ to describe our epoch. These changes have two interconnected origins. The first is that a growing number of authors claim that it is not possible to understand evolution without accounting for development in all its dimensions. This perspective is rooted in the Evo-Devo (Evolution-Development) approach. Second, evidence is mounting that heredity is not limited to the sole transmission of genes across generations but includes several processes of information inheritance that may deeply affect evolutionary dynamics. In this context, many authors over the last few decades have claimed that heredity is not limited to the inheritance of genetic information across generations. The implications of non-genetic information inheritance has been

underlined in several domains of biology and the currently most productive domain is that of epigenetic inheritance. Epigenetics is often defined as the study of the variation that is transmitted (we say that it is ‘heritable’), which is not due to changes in the sequence of the DNA molecule but instead involves changes in gene expression. Such changes are often called ‘epimutations’ because they look very similar in their effects and properties to mutations (that is, changes in the ADN sequence). Epimutations result from changes in the DNA packaging in the cell nucleus that can increase, reduce or even silence the expression of some genes. Epimutations can deeply change the phenotype (that is, the external aspect) of individual organisms and explain how cells of a metacellular organism can take on shapes as varied as neurons or the liver, bone and skin cells, despite the fact they all carry exactly the

1. Dobzhansky T (1973) *Nothing in Biology Makes Sense Except in the Light of Evolution*. *The American Biology Teacher* 35: 125-129.



>>> The various forms of inheritance form an intricate network of interacting mechanisms. They are placed along a gradient from 'hard' (digitalized, not easily altered information) to soft inheritance (analogically encoded information more likely to change during transmission processes).

same genetic information. Epimutations are also responsible for drastic changes in flower shape. For instance, one epimutation is responsible for the switch from bilateral to axial flower symmetry in *Linaria*. The important point is that these epimutations can be transmitted to subsequent offspring plants thus leading to lineages with very different phenotypes. Epigenetic variation can therefore be heritable, and so open to natural selection. Furthermore, because epimutations can be inherited over long periods of time they may deeply affect these plants' fitness (that is, their capacity to transmit their genes) as well as gene flow among plants with or without the epimutation. We are only just beginning to study the evolutionary impact of epimutations.

Many scientists are now calling for the "modernisation of the modern synthesis" by incorporating development as a major evolutionary process. Researchers in the 'Centre de Biologie du Développement' (CBD, joint UPS/CNRS lab) are working on the role of development as an evolutionary process. However, other scientists claim that we should go even further by also accounting for non-genetic inheritance. This is the claim of researchers of the "Laboratoire Évolution et Diversité Biologique" (EDB, joint UPS/CNRS lab) who are studying certain forms of heritable non-genetic information, namely cultural inheritance.

Accounting for all forms of non-genetic inheritance will, in effect, bring heredity back to its original definition, which was

multidimensional in essence. Researchers at the UPS are striving to help get this emerging new synthesis accepted because it challenges the current widely-accepted belief that only genes, and nothing else, are likely to really affect evolutionary dynamics.

The new synthesis will hopefully allow us to account for all the richness of evolutionary mechanisms, a richness that is currently largely underestimated because it ignores non-genetic inheritance. In other words evolutionary biology is undergoing a profound evolution.

The set of articles in this issue is set within this context. It provides a series of flashes illustrating the diversity of evolutionary approaches adopted within laboratories of our university while showing their role in current developments in the field.

**Contact:** [edanchin@cict.fr](mailto:edanchin@cict.fr)

EBD: Laboratoire Evolution et Diversité Biologique/Evolution and Biological Diversity Laboratory

CBD : Centre de Biologie du Développement/ Center of Developmental Biology

LMTG: Laboratoire des Mécanismes et Transferts en Géologie/ Laboratory for Mechanisms and Transfer in Geology

LIPM : Laboratoire des Interactions Plantes Micro-organismes/Plant-Micro-organisms Interactions Laboratory

# Morphological evolution in insects



>>> François PAYRE, CNRS senior scientist at the Centre Biologie du Développement (CBD, joint UPS/CNRS lab). Credit: C. Fresillon/CNRS.

Deciphering various animal genomes has deeply modified our view of evolution. While genes appear to be strongly conserved across species, new data reveal the importance of variations in the interaction between genes.

Animals display extraordinary morphological diversity and the study of this diversity has had a major impact on the formulation of evolutionary theories. We now know that the entire gene set, the genome, governs how the body in each species is formed. Genes are organized in complex regulatory networks needed to build morphological features during development. Genome sequencing has shown that animal genes, as well as their protein products, are surprisingly similar between species. Therefore, the question remains as to how evolution has produced such diversity in different animals?

As often, multidisciplinary approaches have led to significant advances. Our team at the Centre Biologie du Développement focuses on epidermis differentiation, which leads to the production of a pattern of cuticular extensions. These extensions are called trichomes and characterize the external morphology of insects. There is a wide range of different trichome patterns in even closely related insects. To understand this evolutionary diversification, we are collaborating with David Stern's group at Princeton University in an effort to unravel the molecular basis underlying this variation. Coupling studies of evolution and development have also shed new light on mechanisms behind evolution.

### Parallel evolution

Genetic analysis of *Drosophila* species hybrids with divergent trichome patterns has allowed us to identify the genetic basis of this diversification. Surprisingly, while hundreds of laboratory-induced mutations are known to modify trichome patterns, trichome evolution in the wild is due to the modification of only a single gene, called *shavenbaby*. This gene has been independently modified in several *Drosophila* species that have evolved separately over a time period as long as 40 million years! This finding shows that genes in the same network can evolve differently so there must be developmental constraints that favour only certain genetic modifications.

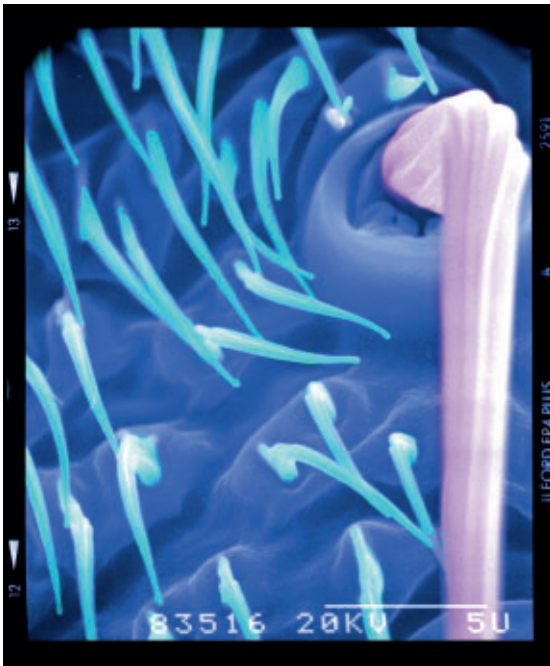
### Micro- or Macromutations

The nature of the molecular mechanisms underlying evolution is still poorly understood and has generated strong theoretical debate. On one hand, evolution might result from the accumulation of mutations over time of a weak effect, called micromutation. In contrast, only strong mutations, or macromutations, might significantly modify development during evolution. Trichome evolution offers the opportunity to study these possibilities in experiments. Our work has shown that only the absence of *shavenbaby* gene activity in epidermal cells leads to changes in trichome patterns, therefore confirming the importance of major variations. However, these apparent major modifications have resulted from weak mutations in at least three different sites in the *shavenbaby* gene! We have shown that the modification of all three regions is needed for morphological changes. At least in this case, a major modification at macroscopic scale is due to the accumulation of several small mutations each with a small effect.

### Evolution between genes

Interestingly, the evolutionary modifications we have identified do not directly affect the gene, that is, the protein coding region. Instead, these mutations modify neighboring genomic regions that regulate the expression of the gene. Deciphering the interaction between developmental genes will be required if we are to fully understand the mechanisms behind evolution. Unfortunately, the regions lying between genes constitute the major part of our genome (>90%) and remain poorly understood. Functional approaches in model organisms will continue to be of great help if we are to fully decipher gene regulation and evolution.

Contact: [payre@cict.fr](mailto:payre@cict.fr)



>>> Electron micrograph of *Drosophila* trichomes.

dos

# headlines

## Evolution and palaeontology: what's new?

Tracking the evolution of life and biodiversity through geological times is the main aim of paleontologists. Recent technological advances are now allowing their analyses to be refined.

Paleontology developed over the last two centuries as a discipline encompassing both biology and earth sciences. Leading figures in the field throughout the 19th and 20th centuries include Georges Cuvier, Jean-Baptiste Lamarck, Alcide d'Orbigny, George G. Simpson and Stephen J. Gould.

The theory of evolution, proposed by Charles Darwin (and Alfred R. Wallace) 150 years ago, played a considerable role in understanding fossil observations, either in terms of morphology or diversity. Today, our understanding has improved thanks to more recent scientific advancements, such as plate tectonics, radiometric dating (we now talk of periods as long as millions or billions of years) and the emergence of genetics, which allows us to interpret evolutionary processes in recent organisms.

### A new approach

In the last two decades, computerized phylogenetic reconstructions – also known as cladistic or parsimony analyses – have allowed us to reconsider the tree of life, both as a whole and in detail. Researchers now tend to reconstruct phylogenies as “genealogic trees”, in terms of sister groups and based on shared derived characters, rather than traditional “ancestor-descendant” relationships. The information (morphological characters or genetic mutations) is treated thanks to dedicated software that allows a huge amount of data to be treated in an objective way.

chronostratigraphical framework and allow scientists to calibrate divergence ages within phylogenetic trees. Once established and chronologically defined, phylogenetic relationships may be interpreted in terms of geographic dispersal, for both fossil and living species. Geologists may then use this data with confidence for paleogeographic reconstruction.

The recent study of a giant rhinoceros fossil, found with other mammals and dating back to more than 25 million years in Anatolia (Turkey), proves that the Balkans and Asia were closely connected throughout Oligocene times. Contrary to what was believed previously (before these fossil studies), Anatolia was not an archipelago during this period. This is what an international team of paleontologists and geologists from our lab, the Muséum National d'Histoire Naturelle (Paris), and the Turkish Geological Survey found by analyzing a few bones<sup>(1)</sup>

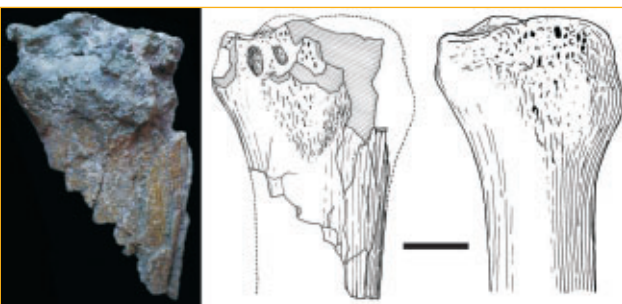
Similarly, the discovery of fossil bamboo belonging to the *Guadua* genus in Peruvian Amazonia<sup>(2)</sup>, by ecologists, geologists, and paleontologists from EcoLab and our lab, allowed to refute the classical and widespread hypothesis of an anthropic-inferred dispersal of such bamboo from North America.

In other terms, paleontology will always benefit from exchange with related sciences. Indeed, it might be only way forward for this “old-fashioned” naturalist subject.

Contact: [poa@lmtg.obs-mip.fr](mailto:poa@lmtg.obs-mip.fr)



>>> Pierre-Olivier ANTOINE, assistant professor at UPS, researcher at the Laboratoire des Mécanismes et Transferts en Géologie (LMTG, joint UPS/CNRS/IRD lab).



>>> Radius fragment of a giant rhinoceros from the Oligocene of Anatolia (Turkey, ca. 25 Myr). Right: comparison with the largest specimen known so far (Oligocene of Mongolia). Both of them are at the same scale (scale bar = 10 cm). © P.-O. Antoine.

### Phylogenetic relationships

In terms of phylogeny, only paleontology provides direct information on morphological changes and the evolution of biodiversity over time: the taxonomic sampling available in paleontology is considerably wider than those based on living organisms, notably because paleontologists work on both fossil and recent organisms.

Finally, fossils offer a well-defined

(1) Antoine, P.-O et al., *Zoological Journal of the Linnean Society*, 152: 581-592.

(2) Olivier, J. et al., *Review of Palaeobotany and Palynology*, 153: 1-7.

# Evolution involves more than just genes

Long perceived as only resulting from genetic transmission across generations, evolution is considered more globally today. The environment shapes an individual's development and thus what is transmitted to offspring.

Life is essentially a matter of information transfer across generations. Because Darwin did not know anything about inheritance, he had a rather open vision of heredity. One sentence in the first edition of his well known "On the Origin of Species" (1859) summarizes his perception "Any variation that is not inherited is unimportant for us". According to this viewpoint, phenotypic variation has two components, one that is transmitted to the next generation and one that is not.

However, the discovery of the amazing ability of DNA to digitally encode and transmit information across generations later led scientists to reduce heredity to genetics alone. Today, researchers believe in either genetic or non-genetic sources of variation. While correctly insisting on the major role of genes, this separation of phenotypic variance mistakenly denies any evolutionary role compared to other forms of inherited variation. In effect, however, as Darwin understood, any variation that is transmitted is open to natural selection and thus to evolution.

## Social influences

The notion of cultural inheritance has emerged in tandem. Cultural inheritance results from information that is transmitted across individuals and generations as a result of social learning.

This form of learning affects many behavioral patterns previously viewed as mainly, if not exclusively, determined by genes. For instance, while scientists have often envisioned differences in sexual preference as solely resulting from genetic variation, recent studies have demonstrated a strong influence of social learning on these preferences, both in vertebrates and insects. Female preferences are influenced by the choice of other females for a certain type of male. It is even possible to create strong liking for artificially created traits, such as coloured feathers on the forefront of a male bird. Indeed, we recently showed that it is possible to trigger sexual preferences in female *Drosophila melanogaster* for males that were painted pink or green.

Such social influences, which can be likened to that for fashion in humans, can lead to sets of isolated populations in which females develop very different

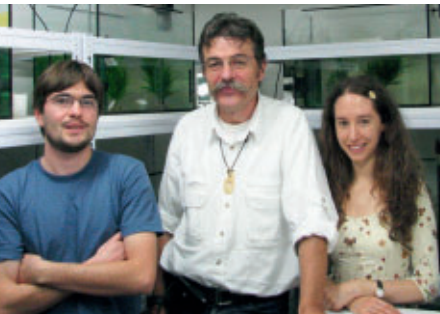
sexual preferences. These may, in turn, affect the evolution of male traits. Males of other isolated populations might hence become so different in appearance that females might ignore males in other populations when the two populations come in contact again. This would then prevent any gene flow between the populations. At this point, the two populations would be isolated for purely cultural reasons and not inter-breed, thus creating a new species.

## Cultural transmission

Researchers in the EDB lab are studying the role of cultural heredity in animal evolution. We work on behavior such as sexual preference in fish and insects and recently showed, for instance, that female *Drosophila melanogaster* show cognitive abilities that are surprising considering their small brain size<sup>(1)</sup>. Such cognition may suggest the existence of culturally inherited behavioral traits in this species<sup>(2)</sup>. Cultural inheritance is unique among such systems because it is not only transmitted vertically (from parents to offspring) but also horizontally (among individuals of the same generation) and obliquely (among non-kin individuals of different generations). Hence cultural transmission profoundly affects evolutionary dynamics and processes that are not possible with purely vertical transmission (as is the case for genetics) may become possible with cultural transmission. Integrating every form of inheritance into our evolutionary thinking may thus considerably broaden the range of possible evolutionary dynamics. We predict that accounting for all forms of inheritance will probably change our perception of evolutionary processes in the near future.

Contact: [edanchin@cict.fr](mailto:edanchin@cict.fr)

1. Mery F et al., *Current Biology* 19: 730-734 (2009)
2. Danchin É et al., *Communicative & Integrative Biology* In press.



>>> Etienne DANCHIN, CNRS senior scientist with Simon Blanchet, postdoc and Susana Varela, PhD student. Team working on cultural evolution in the Laboratoire Évolution et Diversité Biologique (EDB, joint UPS/CNRS/ENFA lab).



>>> *Drosophila* females tend to mate more with pink males than green ones after having seen three pink males successfully mating and three green males being rejected by several other females.



# headlines

## Experimental evolution of legume symbionts



>>> Catherine MASSON-BOIVIN, INRA senior scientist, at the Laboratoire des Interactions Plantes Micro-organismes (LIPM, joint INRA/CNRS lab associated to UPS) and at the Institut Fédératif Agrobiosciences, Interaction et Biodiversités (IFR 40).

Microorganisms need to adapt quickly to their environment because they are very sensitive to change. Their evolution is now better understood thanks to progress in sequencing and proves that the environment greatly affects biological development.

Ecological transitions have an important impact on the environment as they are a major source of biodiversity. Bacteria are particularly prone to ecological transitions because they have a very plastic genome. Indeed, bacterial genomes have evolved over billions of years in response to changing environmental conditions. Experimental evolution allows to see evolution in action at the lab scale and can be used to analyze mechanisms underlying lifestyle changes. New high throughput sequencing technologies allow resequencing of bacteria at various stages of experimental evolution and help to identify adaptive mutations.

### Genus variation

Bacteria collectively referred to as rhizobia represent an interesting case of microorganisms that originate from repeated and independent ecological transitions. Rhizobia are soil bacteria that can establish an ecologically important nitrogen-fixing symbiosis with leguminous plants. Rhizobia elicit the formation of new organs (the nodules) on roots, within which they fix atmospheric nitrogen (N<sub>2</sub>). Nodulated plants are thus able to grow independently of environmentally polluting nitrogen fertilizers. The interaction between rhizobia and plants is a sophisticated process. It involves organogenesis, plant tissue invasion via infection thread and intracellular infection of plant cells, and relies on complex molecular exchange between both partners.

Although rhizobia can fix nitrogen in symbiosis with legumes, they do not form a homogenous taxonomical group but are distributed in more than 10 genera and 60 species intermixed with pathogenic and saprophytic bacteria. Such biodiversity raises fascinating questions about the emergence and the evolution of rhizobia.

### Adaptive symbiosis

To address these questions, we are studying the experimental evolution of a phytopathogenic bacterium *Ralstonia solanacearum* into a legume symbiont in collaboration with P. Heeb (EDB, Toulouse). The evolution approach is based on a “design then evolve” strategy consisting of i) designing a *R. solanacearum* strain with a symbiotic potential by genetic engineering and ii) optimizing this potential by using a legume plant as selective force. Using this strategy, nodulating and intracellularly infecting *R. solanacearum* derivatives were evolved from extracellular pathogens. Genome resequencing of these evolved clones is underway (in collaboration with C. Medigue, Genoscope, Evry) with the aim of identifying adaptive mutations that have occurred during the evolutionary process. The analysis of molecular events accompanying symbiotic adaptation should help in our understanding of evolution of rhizobia and the spread of this symbiosis in nature.

Contact: [catherine.masson@toulouse.inra.fr](mailto:catherine.masson@toulouse.inra.fr)



>>> Infection of *Mimosa pudica* by the rhizobium *Cupriavidus taiwanensis* (in green).

# Genetic diversity and human evolution



>>> Lounès CHIKHI, CNRS senior scientist at the Laboratoire Evolution et Diversité Biologique (EDB, joint UPS/CNRS lab), and presently at the Instituto Gulbenkian de Ciência, in Portugal.

The study of human evolution has long been the realm of anthropologists, linguists and archaeologists, but things are changing and geneticists are now becoming increasingly involved in research on human diversity and evolution.

Fossil data suggest that the first modern humans most probably appeared in Africa some 150 to 200,000 years ago. It would be rather naive to believe that genetic data obtained 5 to 10,000 generations after the emergence of our species will provide us with precise information on the complex demographic history of the human “race” made up of expansion, colonisation of new territories, extinction, encounters and other events. At the same time, it would be just as naive to ignore that, in the last few decades, genetic data have revolutionized the way we look at our species.

For instance, until the 1960s, most specialists thought that humans had diverged from other primates at least 15 million years ago. Molecular data have since demonstrated that (i) we are genetically closer to gorillas and chimpanzees than they are themselves to orangutans, and (ii) that this divergence is very recent, on the order of 5-7 million years.

## Young species

Genetic data have also repeatedly shown that human populations are genetically very similar, in agreement with the idea that our species is a young one that colonized the planet very recently, and in which the notion of race is meaningless. These results are thus at odds with the multiple-origin theories which stated, until very recently, that different human species or races appeared independently on different continents from the *Homo erectus* that left Africa, more than one million years ago (the famous Java and Peking men).

In the last 30 years, several studies have improved our understanding of how demographic events such as expansion (during the out-of-Africa expansion), contraction (during the last ice age in Europe) or mixing events (during the European Neolithic transition, which brought the first near-eastern farmers and hunter-gatherers into contact) influenced the patterns of genetic diversity in present-day populations. It is, for instance, now well-established that the human species is a young species whose current distribution is the result of an expansion from human populations that lived in Africa 50 to 100,000 years ago (that is, quite some time after the



>>> The golden-crowned sifaka (*Popithecus tattersalli*) is an endangered lemur living in a small region in the north of Madagascar. We study the impact of habitat fragmentation on its genetic diversity. We aim at quantifying the relative contribution of recent or more ancient fragmentation due to human activities and climatic changes, respectively, on patterns of genetic diversity (Credit: Erwan Quéméré, PhD student at EDB).

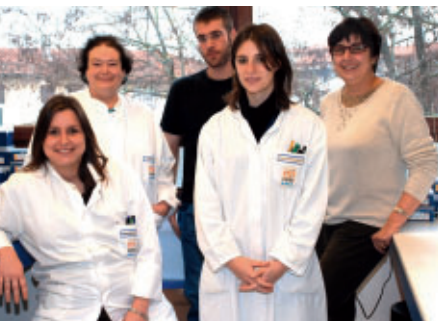
emergence of the first modern humans, also in Africa). Genetic data also suggest that humans did not mix with Neanderthals, or only in a very limited way).

In our lab we aim to understand how mixing between populations can be quantified even when such mixing events are old (as for the Neolithic transition in Europe). We analyze published data and study the properties of simulated data. The applications of our work are not only limited to humans and allow us to reconstruct the demographic history of species under threat, in order to better understand the impact of natural and anthropogenic changes (see photo).

One of the challenges faced by human population genetics (or that of other species) will be to reconstruct their recent demographic history within the framework of models less simplistic than those that we sometimes have to use today.

Contact: [chikhi@cict.fr](mailto:chikhi@cict.fr)

# Iron, a molecule to use with caution



>>> Marie-Paul ROTH (right) and Helene COPPIN (left), INSERM senior scientists with their team at the Toulouse Physiopathology Centre in Purpan (CPTP, joint INSERM/UPS lab).

Although iron is a common food supplement, we only require a small amount of this nutrient. Too much iron is toxic as can be attested by 180,000 patients in France who suffer from hemochromatosis. A French research team from Toulouse has just discovered the molecule that regulates absorption of iron in the duodenum (1).

## → What makes iron a special nutrient?

Iron is needed for the synthesis of hemoglobin in red cells as well as for oxygen transport and cellular respiration. It is therefore crucial for organisms, but iron deficiency or excess iron leads to serious diseases. Iron is taken in via food and absorbed by intestinal cells, but it cannot be excreted. It is therefore important that iron levels are regulated so that an excess of the metal does not build up inside the body.

## → What exactly is hemochromatosis and who is affected?

Hemochromatosis is the most frequent genetic disease in populations of Northern European origin and affects about 180,000 individuals in France. It is more common than cystic fibrosis, phenylketonuria, and muscular dystrophy put together. Hemochromatosis is characterized by progressive iron accumulation in the liver and severe hepatic lesions may occur in the absence of appropriate treatment,.

## → What led Toulouse researchers to this discovery?

In 2001, scientists from Rennes and Paris discovered the role of hepcidin, a small molecule

produced by the liver when iron concentration exceeds body requirements. Hepcidin is transported by blood circulation to the gut where it blocks ferroportin, the port of entry of iron into the organism. The regulation of the synthesis of this small peptide was a mystery until now. Our team found the molecule that regulates this synthesis - BMP6 (Bone Morphogenetic Protein), which, for a long time, was thought to be implicated in skeletal development. Using DNA micro-arrays, we found that the synthesis of BMP6 increases when iron concentrations increase and decreases when the organism is iron deficient. We then showed that mice lacking BMP6 are unable to produce hepcidin. As a consequence, iron flow from the gut into the blood circulation is not blocked, resulting in iron accumulation in the liver.

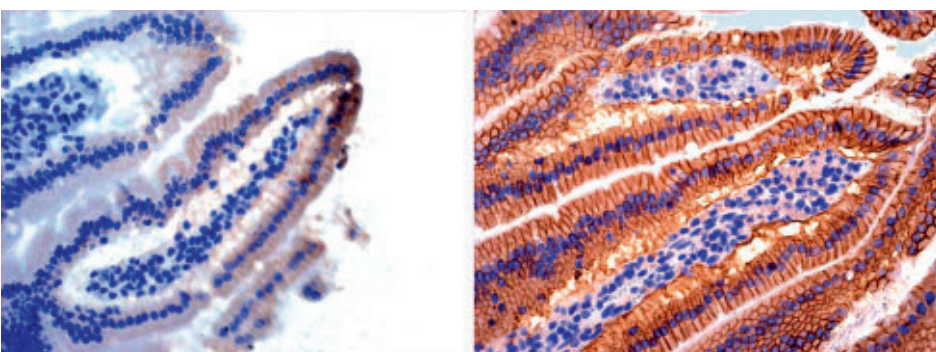
## → Is a new therapy possible?

The protein BMP6 is needed so that iron can be absorbed according to the body's needs. Potential therapeutic applications can thus be envisaged. For example, we hope that administering BMP6 might help prevent iron loading in hemochromatosis patients, thus providing an alternative to current treatments that consist of regular venesections.

(1) Meynard D, Kautz L, Darnaud V, Canonne-Hergaux F, Coppin H, Roth MP. Lack of bone morphogenetic protein BMP6 induces massive iron overload. *Nature Genetics* 2009, 41: 478-481.

Interview by Gaël Esteve

Contact: roth@cict.fr



>>> The absence of BMP6 in a mouse (right) leads to a huge increase in the ferroportin (in brown) in intestinal cells. Iron can now enter the organism.

# Research at Paul Sabatier University

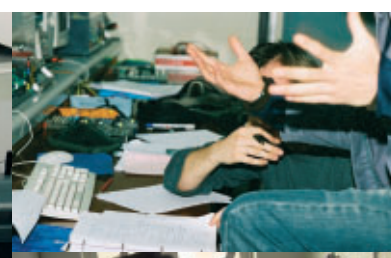
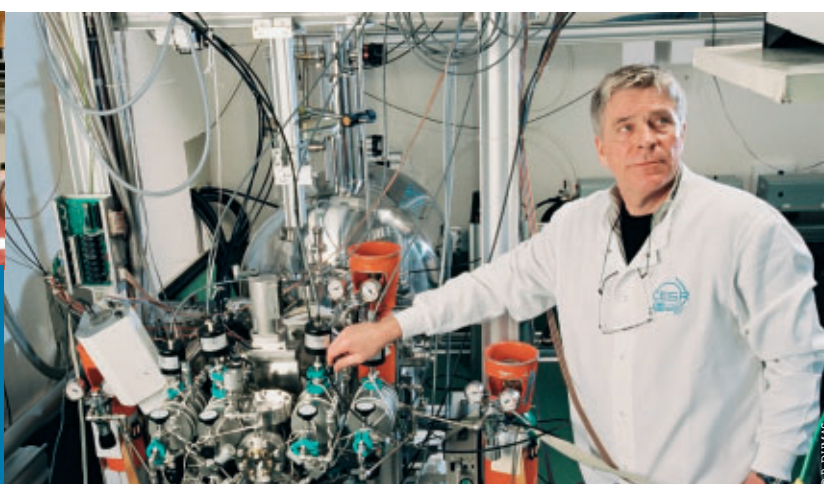
Research at Paul Sabatier University is developed in 64 laboratories organised in research units, supported both by the University and by at least one of the following research institutions: CNRS, INSERM, IRD, INRA, CNES...

The research staff includes about 2350 scientists whereas the administrative and technical staff consists of 1400 people. The number of graduate students is around 1500 in six doctoral schools.

**The main research themes developed on our campus site are:**

- > **Mathematics:** 1 laboratory.
- > **Physics and nanophysics:** 5 laboratories.
- > **Chemistry and Materials Sciences:** 6 laboratories.
- > **Engineering Sciences:** 6 laboratories.
- > **Computer sciences and information systems:** 2 laboratories.
- > **Sciences of Earth, Space and Universe:** 7 laboratories.
- > **Life and Health Sciences and Biotechnologies:**
  - > **Biology and Life Sciences:** 11 laboratories.
  - > **Health Sciences:** 14 laboratories.
- > **The Humanities and Social Sciences,** 4 laboratories.

[www.ups-tlse.fr](http://www.ups-tlse.fr)



FRANCE