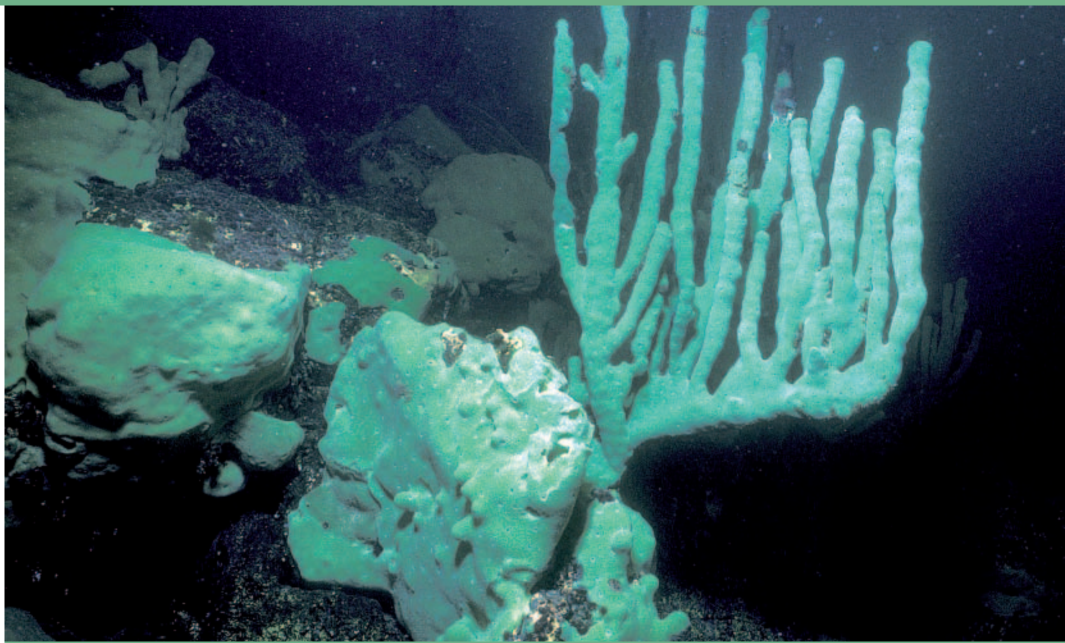
NEST
Pathfinder

VIRTUAL EXPERIMENTATION

MORPHEX



Growth of biological organisms is influenced by genes in individual cells and by interactions between cells. MORPHEX seeks to understand how interactions between genes cause cells to differentiate, grow and divide, and how exchanges between cells contribute to this process. The results should improve understanding of why the growing process sometimes fails, and how to overcome this. It will also lead to the expansion of computer-based experimentation on virtual organisms, and to the development of a generic platform for model-driven experimentation.

Biological organisms consist of complex systems involving genes and cells. Growth in plants or animals is governed by what happens inside the cell – regulated by genes and their interactions – and by the exchanges between cells. The goal of the MORPHEX project is to understand how these two levels of complexity combine to create the form of the final organism.

This shape-forming or morphogenesis is influenced by both internal and external environmental factors. So it is necessary not only to carry out experiments to see what is happening, but also to model the overall growing process mathematically, and then in the computer. This involves modelling cells, gene regulatory networks and, more difficultly, their interactions and what will emerge from these interactions.

Plant and sponge development

MORPHEX will focus on the development of the reproductive organs in the flowering plant *Arabidopsis thaliana* and that of two sponges, *Suberites domuncula* and *Lubomirskia baikalensis*. Sexual organs in flowering plants are formed from populations of dividing undifferentiated stem cells known as shoot apical meristems at the tips and branches of the plant, a process that continues throughout the life of the plant.

A great deal of data has been collected about the regulatory networks involved in the development of these organs but its analysis – without the use of modelling and simulation methods – is very difficult. This project will synthesise and expand existing gene-expression studies to determine the mechanics of morphogenesis in the plant, and so improve overall understanding of floral architecture.

On the animal side, major advances have been made in modelling quantitative and dynamic pattern formation in sea urchins. Currently, the interest is linking the quantitative model of gene expression in such models to

> **"The project should enable us to understand why the growing process sometimes does not work."**

a biomechanical representation, and determining the influence of the environment on the morphogenetic process.

The two sponges offer simpler structures than sea urchins for such a study. MORPHEX will model early development before growth in the adult sponge. Optimisation techniques will be applied to determine causal relations between genes in the regulatory networks, as well as the dynamics involved. Spatial and temporal expression patterns in the developmental processes will be simulated and compared with observed patterns. Attempts will also be made to understand the physical coupling between cells and shape formation.

Shape creation in the sponges and the plant share many common elements, justifying tackling their morphogenesis in the same complex systems framework. The total number of genes, for example, is around 30 000 for the sponges and about 25 000 for the plant. However, there are sufficient differences in the number of cells involved, the levels of emergence, and the development time scales, to be able to guarantee a generic approach to the design of the modelling and simulation tools.

The MORPHEX project will focus on establishing a general model to describe the underlying complex systems, developing tools to extract concrete models based on experimental data provided by biologists, and then determining how to describe, execute and analyse relevant protocols for computer simulation. All this will involve a highly interdisciplinary team bringing together biological development experts, mathematicians, physicists, computer scientists specialised in modelisation, as well as software specialists and engineers from across Europe.

Such an approach makes it possible to construct models of complex systems from incomplete, missing or inconsistent data. It also allows prediction and control of the models and the overall systems. As a result, although the focus will be on biological questions, with concrete results expected on how the sexual organs in the flower and the form of sponges develop, the concepts and software tools developed will be sufficiently generic for reuse in other biological or even non-biological domains. Moreover, the ability to model and validate such simulations will bring more rigour to the verification of results in parallel fields.

Global benefits foreseen

The results should enable us to understand why the growing process sometimes does not work, and how to overcome the problem of a missing gene by manipulating the interaction of surrounding cells. The software and procedures developed in the project will enable the development of model-driven experimentation, markedly cutting the cost of studies on genes, gene interactions and relations with cells.

MORPHEX should also lead to the creation of virtual plants or animals, allowing a large part of experimentation to be carried out on the computer rather than on real plants or animals – reducing risks and avoiding ethical dilemmas. This could, for example, enable crop yields and quality to be improved, and make it possible to optimise farming methods to enable us to feed an ever-growing population.

AT A GLANCE

Official Title
Morphogenesis and Gene Regulatory Networks in Plants and Animals: a Complex Systems Modelling Approach

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Project cost
€ 2 222 961.60

EU funding
€ 1 599 990.40

Project reference
Contract No 043322 (NEST)

The freshwater sponge Lubomirskia baicalensis represents one of the most structured sponge species. The green colour of the specimens originates from the green algae which live in symbiosis with this animal.

An x-ray image of the freshwater sponge Lubomirskia baicalensis demonstrates the complex architectural structure of the hard skeleton of this animal.