

★ The Structural Biology and Chemistry Group (SBCG) of the National Hellenic Research Foundation have overseen a project, EUROSTRUCT, which has dramatically transformed their capabilities by creating a centre of excellence in structural biology in Greece



Crystal and
Structure
from SBCG

The new centre for structural biology

The general theme that underlies the work of SBCG is macromolecular structural biology and chemistry in which structures are used as the starting point for further studies on the mechanisms of catalysis, mechanisms of inhibition, regulation, molecular recognition, and structure-based drug design.

“The overriding objective of the project was to unravel the research potential of the SBCG and the Institute of Organic Pharmaceutical Chemistry (IOPC) of the National Hellenic Research Foundation,” explains Spyros Zographos, associate researcher at the IOPC and project leader. “This was achieved through the creation of a centre of excellence in structural biology, with an emphasis on structure-based drug design and discovery.”

In the past, without access to adequate facilities in Greece, Zographos and his colleagues had been using facilities in

other European countries to carry out their research, the money for which was provided by minor grant applications. However, over the years these facilities became more and more difficult to gain access to, and so the EUROSTRUCT project has opened up an opportunity for research growth that would not have been possible before.

“We work with proteins,” he explains, “which are some of the most important constituents of living things. Through our work we try to determine the three-dimensional structures of proteins, and then use those templates to design molecules that can modify the way in which those proteins work. In this way we can manipulate the function of proteins to block diseases, amongst other things.”

One of the most widely used techniques in this field is x-ray protein crystallography, which is extremely useful in revealing the

3D structure of proteins. Thus, one of the main accomplishments of EUROSTRUCT was the setting up of a state-of-the-art x-ray facility, and the recruiting of a large number of experienced personnel in order to build a critical mass of research capacity.

“Since the creation of the new facility, the number of collaborations we have had with other laboratories from around Europe has increased dramatically,” says Zographos. “We now have an x-ray facility together with protein purification, robotic crystallisation, NMR and mass spectroscopy facilities as well as a computational facility all hosted in the same place, and so by bringing these techniques together, along with the increased transfer of knowledge, we are now achieving a much more integrated approach.”

With the newly built facility in place,



X-ray facilities of SBCG



Workshop lectures and practicals (left to right: E. Garman, P.S. Stewart and I. Kolossvary)

the next step was to extend the amount of research being carried out by branching out to new target proteins. One of the main areas focused on at the IOPC is glycogen metabolism. By modelling and manipulating the proteins involved in this process, it is possible to control blood-sugar levels and thus the molecules involved can be used as therapy for diabetes mellitus.

“When we began this research, we had one main target: glycogen phosphorylase,” Zografos explains. “Now, through collaboration with a laboratory in France, we are also looking at structural and modelling studies of phosphorylase kinase, another enzyme in the glycogen metabolism pathway.

We also have an expert in computational approaches helping us with the design, which is again a benefit derived from the integrated approach.”

Another main target for research are proteins present in olfactory antennae of the mosquito *Anopheles gambiae*, one of the main vectors of malaria. “We have attempted to design molecules that block the protein that mediates how a mosquito senses its human target. If the mosquito loses this ability then it will be unable to find a blood meal, thus potentially halting the spread of malaria,” says Zografos. “This line of work is really very exciting; the implications behind it are massive.”

There are a number of other proteins under investigation at the institute, and the scope is not necessarily limited to drug

design. One enzyme under investigation is of biotechnological interest, and has applications in the processing of wood for the pulp and paper industries.

“There is now a really wide range of interests and subjects being investigated,” enthuses Zografos, “and this is due to the new collaborations and knowledge transfer that has occurred due to the new facility and personnel.”

In terms of the future, Zografos is very positive about the new potential that EUROSTRUCT has unlocked.

“We now just have to focus upon expanding and increasing the number of target proteins that we are investigating. With our state-of-the-art facility, we will be collaborating with many more people in the future and so can really become a focal point for this type of research.”

It would seem that this process has already begun to a certain extent, exemplified by the two international events sponsored by EUROSTRUCT.

“In the first year we held an international symposium,” says Zografos, “and then more recently we held a five-day workshop, which had some very prestigious participants. This workshop provided an opportunity for hands-on experiments using the new facility, and there were also tutorials on subjects such as computer-aided design. These events were very important in terms of disseminating our results and also garnering information from experts from around the world.”

At a glance

Project Information

Project Title:
EUROSTRUCT: European consolidation and promotion of research capacity in the area of structure based drug discovery

Project Objective:
EUROSTRUCT seeks to unravel SBCG’s potential by creating a centre of excellence in structural biology. Key objectives include:

- Set up of a state-of-the-art X-ray facility
- Building a critical mass of sustainable research capacity
- Initiation of new research efforts through collaboration with research groups of international reputation

Project Duration and Timing:
3 years, 2 Feb 2009 to 31 Jan 2012

Project Funding:
€970.300, CSA-SA_FP7-REGPOT-2008-1, SP4-Capacities Coordination and Support Action, Support Actions

Spyros E. Zografos



A Senior Researcher with expertise in Biochemistry, molecular biology, enzyme kinetics, X-ray protein crystallography and structure-based design; Spyros E. Zografos has research interests in the functional and structural studies of enzymes involved in type 2 diabetes mellitus (glycogen phosphorylase, phosphorylase kinase, and glucokinase), nucleotide homeostasis (Adenylate kinase 6) and transmission of malaria (Odorant Binding Proteins from mosquito *Anopheles gambiae*).



Contact

Main contact name:
Spyros E. Zografos
Tel: +302107273850
Email: sez@eie.gr
Web: <http://www.eie.gr/nhrf/institutes/iopc/eu-projects/eurostruct/index-en.html>
Coordinator:
<http://www.eie.gr/nhrf/institutes/iopc/cvs/cv-zografos-en.html>