

## EMBL Grenoble Unit Review

The review of the EMBL Grenoble Unit took place on 6-7 October 2021. The review panel consisted of 10 international experts, including four members of EMBL's Scientific Advisory Committee (SAC). The chair was Poul Nissen, Aarhus University, Denmark. Several observers were present, including the Chair of SAC Paul Nurse, the Chair of Council Eiríkur Steingrímsson, Vice Chair of EMBL Council Anne Paoletti, and the Provisional Head of EMBL Grenoble Kristina Djinovic Carugo. The review took place in a hybrid format, whereby EMBL Grenoble personnel and select review panel members and observers attended in person. The majority of the review panel members and observers attended via video conference.

### Evaluation Summary

The overall performance of EMBL Grenoble was rated as outstanding based both on the quality of its research and services and the training and development of young scientists. The group leader programmes, beamline developments, and user services form a unique and strong unit that was highly appreciated by the panel and was perceived as an excellent fit for the upcoming EMBL Programme. Since the last review in 2017, important changes have or will soon take place. Firstly, the Instrumentation Team has completed a major, highly successful upgrade of the beamlines at the new fourth generation ESRF Extremely Brilliant Source. The cryo-EM facility has been enhanced by the installation of a Glacios cryo-EM system following advice from the last review. Furthermore, after decades of visionary and productive leadership, the Head of Unit Stephen Cusack will retire in 2022. The proposed new Head of Unit, Kristina Djinovic-Carugo from the Max Perutz Labs in Vienna, was considered to be a strong hire for the future of the Unit.

The panel found the RNA and infection biology research programmes at EMBL Grenoble to be of outstanding quality and impact. The Instrumentation Team at EMBL Grenoble were also considered to be impressive, by accomplishing the large and demanding task of updating the beamlines with the required capabilities to exploit the powerful fourth generation synchrotron at ESRF. The world-leading outcome places EMBL-led beamlines at the ESRF at the cutting-edge of macromolecular crystallography services.

Regarding the research directions, the panel discussed and strongly approved of the microbiology and infection biology focus combined with RNA biology. Coupled with the Microbial Ecosystems, Infection Biology and Human Ecosystems transversal themes in the EMBL Programme, the panel found that EMBL Grenoble will be an attractive site for collaboration both within and outside EMBL. For example, collaborations can easily be envisaged on cellular and tissue-based imaging projects with the Barcelona, Rome, and Heidelberg units. However the panel felt that the unit is too small for entirely new research topics such as neurobiology to be added as group leader focus areas.

The panel considered that the Grenoble site offers many opportunities, particularly with the reopening of the ESRF high-energy synchrotron, which is the world's brightest X-ray source. However, it must also rise up to the significant changes taking place in the field of structural biology. The extent to which room-temperature or time-resolved macromolecular crystallography beamlines will be used in the future will have to be considered carefully. The panel also suggested that other uses of bright, coherent X-ray sources should be further explored, in order for the unit to be at the scientific forefront and pioneer new approaches in the life sciences. The remarkable track record of the Instrumentation Team could be used for technologies such as the automation and implementation of high-pressure freezing and microfluidics in

advanced sample preparations for X-ray imaging techniques and cryo-EM. There will have to be significant changes at the unit if it is to seize these future opportunities in structural biology, leverage the infrastructure developments already in place at EMBL Grenoble, and deliver on the ambitions delineated in the next EMBL programme.

The panel proposed that the future directions and needs of structural biology service provision should also be revisited in high-level discussions between EMBL and ESRF, to redefine what the respective partners can and should do in the future. In addition, the strong synergies across the Grenoble science area and region should be exploited further, particularly in light of the new EMBL Programme, for example in areas of integrative structural biology approaches, data sciences, and complex modeling.

The panel felt that there is a critical need to increase resources. This can hopefully be achieved through an overall strengthening of the EMBL Grenoble budget and will be necessary for the important role of the unit in the new EMBL Programme, potential new services in imaging and microscopy, and increasing responsibilities with the local research communities for complex modeling. In particular, productivity of cryo-EM studies would be critically improved with a new Falcon4 detector and Selectris energy filter. This is outside the capacity of the unit on its own, and hopefully EMBL actions can provide sufficient leverage. The panel also felt that the need for scientific computing and data storage is a constantly growing matter and will require attention so as not to hamper research productivity.

Despite the outstanding productivity at EMBL Grenoble, the panel was compelled to mention that the building is in a significant state of disrepair, the consequences of which can significantly distract and inhibit research, as well as threatening precious equipment and facilities. Discussions with relevant stakeholders of the EMBL building complex must be initiated as soon as possible.

The review panel engaged in discussions with predoctoral and postdoctoral fellows over many aspects of research, training, mentoring and work/life balance at EMBL Grenoble. The state of the building was raised by the predocs and postdocs but in general they appear to be very happy with the training, mentoring, administrative and technical support, and the open and interactive research environment. The panel suggested that a formalised forum for cryo-EM training could be beneficial for fellows. They also proposed that mentoring of fellows should include future career discussions.

Overall, the review panel found the Grenoble Unit has performed outstanding research and service provision that will permit its continued success during the upcoming period of transition.

## Response to the Panel's Recommendations

I would like to thank all panel review members, and particularly the Chair, Poul Nissen, for their time, effort, and expertise in reviewing the EMBL Grenoble unit. The review came at an extremely important moment for the future direction of the unit, and the panel's input will be vital. I am certain that the importance of this review will be apparent in years to come.

My sincere congratulations and thanks to Stephen Cusack, for his unwavering leadership as Head of Site. Stephen has taken the Grenoble site through numerous scientific achievements since the late 1980s. During this time, the site has developed an outstanding research programme, as well as exceptional

services, infrastructure, and technologies. The numerous, collective scientific accomplishments achieved by the EMBL Grenoble Unit were possible thanks to Stephen's visionary guidance.

Most recently, the unit has been central to many aspects of the next EMBL Programme and scientists within the unit have played an active role in shaping the EMBL infection biology and structural biology strategies as part of a pan-EMBL effort. Together with other EMBL structural biology groups, a strategy paper on integral structural biology and "4D structural biology" was developed, which serves as the basis for future strategies in structural biology that bridge across scales and time ranges. This paper outlines the significant changes underway in the field of structural biology, highlighting very similar aspects to the unit review. In recent years, novel, in situ structural biology techniques have been developed; the importance of integrative phenomics approaches is being realised; and the use of open access AI-based structural prediction tools such as AlphaFold (part of a Google DeepMind/ EMBL-EBI collaboration) is revolutionising structural biology.

Such developments, in conjunction with the start of the new EMBL Program, the retirement of Stephen at the end of 2022 and Kristina Djinovic Carugo's start as the new Head of Site during the same year, mean that this is a critical time for the unit. I am confident that Kristina will lead the site based on its multifaceted focus on research, service, and technology development. I agree with the panel that there are many exciting opportunities for EMBL Grenoble and some strategic choices need to be made.

The panel's suggestion that the expertise of the Instrumentation Team should focus on technologies other than macromolecular crystallography, is one that will be carefully considered with the new head of site. For example, instrumentation development for X-ray imaging or cryo-EM sample preparation could be a new focus, given the high level of interest in these methodologies across EMBL and at local Grenoble institutes. In this context, the suggested investment by the panel in a Falcon4 detector and Selectris energy filter would not only critically improve the productivity of cryo-EM studies at EMBL Grenoble. It would also enable the Instrumentation Team at EMBL Grenoble to develop a novel and innovative robotic instrument for automated production of normal and time-resolved cryo-EM grids and could be offered to external users as a service.

Regarding the panel's comments on the research focus of EMBL Grenoble: at EMBL, group leaders are hired based primarily on scientific excellence, as well as an alignment with the thematic interests of the Site set by the leadership. I would agree with the panel that the unit is too small to add a neurobiology focus at this stage, as there would be a risk of the group feeling isolated even with the collaborative opportunities at other EMBL sites.

I also agree that it will be very important that the EMBL Grenoble unit becomes better connected to the French research landscape and national institutions. With the start of the next Programme and new Head of Site in 2022, there will be more opportunities to integrate and enable a critical mass of scientific collaborations. This could be explored through more formal connections with University, INSERM, CNRS and CEA units, or by forming new integrative systems with EMBL Grenoble's campus partners.

I fully concur with the panel that the relationship with the ESRF is absolutely critical, both in the coordination of providing joint beamline services and in developing new research areas, such as X-ray imaging for the life sciences. Strengthening this partnership at multiple levels, in order to be more coordinated and consultative will be a major priority.

The poor state of the building and the issue of refurbishment that were raised by the panel are indeed of great concern and this will be urgently looked into with our campus partners and proprietors to clarify the situation and ensure swift action. Scientific computing and data storage have been and will continue to be issues requiring attention. I would like to emphasise that EMBL's Data Sciences strategy for 2022-2026, described in the next EMBL Programme, was developed to focus on and solve these problems across each EMBL site.

In terms of training, the panel's recommendations regarding the fellows will be taken on board. The EMBL Fellow's Career Service provides career support and guidance to predoctoral and postdoctoral fellows across EMBL's six sites. I was pleased to hear that overall, fellows feel that they are working in a supportive environment.

In conclusion, I would like to congratulate Stephen once again, and all the groups and teams at EMBL Grenoble for a very successful review and for their exceptional work and dedication, particularly in the last couple of years during the pandemic. This review has highlighted the outstanding science ongoing at EMBL Grenoble, as well as the many opportunities ahead, through rich discussions. My thanks to Poul Nissen and all of the review panel for their discussion and very valuable input. The advice from this review will be critically important for the evolution of the site, and for Kristina as its new head will, I am certain, ensure that EMBL Grenoble continues to play a significant role in the field of structural biology. We will of course do everything we can to accompany Kristina through this period of installation and transition, and help her achieve her vision launching EMBL Grenoble into a new era.



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