

Cell Biology and Biophysics Unit Review

The review of the Cell Biology and Biophysics Unit activities took place on 3-5 May 2021. The review panel consisted of 19 international experts, including seven members of EMBL's Scientific Advisory Committee (SAC). The review was chaired by Brenda Andrews, University of Toronto, Canada. Several observers were present at the review; the Chair of SAC Paul Nurse, the Chair of Council Eiríkur Steingrímsson, the EMBL Director General Edith Heard, the Director of EMBL Heidelberg's Scientific Activities Peer Bork, Head of EMBL Council Secretariat Michael Thompson, Senior Administrative Officer of the Council Secretariat Judit Gulyas, and Strategy Officer Emma Steer. Due to the SARS-CoV-2 pandemic and the resulting travel and physical distancing restrictions, the review was convened exceptionally via video conference.

Evaluation Summary

The Cell Biology and Biophysics (CBB) Unit is highly interdisciplinary, applying and developing new imaging technologies and computational tools to explore cell biology at multiple scales. Since the last review period, the unit has seen a significant turnover of group leaders. Seven group leaders left the CBB Unit to take positions at world leading institutes and two more are expected to leave the unit soon. The outstanding performance of individual groups attests to Jan's exemplary leadership and direct mentoring and support of group leaders. Group leader departures have been balanced by new recruitment of an impressive cadre of six junior investigators. The new recruitments include five women, which has positively shifted the skewed gender balance noted in the last review.

The review panel was impressed with all of the high-quality research performed in the CBB Unit over the past four years. The panel supported the overall philosophy of the unit, which involves combining technology development with mechanistic cell biology, physics, computational modelling as well as cell and molecular biology to advance an understanding of cell biology. Indeed, the CBB Unit has successfully integrated physicists, computer scientists, and biologists to carry out innovative research that demands a multi-disciplinary approach. This is a challenge that is internationally recognised but unlike in the CBB unit, is not always overcome.

The review panel discussed several highlights including work by Julia Mahamid's group (affiliated to the CBB Unit and part of the Structural and Computational Biology Unit) which published a landmark study that implemented a number of breakthrough advances in electron cryotomography of cells, revealing near-atomic resolution information from large complexes *in situ*. The Haering group published an important study demonstrating that condensin, a protein complex with key roles in chromosome assembly and segregation, has DNA loop extrusion activity. The Kreshuk Group and the Schwab Team have collaborated with Detlev Arendt's group in the Developmental Biology Unit to produce a remarkable whole-body cell atlas, integrating gene expression and cell morphology, using a powerful segmentation approach on the > 11,000 cells in the marine worm *Platynereis dumerilii*. Finally, the Diz-Munoz and Neveu Groups measured membrane tension during early mesenchymal stem cell differentiation and discovered that naive stem cells release their plasma membrane from the underlying actin cortex when transitioning to a primed state.

The development and optimisation of new imaging and physical technologies for cell biology have continued to be a major focus in the CBB Unit. New imaging techniques include deep tissue (Brillouin) and 3D imaging, and new analysis tools include computational methods for cryo-EM data and highly performant cell

segmentation tools. The aim is to transfer new technologies, when they become robust, to the Imaging Centre where they can be offered as a service to the community. The future possibilities for broad impact of these technologies across Europe are substantial. It was also noted that it will be important to develop mechanisms that ensure continued engagement between CBB research groups and the activities of the EMBL Imaging Centre.

Due to its focus on technology development and quantitative biology, the CBB Unit is well positioned within EMBL. The CBB Unit should be able to embrace the goals of the new EMBL programme in the future, as imaging is central to understanding molecular and cellular functions ‘in context’ and theory is one of the new Transversal Themes. The unit could become relevant to many facets of the new programme to study not just eukaryotic cells but also microbes and ecosystems.

The panel was greatly impressed with the quality of the science and technology and the future plans of the unit, but the panel also advised that the CBB unit should aim for a critical mass of groups studying important biological problems using the technologies being developed. This would mean enhancing more mechanistic research at the frontier of cell biology, including genetic and biochemical approaches through future hires. Strengthening collaborations and training opportunities with the other units such as Structural and Computational Biology and Genome Biology could also facilitate this.

Given the interdisciplinary nature of the unit, the panel noted that concerted efforts should be made to establish relevant academic relationships with various faculties, in addition to biology, at the University of Heidelberg. This would help in the direct recruitment of students in physics, chemistry, and computer science. Such students would need to have courses in basic principles of biology and have appropriate experts from different fields on their thesis committees. Indeed, non-biology thesis committee experts could be international, if participation could be virtual.

It will also be important to continue to ensure that research themes pursued by theoreticians and physicists resonate with biologists. The panel suggested that formal mentoring involving non-biology external experts could be useful for some junior group leaders as they develop their programmes.

The panel noted that active promotion of training opportunities in quantitative biology at EMBL should be continued and enhanced. Generally however, the CBB Unit is clearly a wonderful training environment - the students and postdocs expressed appreciation for the unique training opportunities available in the unit and at EMBL. The panel was impressed by the positive experiences of the graduate students and postdocs, despite the challenges of the past year.

Overall, the panel found that the CBB Unit is performing exceptional research and is a paradigm for how to address the considerable challenge of making interdisciplinary life science really work.

Response to the Panel's Recommendations

My sincere thanks to the Panel for their time and effort in reviewing the CBB Unit, especially in the circumstances due to the ongoing pandemic. I would like to congratulate everyone in the Cell Biology and Biophysics Unit and in particular Jan Ellenberg as the Head of Unit for an outstanding review that showcased the unit's remarkable interdisciplinarity and scientific output. Interdisciplinary research is a vital part of

EMBL's upcoming future plans and I am very pleased that this has already been recognised and lauded by the panel in the context of this review.

Thanks to the supportive leadership provided by Jan Ellenberg, I am extremely happy to see how many talented early career scientists have flourished within the CBB Unit before taking up leadership positions elsewhere. EMBL's nine-year turnover policy ensures that skilled people are seeded throughout Europe and beyond, and the CBB Unit has excelled in achieving this during the past 4 years. Given the resulting large number of open group leader positions, I am pleased that Jan Ellenberg has seized the opportunity to hire a new set of excellent and diverse group leaders. The recent recruitments have also led to a more gender balanced unit. This contributes to ensuring a more equal, diverse, and inclusive EMBL.

The panel's recommendation that the unit should consider a stronger focus in studying research questions at the frontier of cell biology is well noted. The very recent recruitment of Niccolo Banterle, who will start in CBB in November to study structure and function of the centriole using a combined biochemical and cell biological approach already goes into this direction. EMBL's success relies on the virtuous cycle of novel research, technology development, and services. The balance between these constituent parts is continually considered and I am sure that Jan Ellenberg will ensure that a rich ecosystem of biological research questions will be nurtured within the unit, as this is definitely needed to sustain the relevant and applicable technology development. Interactions with other units are also key in this context. I also look forward to seeing the unit become involved in many facets of the new Programme, including the mechanistic understanding of microbes and ecosystems at the cellular scale and beyond, as this has the potential to open up new biological questions that can benefit from and drive new imaging technologies.

The CBB unit and EMBL leadership are very much aware of the need to connect even more with experts in scientific fields outside of biology. In this context, I am very happy to note that CBB group leader Anna Erzberger has now formally joined the faculty of physics of the University of Heidelberg. Indeed, in the context of the new Programme, EMBL plans to invite international experts in theory, physics, chemistry, and computer sciences to take part in advisory panels including Thesis Advisory Committees and Transversal Theme Expert Panels. The past year has illustrated the benefits of virtual meetings and the diversity of experts to be consulted can be widened.

The topic of Theory is one of the upcoming Transversal Themes within the next EMBL Programme, and in this context there have been ongoing discussions about how theoreticians at EMBL can be best supported. Over the past year or more, many groups interested in theory have started to build a strong and very active internal community, allowing them to connect and support each other. This includes scientists within the CBB Unit, some of whom were among the first theory groups to be hired by EMBL. Support and advisory mechanisms will be furthered and formalised with the start of the next Programme in 2022, when the Transversal Themes are implemented. Furthermore, the Theory at EMBL Visitor Programme will welcome theoreticians for sabbaticals at EMBL, to facilitate knowledge exchange. I realise that creating these mechanisms is a necessary step to ensure that theoreticians at EMBL can thrive.

I do take on board the suggestion from the panel to actively promote training opportunities in quantitative biology through mechanisms such as workshops, summer student opportunities, recruitment days and other activities. These are facilitated by EMBL-wide initiatives such as the EMBL Fellows' Career Service which offers career events, and the Visitor Programme which enables Master's students the opportunity to conduct research at EMBL.

Finally, I agree with the panel that it will be important to ensure a proper synergy between the unit and the Imaging Centre, once it opens. I am certain that Jan Ellenberg will enable this. The Imaging Centre represents a unique opportunity for EMBL to accelerate the transfer and translation of the tools and techniques developed in the CBB and other Units, as technology companies and external service users are exposed to them.

I would like to conclude by joining the panel in warmly congratulating all members of the CBB Unit and Jan Ellenberg for an extremely successful review. The unit's interdisciplinary strengths combined with the creative and collaborative spirit of the unit have enabled the unit to excel and are a testament to Jan Ellenberg's leadership.



Professor Edith Heard, FRS
Director General
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