Submission
2016 National Research Infrastructure Roadmap
Capability Issues Paper

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Declaration of Interests
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Response Preparation
Contributions to the submission below include generous contributions from members of EMBL Australia, EMBL ABR, EMBL (with particular thanks to Plamena Markova and Paul Flicek), BioPlatforms Australia (BPA), Monash University, the Australian Regenerative Medicine Institute (ARMI), The South Australian Health and Medical Research Institute (SAHMRI) and the University of New South Wales (UNSW).

Executive Summary and Introduction

The European Molecular Biology Laboratory (EMBL) is Europe's flagship intergovernmental research organisation for the life sciences with its headquarters and main laboratory in Heidelberg, Germany and four outstations in Hinxton (the European Bioinformatics Institute, EMBL-EBI), Grenoble, Hamburg and Monterotondo (Rome). EMBL has 22 Member States, and two Associate Member States: Australia and Argentina. The long term commitment of its member states allows EMBL to produce state-of-the-art research, to provide services to the member states' research communities, to engage actively in technology development and to train the next generations of scientists. In addition, EMBL activities contribute substantially to the world research-related economy. For example, it is estimated that the annual worldwide efficiency impact of EMBL-EBI is ~£1 billion and, that the annual return on Research and Development in this institute equates to ~£920 million.

Australia became EMBL's first Associate Member State in 2008 for an initial period of seven years. In 2015 the Department of Education, on behalf of the Australian Government, and EMBL signed an agreement for the renewal of the associate membership of Australia in EMBL.

Australia has been extremely proactive in taking up all initiatives available under the associate membership and, as a result, today there is a multitude of well-developed collaborative links between the Australian research community and EMBL that allow for cross-fertilization of ideas, sharing of expertise, use of services and scientific facilities, and training of young researchers.

Through flagship initiatives such as the EMBL Australia Partner Laboratory Network we have successfully contributed to the internationalization of Australian science. These include 10 current EMBL Australia Partnership Group Leaders (EMBL Australia Group Leaders) across New South Wales (3), South Australia (3) and Victoria (4). Two more EMBL Australia Group Leaders in Victoria will be recruited in late 2016. One Alumni from the Group Leader Program has completed his tenure and taken up a leadership position in A*star (Singapore). In total, to date the contributing organisations have invested or committed in forward funding ~$50 million in the EMBL Australia Group Leader Program. Furthermore, EMBL Australia has also overseen the establishment of the EMBL Australia Bioinformatics Resource (EMBL-ABR) and the EMBL Partnership PhD program.

We continuously work together to increase the breadth, quality and impact of global collaborative research. This initiative has also helped consolidate existing pockets of excellence across the country, thus increasing the interconnectivity of Australian research but also linking it through a sustainable mechanism to Europe's largest excellence hub in the field of molecular biosciences.

As the political and scientific benefits of international cooperation in research are often intertwined, the associate membership offers a forum to discuss a range of science policy issues that stimulate excellence in science. Australia is represented with two delegates in the EMBL Council. EMBL Council consists of representatives from the member and associate member states coming from national governments and research institutes. This is an important international forum where top scientific and science-policy actors meet and engage in strategic discussions with broader societal impact.

Here, we highlight some of the key outcomes that Australia's associate membership of EMBL is bringing. These include the internationalization of our research, the sharing of expertise, access to key international infrastructure, access to European research funding, training the next generation of scientists and revolutionizing our ability to handle massive amounts of biological data. Collectively these activities are substantially leveraging on our national research investment and are enabling Australian scientists to address major future research and societal challenges.

Question 1: Are there other capability areas that should be considered?

Our international relationship with Europe (through our Associate membership of EMBL, which is funded through NCRIS) provides a series of key strategic opportunities. These include

Access to major infrastructure funded through investment by multiple nations: EMBL has established key international capabilities in genomics, computational biology (bioinformatics), imaging instrumentation, synchrotron beamlines (particularly in the structural biology arena) and X-ray free electron lasers (e.g. the European XFEL). Such capabilities have been built up in Europe over many years, and represent the investment of many 100's of millions of Euros. Replicating such capabilities nationally would not be possible, particularly in the current climate of financial austerity.

International training opportunities: Many of the key technology platforms we establish in Australia involve instrumentation built and developed elsewhere. Accordingly, there is often a significant "lag phase" with respect to developing the appropriate communities of expert users in new areas. Through collaborative arrangements with international centres of scientific excellence such as EMBL, training in existing as well as new technology areas can and should be expedited. A particular case in point relates to Bioinformatics, where access to the European Bioinformatics Institute (EBI) provides a wealth of opportunity for training, both in Australia and in Europe.

Development of life-science-related instrumentation: Major scientific discoveries in life science commonly rely on the development of bespoke instrumentation designed to address a particular problem. Nowhere is this more apparent as in the fields of optical and electron microscopy where specialized adaptations to equipment are common. Similarly, development of major national capabilities such as synchrotron and neutron beamlines requires the development and adaptation of specialized instrumentation.

While Australia has, in the past, had a history of great innovation in instrument development, we currently have very limited national capability in these regards, particularly in comparison to international facilities. Indeed, very few places in the world have the capacity to analyse, visualize and quantify the dynamic inner workings of life across the whole range of biological organization. Thanks to its breadth of expertise, its collaborative culture and its comprehensive technology portfolio – ranging from structural biology methods over light microscopy at the cellular scale to live imaging of entire organisms – EMBL is one of these places.

Major advances in electron and light microscopy have led to an enormous demand in the life science community for access to the new technologies and support in the accompanying sample preparation, data acquisition and image processing techniques. Imaging data is also a frontier where new resources and software must be developed to allow data storage and provision to the community.

EMBL, with its leading expertise in both electron and light microscopy development and use together with its broad experience in providing services, data resources and training courses for the life science community of its member states, can provide access to state-of-the-art imaging facilities and expertise in instrument development to Australian scientists and engineers. Further, to create a multiplier effect that goes beyond simply providing access to a technology that is in high demand, EMBL offer training to Australian users in the operation of the technology.

Accordingly, and in order to begin capitalizing on the expertise within EMBL, the EMBL Australia Partner Laboratory Network (through its current nodes at the University of New South Wales (UNSW Single Molecule Science / Optical Imaging, led by Prof. Katharina Gaus) and Monash University (within the Electron Microscopy Group) have recruited technical expertise and is starting to develop new microscopy-related instrumentation. Similarly, access to the state of the art light imaging facilities at the EMBL Heidelberg and development of complementary facilities within the Monash Micro Imaging platform has proven invaluable for supporting animal cell imaging experiments that relate to regenerative medicine research within ARMI. We argue, however, that there is an urgent and current need to build on this foundation and develop a strong national capability that permits engineers, physicists and computer scientists to be “married” with the key problems in biology that are the focus of Australian scientists.

Structural biology: We agree with the statement in the roadmap with respect to stronger support of national structure biology infrastructure and capability. In order to be competitive on the international stage structural biologists typically require scientists to conduct experiments at national and international synchrotron micro-focus X-ray beam lines. Furthermore, the most challenging problems in structural biology require cryo-Electron Microscopy in order to determine structures. The latter approach typically requires specialized supercomputing capabilities designed to rapidly process the large quantities (terabytes) of EM images collected.

Electron Microscopy in particular is revolutionizing the study of large and dynamic molecular structures. Indeed, EMBL Australia is instrumental in supporting (through recruitment of EMBL Australia group leaders at Monash University) the development of Australia’s first (and currently only) automated Electron Microscopy platform (featuring an FEI Titan KRIOS). Installation of similar automated microscopy platforms is planned around the country, for example at UNSW and the University of Wollongong. In the latter University, and in order to support scientists in and around the state of NSW, it is planned to install a Titan KRIOS in 2018/19.

As these new resources come on line, it is important that these instruments be properly linked and networked, for example to permit sample queues to be balanced across the nation and such that periods of downtime and maintenance can be coordinated. Further, given the large amounts of data output by such instruments (terabytes / day), access to extensive imaging related bioinformatics and supercomputing is critical. Such networked infrastructure has already been built and coordinated in EMBL. Accordingly, we reason it would be valuable to build on this experience and deploy many of the international computational tools developed to facilitate data sharing and analysis (e.g. the bioinformatics and research infrastructure frameworks ELIXIR [https://www.elixir-europe.org/] and the Coordinated Research Infrastructures Building Enduring Life-science Services [CORBEL]).

Through the associate membership, EMBL offers to the Australian user community access to its structural biology sites, thus continuing to support Australia in building a larger capacity for structural biology. EMBL plans to make a new generation of unique infrastructures available to the life science community. In Hamburg, in addition to a continuation of the development of the EMBL@PETRA3 beamlines and structural biology support infrastructure towards robust service functionality, the European X-ray Free Electron Laser (European XFEL), the most powerful X-ray laser in the world, will start operation in 2017. EMBL is eager to help make this opportunity available to the life science user communities in its member states and is therefore playing an important role in the development of a dedicated sample preparation and characterisation facility for life science users at the European XFEL as part of an international consortium.

A coherent national bioinformatics strategy: The trend towards Digital Biology, new technologies and resulting new data types, translates into new challenges regarding data processing, storage, and analysis. Moreover, dealing with the rapidly increasing wealth of image data will become a priority over the next years. EMBL is an obvious place to lead the development of image data repositories and standards that allow effective data sharing and the integration of images with other data types in Europe and globally, because it combines expertise in developing data standards and resources with in-depth understanding of imaging technologies and the needs of imaging communities.

Bioinformatics is becoming the conduit to allow translation of new discoveries in human biology in research laboratories to enter clinical practice. This process is only just beginning and at this stage EMBL and Australia can work together to ease the bottleneck to translation by increasing biological knowledge, especially for humans and pathogens; by handling and integrating data and by championing open data, as well as helping to develop international standards for the ethical handling and secure, confidential sharing of data. Capitalizing on EMBL-EBI's expertise in this area, and combining it with a unique Australian perspective to global problems, we work together to use our computational expertise to identify and quantify genetic, environmental, demographic, social and lifestyle determinants of diseases and make reference datasets available to clinical researchers. In pharmacogenomics we will work on applications to specific diseases and use data integration and systems readout for therapeutic target validation. These activities are enhanced through the provision of dedicated EMBL training courses on-site, in Australia but also online training open to the Australian community of bioinformaticians.

In addition, EMBL and Australia have worked together to support the establishment of a strong national bioinformatics capability. Our associate membership of EMBL has driven the establishment of the EMBL Australia Bioinformatics Resource (EMBL ABR; additional detail in regards to the national activities of EMBL-ABR is provided in a separate submission). The goal of our strategy is to develop a similarly EBI federated group of bioinformatics nodes around the country and, in the longer term to connect our community to European scientists and provide a gateway to apply for membership of bioinformatics frameworks such as ELIXIR.

ELIXIR is a distributed research infrastructure for life-science information. It is a special project of EMBL and its mission is to unite the leading life science organizations in managing and safeguarding the increasing volume of data being generated by publicly funded research. It follows a Hub and Nodes model, with a single Hub located alongside EMBL-EBI in Hinxton, Cambridge, UK and a growing number of Nodes located at centres of excellence throughout Europe and, in the longer term, in selected international partner countries. It coordinates, integrates and sustains bioinformatics resources across its member states and enables users in academia and industry to access vital data, tools, standards, compute and training services for their research. EMBL will support the building of national bioinformatics network across Australia so as to prepare the community for joining ELIXIR.

Question 2: Are these governance characteristics appropriate and are there other factors that should be considered for optimal governance for national research infrastructure.

Associate membership of EMBL is funded by the government (rather than by institutions) and, as a consequence has the provision for transparent, comprehensive and independent oversight. It also means that the membership is open to the entire national community of researchers. Strong high-level governance is, for example, provided through our observer status on EMBL Council. Further, having a seat at a major scientific international collaborative table provides a wealth of experience in terms of building, running and oversight of major national research capabilities.

Question 3: Should national research infrastructure investment assist with access to international facilities?

In addition to the points raised previously (Question 1), we argue strongly that proper international engagement is key to the success as well as proper training of our life science community. As is the case in physics and astronomy, the scale of problems that we seek to address in biology have grown to the point that the traditional approaches to research (involving a single research team or a small collaborative grouping) will not be competitive. Accordingly, as a nation we need to be engaged with international communities that seek to assemble and apply the resources of multiple nations in order to address the most significant problems.

A particularly important example of the key opportunities afforded by international collaboration relates to both genomic medicine and agriculture. Expert teams in the EMBL-EBI are developing and applying massive specialized resources such as the ChEMBL chemical compounds database, the Gene Ontology and the Variant Effect Predictor Tool. Together, such resources are widely used by academia, industry and the medical community, and are essential for the analysis of the effect of genomic variation on human, animal and plant health, on the progression of diseases such as cancer and on the evolution of dangerous pathogens. Such tools lie at the heart of personalized medicine, the discovery of new therapeutics / pest control solutions, and the development of innovative crop solutions. For example, access to the expertise and computational approaches at EBI has been essential for EMBL-Australia Group Leaders within ARMI to conduct whole genome and systems biology experiments in regenerative medicine that are leading to the development of new cell-based therapies in this arena.

Australia's associate membership of EMBL furthermore presents a key advantage in terms of providing opportunities for our scientists to engage in major international collaborative projects. For example, Dr David Lynn (EMBL Australia Group Leader at SAHMRI) leads the computational biology aspects of the PRIMES project, a €12 million European Commission funded project in cancer systems biology. Similarly Dr Lynn also leads the InnateDB.com project, an internationally recognised platform for systems level analyses of the mammalian innate immune system and that involves a collaboration with the EBI as part of the International Molecular Exchange Consortium.

Similarly, through such international relationships Australian scientists are gaining access to major life-science related databases. These include clinical databases that, as a result of privacy regulations, cannot be transferred elsewhere and instead must instead be remotely interrogated and analysed.

Finally, there is a strong structural engagement between EMBL Australia's associate membership and some of Australia's capability organisations such as Bioplatforms Australia, and the APN. Further engagement with other capabilities (Synchrotron, ANSTO, NIF and others) is highly desirable and would provide further significant direct opportunities for engagement including sophisticated intercontinental training, exchange opportunities and thematic collaboration.

Question 4: What are the conditions or scenarios where access to international facilities should be prioritised over developing national facilities?

Many international facilities that our scientists need to remain competitive would be very difficult to replicate within Australia. Annual infrastructure investment by a super-power such as the United States of America, or formal alliances of nations (such as Europe) is far greater than the Australian national science budget. Examples of such infrastructure that our scientists rely on accessing overseas include 4th generation synchrotrons and associated beamlines (for example the EMBL structural biology beamlines at the DESY PETRA-3 synchrotron) and X-ray free electron lasers. The cost of the building the European XFEL, which will come online next year, has exceeded €1 billion.

Similarly, in bioinformatics, major international groupings have developed resources and infrastructure that exceed our current national capabilities. For example, EMBL-EBI, is an organisation that hosts petabyte scale international databases, employs 600 staff and has a budget of over €50 million / annum. Accordingly, effective collaborative linkages to such institutions are critical. Within EMBL Australia, for example, our team in the South Australian node (SAHMRI) includes two EMBL Australia group leaders specializing in Bioinformatics, both of whom have developed close collaborative interactions with the EBI in order to conduct their research. Similarly, from the resource perspective, close linkages have been built between EMBL-ABR and the EBI.

We argue that it is critical that we develop national facilities where possible, but that these should optimally provide key strategic capabilities that complement (and thus potentially) contribute to the broader international scientific community to avoid duplication of efforts or resources. For example, in the field of imaging our national synchrotron provides world-leading capabilities in small animal imaging, however, for certain experiments our scientific community accesses international synchrotrons or new imaging capabilities such as XFEL. Similarly, in Bioinformatics through our associate membership of EMBL our scientists are directly engaging with the European Bioinformatics Institute.

International facilities further provide great prospects for collaboration and engagement with major international projects, thus strengthening and increasing the reach and impact of our national capabilities. For example, particularly notable opportunities in these regards relate to field of Phenomics and in growing engagement between national capabilities such as the Australian Phenomics Network, the EMBL-EBI, the International Cancer Genomics Consortium (ICGC) and the Global Alliance for Genomics in Health. Lastly, and as previously discussed, we believe that national membership of international collaborative groupings such as ELIXIR provide, in the longer term, the best opportunity to develop a coherent and efficient framework around which we can organise, support and grow our national bioinformatics community.

Question 5: Should research workforce skills be considered a research infrastructure issue?

In short, yes. We argue strongly that it is critical that strategic infrastructure is run by highly skilled and motivated people with the management and technical expertise to run sophisticated technology platforms. Funding and career development for such individuals is often difficult to provide within standard University or Institute enterprise agreements which tend to be designed to support "teaching and research academics", "research-only" and "administration-focused" staff. A particular case in point relates to Bioinformaticians; these scientists play critical roles in data analysis, but may not have overall leadership of the project. Accordingly, and despite their critical skill-set, such individuals often struggle to win the grants and fellowships required for a sustained academic career.

Research infrastructure is furthermore intimately linked to our national ability to recruit and retain high quality scientists from overseas. Such individuals expect and require access to the best facilities in order to effectively address the most important scientific questions. Through our associate membership in EMBL, for example, we are recruiting exceptional EMBL Australia group leaders, all of whom rely on access to high quality national infrastructure in order to pursue their scientific goals.

Question 6: How can national research infrastructure assist in training and skills development?

Successful training models include dedicated training workshops supported and complemented by in house training conducted within major research platforms. For example, in structural biology the worldwide community conducts international training workshops (e.g. "ccp4 workshops") that include bi-annual events held in Australia. Such workshops involve our national experts engaging with visiting international scientists who collectively conduct focused training events. Other invaluable training opportunities relate to areas where we have a recognized and long-term national skills shortage. In bioinformatics, for example, the EMBL-EBI "train the trainer" series of international workshops is helping build our skill base in that discipline. Such international training events also provide invaluable opportunities for our scientists to develop new international collaborations. Indeed, through the existing collaborative network between EMBL-EBI, EMBL Australia, EMBL-ABR CSIRO and Bioplatforms Australia, over 1000 bioinformaticians have been successfully trained, thus demonstrating how European connection has extended Australia's national capability.

A close relationship between academia and research infrastructure is also critical to ensure our PhD students graduate with an attractive technical skill set. The engagement of national research platforms is key in these regards, since these house and / or operate major infrastructure that could not otherwise be located within individual scientists' research groups.

Maximizing the benefit of disruptive technology through effective training strategies

Research infrastructure and capitalizing on our international relationships also have a critical role to play in helping our nation properly train in and effectively use disruptive technology. Examples include:

1) The utility of cryo-Electron Microscopy in obtaining near-atomic resolution structures of large macromolecular assemblies: In this area, and as a consequence of engineering breakthroughs together with developments in optics, detector technology and software, cryo-EM can now yield molecular structures at resolution previously only obtainable through X-ray or NMR-based techniques. Accordingly, around the world, structural biologists have to re-train in EM-based techniques in order to remain competitive. Further, EM facilities have to transform their operations to account for the demands of high throughput biological cryo-EM. As a consequence, there is now a worldwide shortage of experienced biological microscopists.

We argue the only long-term way of addressing this issue is through effective national and international training strategies that, by necessity must be integrated with appropriate research infrastructure. Our relationship with EMBL is particularly important in these regards and in helping address this paucity of talent, both through access to EM training workshops in Heidelberg and through organising visits of experienced EMBL trainers to run courses in Australia.

2) CRISPR/CAS9 technology for altering a genome sequence*:* CRISPR / CAS9 genome editing approaches have completely changed our ability to rapidly introduce specific mutations in the genome of model organisms (and potentially from a therapeutic perspective in humans). Experiments such as making a knockout mouse that commonly took years from conception to delivery can now be delivered in a matter of weeks at a fraction of the price and thus changing the scale on which phenomics related experiments can be conducted. Accordingly, scientists in the phenomics and in the "knockout / knock-in" space have had to re-train and re-skill in order to take advantage of CRISPR/CAS9 related approaches. In these regards our community can take advantage of regular EMBL training courses such as Genome Engineering (CRISPR/CAS)

3) Next generation sequencing techniques: The advent of next generation sequencing approaches has all but eliminated traditional capillary based sequencing approaches and, furthermore, brought us into the era of the $1000 human genome. As a consequence, our scientists now have the ability to sequence large groups of patients that suffer from a particular disease. Accordingly, we can learn from major genome-related projects being conducted in Europe and involving EMBL. These include the 100,000 genomes project in the UK. This latter project involves a collaborative alliance between the British National Health Service, the sequencing company illumina and software produced by the EBI that is critical for analysis of the vast amount of genomic data (the Variant Effect Predictor annotation engine). These exciting advances bring important new challenges in data management and training that can only be addressed through dedicated national and international workshops and pooling of efforts.

4) New optical microscopy approaches: Over the past five years, developments in optical physics and engineering have seen the invention of new and sophisticated optical microscopy approaches. One recent such example is SPIM, a technique pioneered at EMBL (and that later led to the development of the Lattice Light Sheet [LLS] microscopy). These new types of microscopy are revolutionizing our understanding of biology by providing extremely high resolution 3D images of living cells in real-time. However, such instrumentation also requires microscopists to gain new skill sets, a requirement that can be met, for example, through the EMBL Course in Advanced Fluorescence Imaging Techniques.

5) Unprecedented volumes of data: The new wave of microscopy and genomic techniques is leading to an explosion in the quantity of data that a typical research team must be capable of analysing. EBI expertise in operating data resources, together with its training opportunities, will form a critical part of our scientists to seamlessly handle new scales of biological data.

Training the next generation of scientific stars

Finally, from the perspective of training, our NCRIS funded associate membership of EMBL provides several unique opportunities for training. The EMBL PhD and Postdoctoral program presents excellent opportunities for Australian students and postdoctoral scientists to train in Europe. Such an experience gives these individuals a global career opportunity and permits early development of lifelong international networks. World class research labs and facilities, high quality seminar programmes and the vibrant international atmosphere combine to ensure that talented young researchers have access to all they need at this critical career stage. The EMBL EI3POD programme is designed to support interdisciplinary research projects involving two EMBL labs and a lab in an EMBL member or associate member state. This new scheme offers the possibility for fellows to take part in international/inter-institutional collaborations or an intersectorial experience while carrying out interdisciplinary research. Australian academic partners can benefit from the EI3POD scheme.

To complement these international initiative, in the past two years we have launched the EMBL Australia Partnership PhD Program (led by Prof Katharina Gaus, EMBL Australia Node Leader, UNSW). This initiative provides access to the EMBL shared pool of potential PhD students and is helping our community attract outstanding international PhD students to Australia. The program is still in its infancy, but to date has recruited >10 international PhD students to Australia.

Question 7: What responsibility should research institutions have in supporting the development of infrastructure ready researchers and technical specialists?

Briefly, and building upon our response to Q5 and 6, we argue that a synergistic approach that involves a network of research institutions, research infrastructure platforms and the relevant national and international communities is key to ensure the healthy development of trained and capable scientists. EMBL for example, has a long and distinguished track record in achieving that goal across several fields of biology. To date, for example, 26 Max Planck Directors have received training at EMBL during their career.

Question 8: What principles should be applied for access to national research infrastructure, and are there situations when these should not apply?

Ideally capabilities should be designed and supported such that they can meet the growing and ever changing needs of the scientific community. For highly specialized infrastructure where an instrument may be oversubscribed, we support merit-based access. The Australian Synchrotron collaborative access program (CAP) is an excellent and successful example of such a scheme. Here, leading scientists performing impactful science are prioritized through peer review of applications for beam time. Factors typically considered in peer review include demonstrated track record of the team's prior success, preliminary data (that may support likely success of experiment) and importance of the problem under investigation.

With regards to infrastructure localized internationally, to complement the excellence-based approach EMBL prioritizes applications from member and associate member states for access to the infrastructure it hosts. Accordingly, Australian scientists are considered equal to all other EMBL member nations in these regards. Key Core platforms to which the Australian community receives access include Bioinformatics, structural biology, optical and electron microscopy, chemical biology and metabolomics.

Question 9: What should the criteria and funding arrangements for defunding or decommissioning look like?

We argue that rather than defunding or decommissioning, the national strategy should instead generally include approaches to facilitate and promote the rapid evolution of and / or merging or reprioritization of technological capabilities. Such an approach will maximize the ongoing impact of past investment particularly (as is often the case) where a disruptive technology may suddenly come into play.

Related to the above, areas where decommissioning may be of importance is in bioinformatics where developing appropriate strategies for closing down redundant or out-of-date databases and software may be needed (i.e. where better capabilities are provided by newer resources). Similarly, in the field of computing and supercomputing criteria for planned redundancy may include cost benefit analysis with respect to maintaining and running older hardware versus establishing new machines.

Question 10: What financing models should the Government consider to support investment in national research infrastructure?

Both discovery driven research and infrastructure require appropriate time-horizons to be successful. We argue that long term Federal investment (over the 10+ year timeframe), in combination with appropriate access models, should be at a sufficient level to ensure that the national community as a whole has the opportunity to benefit from major capabilities.

Question 11: When should capabilities be expected to address standard and accreditation requirements?

In order to maximize impact, particularly with respect to engagement of industry, technology platforms should have world-class standard operating procedures (SOP), for example through metadata requirements (Bioinformatics) or through systems monitored through the International Standards Organisation (ISO).

Question 12: Are there international or global models that represent best practice for national research infrastructure that could be considered?

Yes, we argue that EMBL and EBI provide excellent examples of best practice. For example, the Group of Senior Officials (part of G7) listed EMBL, the International Mouse Phenotyping Consortium (a group that includes the Australian Phenomics Network) and ELIXIR as exemplar research infrastructures with global impact and significance.

We further argue that the guided development of scientific networks, such as national engagement through EMBL and, in the longer-term, ELIXIR present an excellent approach to reduce duplication of resources and research effort while maximizing collaborative gain.

Question 13: In considering whole of life investment including decommissioning or defunding for national research infrastructure are there examples domestic or international that should be examined?

No response

Question 14: Are there alternative financing options, including international models that the Government could consider to support investment in national research infrastructure?

No response

Health and Medical Sciences

Question 15: Are the identified emerging directions and research infrastructure capabilities for Health and Medical Sciences right? Are there any missing or additional needed?

We agree with the capability roadmap that structural biology requires significant national support. Currently in these regards the Australian synchrotron is a crucial national platform heavily used by the structural biology community. Our scientists furthermore should continue to gain priority access to EMBL-supported 4th generation Synchrotron beamlines in Hamburg and Grenoble. Nationally we argue that NCRIS should support disruptive technologies in the structural and cellular biology such as high throughput cryo-Electron Microscopy and next-generation optical microscopes (e.g. the lattice lightsheet microscope). The former EM instrumentation can be considered to be equivalent (both in cost and operation) to a synchrotron beamline.

In relation to bioinformatics we support strongly the development of a federated bioinformatics community, such as is being organised by EMBL-ABR. This strategy should facilitate national collaboration and eliminate duplication of effort. In the longer term we argue that our associate membership of EMBL provides additional opportunities to enable Australian membership of ELIXIR.

As highlighted in Q1 we argue there is an urgent need for the development of national facilities that permit the development of instrumentation that is bespoke for the requirements of the Australian scientific community and capitalizes on already existing instrumentation in EMBL and in the US.

With respect to health informatics and genomics enormous opportunities exist in the fields of personalized medicine and in the control of pandemics and epidemics. With regards to personalized medicine, such approaches may also be combined and developed with rapid phenomic analysis of model organisms, for example, with respect to APN-facilitated analysis of disease-linked mutations.

Finally, it is worth noting that fundamental research is under significant pressure to deliver impact, but we need to remember that real scientific breakthroughs take time and dedication, and require continuing support and vision. In the long-term it is the discovery driven research that often creates the most unexpected disruptive innovation with remarkable impact for society. For example - After 20 years of work EMBL scientists have recently been able to solve the atomic structure of the complete influenza polymerase using one of the beamlines operated by EMBL in Grenoble (Cusack and colleagues, Nature, 2014). This provides insight into the replication mechanism of the influenza virus, and creates new opportunities for the development of antiviral drugs that inhibit polymerase activity.

This work represents a concrete example of how structural biology and the use of beamlines can directly benefit human health. Its societal impact is evident by the potential of this work to improve public health (i.e. by providing new opportunities to treat both seasonal and pandemic flu), while the economic impact is given by the opportunity to enhance competitiveness of the pharma sector through commercialisation of new drugs. The work has also led to the birth of the spin-off company Savira for the development of anti-influenza drug candidates.

Question 16: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

We argue that our continuing and stable associate membership of EMBL is critical for the internationalization of our science, for training of our scientific community and for our scientific community to access major international infrastructure such as the EBI, state-of-the-art imaging facilities and a variety of international synchrotron beamlines. Representation within the premier European scientific organisation further provides a route into international consortia and collaborative projects that would otherwise be difficult for our scientists to access and engage with.

The value of such interactions cannot be overstated. For example, in the past, it is worth noting that Australian scientists did not play a significant role in the Human Genome Project. Partly as a consequence of these events, over 15 years later, we are still developing strategies to build and network our bioinformatics community. Through our associate membership of EMBL and our linkages with EBI, we are now well placed to address this problem and engage with initiatives such as ELIXIR and CORBEL.

Question 17: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Health and Medical Sciences capability area?

No Response.

Environment and Natural Resource Management

Question 18: Are the identified emerging directions and research infrastructure capabilities for Environment and Natural Resource Management right? Are there any missing or additional needed?

We would highlight the impact of Bioinformatics on good agriculture practice, disease control and in developing innovate crop solutions. Similarly, given its climate, Australia is particularly vulnerable to the impact of climate change, both with respect to agriculture but also with regards to its tourism industry (e.g. the impact of warming on coral reef bleaching and on the ocean environment).

Question 19: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

We argue that as for health, our engagement with EMBL, EBI and in the longer term ELIXIR is crucial for our successfully developing strategies to manage challenges in relation to climate and our environment.

Question 20: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Environment and Natural Resource Management capability area?

No response.

Advanced Physics, Chemistry, Mathematics and Materials

Question 21: Are the identified emerging directions and research infrastructure capabilities for Advanced Physics, Chemistry, Mathematics and Materials right? Are there any missing or additional needed?

The development of bespoke instrumentation requires successful collaborative engagement of physicists, engineers and computer scientists (particularly in the field of algorithm development, modelling and data analysis).

Question 22: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

No response.

Question 23: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Advanced Physics, Chemistry, Mathematics and Materials capability area?

EMBL provides key opportunities for international linkages into aforementioned Chemoinformatics efforts (e.g. chEMBL).

Understanding Cultures and Communities

Question 24: Are the identified emerging directions and research infrastructure capabilities for Understanding Cultures and Communities right? Are there any missing or additional needed?

Our associate membership with EMBL provides a formal involvement with an organisation that has over 80 nationalities working together. This presents an extraordinarily culturally diverse international scientific community that our scientists can benefit from being part of.

Question 25: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

We argue that Australia should continue its long term engagement with EMBL as it is vital to maintain alliances that can lead the way when it comes to supporting researchers' independence to conduct basic research, while at the same time producing results with real societal impact.

Question 26: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Understanding Cultures and Communities capability area?

No response

National Security

Question 27: Are the identified emerging directions and research infrastructure capabilities for National Security right? Are there any missing or additional needed?

We agree that the fields of genomics and bioinformatics represent critical approaches for helping combat the emerging pathogens (both human and agricultural). An example of the power of such approach includes understanding the evolution, impact and spread of new and dangerous diseases (e.g. flu, Zika virus etc).

Question 28: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

No response

Question 29: Is there anything else that needs to be included or considered in the 2016 Roadmap for the National Security capability area?

No response

Underpinning Research Infrastructure

Question 30: Are the identified emerging directions and research infrastructure capabilities for Underpinning Research Infrastructure right? Are there any missing or additional needed?

The NCRIS funded Australian National Data Service (ANDS) and National eResearch Collaboration Tools and Resources project (NECTAR) both provide support for the development of computational resources such as the Characterisation Virtual Laboratory, an environment for managing and analysing data output by high-end instrumentations such as Synchrotrons, Electron and Optical Microscopes.

Question 31: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

Please see our response to Question 16.

Question 32: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Underpinning Research Infrastructure capability area?

No response.

Data for Research and Discoverability

Question 33 Are the identified emerging directions and research infrastructure capabilities for Data for Research and Discoverability right? Are there any missing or additional needed?

Bioplatforms Australia has overseen significant NCRIS investment in genomics, transcriptomics, proteomics, metabolomics and bioinformatics (for example through investment in EMBL-ABR) and has catalysed significant cultural change across the Life Science communities. BPA has supported open access to instrumentation, and in collaboration with EBI, EMBL Australia and EMBL-ABR it has supported large-scale data and Bioinformatics training initiatives thus addressing some of Australia's pressing challenges in these regards. The governance arrangement at Bioplatforms Australia (not for profit, independent, connected within the sector) has played an important role in achieving these outcomes.

Question 34: Are there any international research infrastructure collaborations or emerging projects that Australia should engage in over the next ten years and beyond?

No response.

Question 35: Is there anything else that needs to be included or considered in the 2016 Roadmap for the Data for Research and Discoverability capability area?

No response.

Other comments

If you believe that there are issues not addressed in this Issues Paper or the associated questions, please provide your comments under this heading noting the overall 20 page limit of submissions.

No response.