EIROforum[1] Paper

Research Infrastructures: Value and Impact for European Science, Industry and Society

May 2020

[1] EIROforum is an organisation of eight European Research Infrastructures, namely CERN, EMBL, ESA, ESO, ESRF, EUROfusion, European XFEL, and ILL. For this document, ESA has abstained from being a signatory.

Executive Summary

The current pandemic has confirmed the decisive role that science plays in delivering sustainable solutions for society. We are witnessing a global effort, in which European Research Infrastructures (RIs) are uniquely placed to play a leading role for Europe by offering expertise, vital scientific services and technologies that will not only help us handle the current crisis, but also devise solutions for mitigation and prevention of future such adversities.

In order to unlock and fully exploit the innovation potential of European RIs in the challenging times that Europe will face in the next years, and to allow Europe to remain a global leader in many scientific and technological domains, strong support to Research Infrastructures should be provided both by Horizon Europe and by the EU Recovery Plan 2021 – 2027.

RIs are pivotal in sustaining and enhancing the competitiveness and world-class excellence of European science, and have significant value for and impact on European industry, society and economy, as demonstrated by examples in the Annex of this paper.

European Research Infrastructures:

- harness scientific expertise that drives discoveries and creation of knowledge;
- offer access to researchers from Europe and beyond to the best and in some cases, unique, state-of-the art facilities;
- enable integration of research communities from all countries in Europe;
- maintain the world-class excellence of European science

RIs are also drivers of innovation as they need to develop advanced instruments and a variety of cutting-edge technologies. These developments are often done in close collaboration with industry, and lead to both incremental and breakthrough innovation. Knowledge and technology transfer from RIs to industry via collaborative R&D activities, procurement of goods, equipment and services, and the creation of spin-off companies is of significant benefit for European industry. RIs now become key drivers for the continuous cycle of technology developments, which can feed the cycle of innovation well beyond their respective scientific areas.

Research Infrastructures provide numerous benefits to European society and economy, either directly, through addressing societal challenges or industrial needs, or indirectly through training and education, as well as knowledge and technology transfer.

Research infrastructures: Cornerstones of European scientific excellence

RIs develop and provide state-of-the-art instruments for carrying out fundamental science: a quest for new knowledge from examining the ingredients of life and matter to unravelling the history of the Universe. This research has contributed to many Nobel Prize-winning discoveries[2]. The scientific enterprise of their design, construction and operation marshals and sustains international collaborations of scientists, engineers, technicians and administrators for the inherently peaceful purpose of advancing the frontiers of knowledge. European RIs strengthen and support their respective scientific communities, including many ERC Grant recipients, continually raising the bar of scientific discoveries and creating competitive forces that drive excellence in science. World-leading facilities, such as those offered by the EIROs and other European RIs, have become essential in structuring and integrating large scientific communities and fostering collaboration across Europe. This community consolidation further enables scientists to conceptualize and provide input into the requirements and design for RI and concepts for future facilities. Moreover, it has resulted in collaborations around ambitious scientific projects that are key to driving scientific excellence in Europe.

Value of Research Infrastructures for European Industry

The collaboration between RIs and European industry is driven by the requirements for cutting-edge instrumentation as well as for access to highly advanced techniques, facilities, data and expertise. Industry acts both as a supplier—often jointly developing hi-tech components with the facilities—and in certain cases as a user, where RIs provide unique capabilities for industrial research and development, such as in testing and development of new components and advanced materials.

RIs have a need for state-of-the-art instrumentation encompassing a multitude of fields including, for example, novel detector and imaging technologies, advanced data acquisition systems, high performance and high capacity computing and communication networks. The resulting technologies of such collaborations often have spill-over applications in other domains and industrial sectors that cover a whole spectrum ranging from cancer treatment and new medicines, to the aerospace and automotive industries.

The precision, sensitivity, tolerance and other technical requirements for RI instruments often far exceed the requirements of conventional industrial uses; thus, RIs are key capability drivers for society. As a result, the continuous cycle of technology developments in RIs feeds a cycle of innovation not only in their respective areas, but well beyond, as demonstrated by the pioneering initiative ATTRACT, which aims at developing breakthrough technologies for science and society and is funded by Horizon 2020[3].

---

[2] E.g. the contribution of ESRF to the 2009 Nobel Prize in Chemistry, the contribution of ESO to the 2011 Nobel Prize in Physics, the contribution of CERN to the 2013 Nobel Prize in Physics, the contribution of the ILL to the 2016 Nobel Prize in Physics, and the contribution of EMBL to the 2017 Nobel Prize in Chemistry.

[3] https://attract-eu.com/

Value of Research Infrastructures for European Society & Economy

Human progress is achieved through new discoveries and their implementation. In current times, scientific breakthroughs are typically realised with the support of a first-class RI. Scientific developments made in RI drive knowledge creation and foster the likelihood of technological breakthroughs with vast societal and industrial applications. The RI missions and science fascinate the general public from school children to grandparents and teachers[4], and inspire young people to pursue careers in science, technology and engineering. As hubs of excellence for their respective scientific communities, RIs provide invaluable training opportunities for young researchers, engineers and technicians, who continue their careers in other academic institutions or in European industry.

Many world-changing technologies and applications that we take for granted today, such as satellite and wireless communications, mobile phones, MRI scanners and cancer treatments, are the result of developments and breakthroughs in fundamental research, such as electromagnetism, Einstein's theories of relativity, or the sequencing of the human genome. The results of such fundamental breakthroughs, sometimes unexpected and often without concrete application in mind, inevitably find their way into everyday life[5].

RIs have evolved and have developed synergies with neighbouring scientific fields. Their technologies often find applications well beyond their initial scientific domain and the use for which they were originally intended. In order to keep evolving and to be able to address the societal challenges of the time, RIs needs both cutting-edge technologies and a solid community of curiosity driven scientists. Their future will depend on continuous development, of innovative technologies as well as accessing a pool of well-educated, well-trained scientists and engineers.

Conclusion

In order to sustain the world-class excellence of European science, to enable European RIs to stay at the forefront of their science and technology fields, and to provide direct and indirect benefits for European industry, society and economy, the EU Recovery Plan 2021-2027 should foresee strong support for European Research Infrastructures.

---

[4] CERN hosts annually around 140,000 visitors of all ages coming from 80 countries around the globe. ESO's education and outreach centre, *Supernova,* has hosted 57,000 visitors including 5,000 school children in the first ten months of its operations, which began in April 2018. EMBL reached over 200 teachers and 3000 secondary school students through its educational activities in 2019.

[5] One of the earliest descriptions of the eventual major impacts of fundamental research was captured in 1939 in the classic essay *The usefulness of useless Knowledge*, by A. Flexner. More recently, for example, by conducting an extensive study of drug development, Harvard scientists made the startling conclusion "most transformative medicines exist because of fundamental discoveries that were made without regard to practical outcome and with their relevance to therapeutics only appearing decades later." Spector, J et al. "Fundamental science behind today's important medicines." Science translational medicine 10.438 (2018). http://stm.sciencemag.org/content/10/438/eaaq1787

ANNEX

European Research Infrastructures contributing to addressing global challenges

- **Fight against Cancer:** Cancer is a major societal issue worldwide and especially in Europe, where close to 4 million new cases per year are diagnosed and related healthcare costs per annum exceed 100 billion EUR[6]. Next-generation cancer detection and treatment will rely on technological breakthroughs in a variety of areas: cross-country genomics studies, pharmaceutical target validations, advanced radiation and hadron therapy, as well as advances in imaging and detector technology. European Research Infrastructures will continue to play a major role in all of the above as well as in the development and testing of novel drug treatments, such as immunotherapy and cancer vaccines, and can contribute to the progress in ion beam therapy and in-vivo imaging technologies.
- **Reversing ocean biodiversity loss:** The ocean ecosystem is critical to life on Earth and ocean biodiversity continues to decline in every region of the world. Analysing and tackling this requires coordination across sectors and policy domains. Combating ocean biodiversity degradation is an interdisciplinary scientific challenge, requiring the integration of research and data from the level of (bio)molecules to cells to organisms to ecosystems to biospheres. This will require the utilisation of state-of-the-art research infrastructures, the development of enabling technologies and the integration of various data sources.
- **Combating Antimicrobial Resistance (AMR)***:* The state-of-the-art instrumentation and computing capacity of EMBL, together with funding from the European Research Council (ERC) played a vital role in three recent discoveries[7] that will help humanity in our efforts against antimicrobial resistance (AMR). One of the major global threats identified by the World Health Organization[8], the spread of antimicrobial resistance could inverse many of the medical breakthroughs of the last century if previously curable infectious diseases become untreatable. These scientists that unravelled the molecular basis of a major antibiotic resistance transfer mechanism, developed the first proof-of-principle for blocking this transfer and carried out the first of a kind large-scale screening of 3000 drug combinations on three different disease-causing bacteria of its kind.

Value and impact of Research Infrastructures for European industry

CERN spends on average annually circa 500 MCHF on procurement contracts for goods and industrial services. Several studies show the impact of CERN's procurement activities on technology transfer and innovation[9]. The results of the study[10] on the technology-intensive procurement (worth ~1.0 billion €) for the LHC project indicate that many corollary benefits are associated with such a procurement activity. For example,

---

[6] R. Luengo-Fernandez, et al Lancet Oncol, 14 (2013), pp. 1165-1174

[7] Maier, L., Pruteanu, M., Kuhn, M., et al. Extensive impact of non-antibiotic drugs on human gut bacteria. Nature, published online 19 March 2018. DOI: 10.1038/nature25979; Brochado, A., et al. Species-specific activity of antibacterial drug combinations. Nature, published online 4 July 2018. DOI: 10.1038/s41586-018-0278-9; Rubio-Cosials, A., et al. Transposase – DNA complex structures reveal mechanisms for conjugative transposition of antibiotic resistance. Cell, published online 15 March, 2018. DOI: 10.1016/j.cell.2018.02.032

[8] WHO: Antimicrobial resistance: global report on surveillance 2014

[9] "Does CERN procurement result in innovation?" S. Åberg, A. Bengtson, 2015

[10] Technology Transfer and Technological Learning through CERN's Procurement Activity, E. Autio, M. Bianchi-Streit, A. Hemeri, 2003

as many as 38% of companies developed new products or services as a direct result of the supplier project; 13% started new R&D units; 14% started new business units; 17% opened a new market; 42% increased their international exposure; and 44% indicated significant technological learning. Other studies[11,12] reveal that the "utility ratio" (increased revenue + cost savings)/(procurement value) was in the range of 3:1, meaning that each CHF that was spent by CERN in procurement generated three CHF worth of additional value to the suppliers of high-tech equipment for the LHC.

The ESRF's synchrotron X-rays provide powerful opportunities for commercial R&D, enabling companies to develop new products, refine existing ones, and improve their manufacturing processes by allowing them to examine materials in manner that goes far beyond what is possible with standard laboratory-based techniques. These advanced analytical experiments have an impact on European industry across a multitude of domains, including drug discovery and development, battery research, catalysis, metallurgy, consumer products and medical devices, amongst many others. For example, studies on formulation carried out at ESRF by one company have opened up a new market worth €1.2 billion. In addition to direct commercial access, around 30% of public beam time used at ESRF has a direct link with industry. As a result of the knowledge transfer that takes place, such academic-industry collaborations can lead to the direct commercial use of the facility, providing a strong added-value for industrial innovation.

A study on European XFEL during its early construction phase[13] (2009-2017) on external effects of RI shows the impact in Technological and organizational learning as well as how companies involved in the construction gained reputation not only in Germany but also in other regions of the world.

The non-destructive determination of residual stresses in engineering components is limited to surface or near-surface regions and offers limited spatial resolution. Bulk stress mapping is generally performed using destructive methods, which not only limits the possibility for further investigations but also involves the destruction of expensive and highly elaborate parts. To give industry the investigation tools it needs to make advances in areas such as additive manufacturing, hardening processes and welding, the ILL operates a "Stress Analyser for Large-Scaled engineering Applications" (SALSA). Using this neutron diffractometer, it is possible to perform truly non-destructive strain and stress measurements, in the form of profiles or maps, beneath several centimetres of metal or ceramic. Thanks to the non-destructive nature of SALSA, investigations can be carried out over full development cycles, since the same sample can be measured time and again, once it has undergone further treatment or ageing tests.

Industry is increasingly utilising the data and software by RI's to create new products, services and business opportunities. A good example of this is the Open Targets public-private partnership[14] which has brought together the some of the world's leading pharmaceutical and biotechnological companies in utilizing the world's most comprehensive range of freely available molecular databases and resources of EMBL-EBI. Combining the latest large-scale genetics, genomics data and computational analysis, the companies carry out pre-competitive collaboration with the aim of improving the success rate for developing new medicines.

---

[11] The economic impact of technological procurement for large-scale research infrastructures: Evidence from the Large Hadron Collider at CERN, P.Castelnovo, M. Florio, S. Forte, L. Rossi, E. Sirtori, 2018

[12] The Impacts of Large Research Infrastructures on Economic Innovation and on Society: Case Studies at CERN, OECD 2014

[13] External effects of Basic research Infrastructure, M. Neumann, 2014

[14] https://www.opentargets.org/

Value and impact of Research Infrastructures for European society and economy

Thousands of hospitals around the globe employ Positron-Emission Tomography (PET) as an aid to the diagnosis of diseases such as dementia and cancer. In modern PET-CT (Computer-Tomography) scanners, three-dimensional imaging is often accomplished with the aid of a CT X-ray scan performed on the patient during the same session, in the same machine. PET technology has been advanced over 40 years thanks to the work carried out at CERN and other research laboratories around the world. The technologies and scientific advances behind high-energy physics – through developments in accelerators, detectors and computing – have had significant contributions to the field of medical imaging.

In 2017, there were approximately 37 million people living with HIV[15] and tens of millions of people have died of AIDS-related causes. HIV treatment includes medications to prevent and treat the many opportunistic infections that can occur when the immune system is compromised by HIV, as well as the use of antiretroviral therapy (ART) to attack the virus itself, with the aim of halting the development of AIDS. HIV-1 protease is an enzyme responsible for the maturation of virus particles into infectious HIV virions, which ultimately leads to the development of AIDS. Without effective HIV-1 protease activity, HIV virions remain non-infectious. Given its fundamental role in HIV replication, the disruption of HIV-1 protease activity is a key target for successful ART drugs. At ILL, scientists have used neutron crystallography to determine the structures of HIV-1 protease/drug complexes, providing vital information to help design new, more effective ART drugs.

Every year, 290,000 to 650,000 deaths and 3 to 5 million cases of severe illness worldwide are associated with flu[16], an infectious disease caused by influenza viruses A and B. Vaccines and anti-viral drugs are available for flu, but viral strains with resistance to these drugs are emerging. The need for an effective drug with a novel mechanism of action is high. A promising target for these drugs is one of the flu virus's enzymes, influenza polymerase. In 2018, scientists at the European Molecular Biology Laboratory (EMBL) succeeded in determining the molecular structure of this enzyme using X-ray diffraction data collected on beamlines at the European Synchrotron Radiation Facility (ESRF). Understanding the structure of influenza polymerase makes it easier to reveal the detailed mechanisms of viral replication and viral host-pathogen interactions that underpin drug development. EMBL researchers are continuously working on influenza polymerase with the aim of supporting the development the next generation of influenza drugs, and are now using their expertise in virology and infection biology to study SARS-COV-2.

In the domain of personalised medicine, we are starting to realise how the use of genomic sequence testing will revolutionise medical treatment and the implications of this for national healthcare systems. These discoveries, often carried out with the help of a RI, underpin many areas of the world's economy. The translation into economic wealth is staggering: the global pharmaceutical market is estimated to reach nearly €70 billion in 2019[17], and the MRI market €5 billion by the year 2020[18]. Moreover, RIs are often able to rapidly contribute to devising long-term public health solutions, and a recent example of this is the creation of the COVID-19 Data Portal[19] by EMBL as a response to the current pandemic. The Portal's goal is to collect and share outbreak sequence data from COVID-19 while also allowing search of clinical and epidemiological data across Europe.

---

15 https://www.hiv.gov/hiv-basics/overview/data-and-trends/global-statistics

16 World Health Organization, https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)

17 https://www.bccresearch.com/market-research/biotechnology/drug-discovery-technologies-report-bio020e.html

18 http://www.axisimagingnews.com/2015/07/analysis-global-mri-market-reach-5-8-billion-year-2020/

19 https://www.covid19dataportal.org/

With the continuous depletion of natural resources and fossil fuels in particular, power consumption is one of the major global challenges that needs to be addressed today in order to secure the supply of energy for the future generations. Electricity production by means of fusion, the thermo-nuclear reaction that powers the Sun and the stars, will provide safe, non-carbon emitting and virtually limitless energy. ITER[20] is the largest magnetic fusion device, currently being constructed in Southern France, which will be used for research and demonstration of the feasibility of fusion as energy source with enormous potential impact for the future of mankind. Many of the novel technologies to be used at ITER to tame the hot plasma have been developed and tested at JET (Joint European Torus) currently exploited under EUROFusion; and the EUROfusion programme is focussed in supporting the ITER construction and preparing ITER operation and scientific exploitation. ITER is also having a significant economic impact. It is delivering almost equal returns in increased Gross Value Added (GVA) in the EU economy and has needed the employment of 34 000 job years in the period of 2008-2017[21] and is expected to deliver a gross extra GVA of €12.7 billion and 61 000 job years between 2018 and 2030[22].

[20] https://www.iter.org/proj/inafewlines

[21] http://trinomics.eu/project/iter-impacts/

[22] *Brussels, 7.6.2018 SWD(2018) 325 final.*