Brussels, 30 October 2015

COST 056/15

DECISION

Subject: **Memorandum of Understanding for the implementation of the COST Action "A new Network of European BioImage Analysts to advance life science imaging" (NEUBIAS) CA15124**

The COST Member Countries and/or the COST Cooperating State will find attached the Memorandum of Understanding for the COST Action A new Network of European BioImage Analysts to advance life science imaging approved by the Committee of Senior Officials through written procedure on 30 October 2015.

MEMORANDUM OF UNDERSTANDING

For the implementation of a COST Action designated as

COST Action CA15124
A NEW NETWORK OF EUROPEAN BIOIMAGE ANALYSTS TO ADVANCE LIFE SCIENCE IMAGING (NEUBIAS)

The COST Member Countries and/or the COST Cooperating State, accepting the present Memorandum of Understanding (MoU) wish to undertake joint activities of mutual interest and declare their common intention to participate in the COST Action (the Action), referred to above and described in the Technical Annex of this MoU.

The Action will be carried out in accordance with the set of COST Implementation Rules approved by the Committee of Senior Officials (CSO), or any new document amending or replacing them:

a. "Rules for Participation in and Implementation of COST Activities" (COST 132/14);
b. "COST Action Proposal Submission, Evaluation, Selection and Approval" (COST 133/14);
c. "COST Action Management, Monitoring and Final Assessment" (COST 134/14);
d. "COST International Cooperation and Specific Organisations Participation" (COST 135/14).

The main aim and objective of the Action is to to establish a BioImage-Analysts network to maximise the impact of advances in imaging technology in Life Sciences and to boost bioimaging-based research. "BioImage-Analysts" recently emerged in research institutions to support biologists with image analysis resources, but their own network is missing, thus hindering the exchange of experience, knowledge and techniques.. This will be achieved through the specific objectives detailed in the Technical Annex.

The economic dimension of the activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at EUR 60 million in 2015.

The MoU will enter into force once at least five (5) COST Member Countries and/or COST Cooperating State have accepted it, and the corresponding Management Committee Members have been appointed, as described in the CSO Decision COST 134/14.

The COST Action will start from the date of the first Management Committee meeting and shall be implemented for a period of four (4) years, unless an extension is approved by the CSO following the procedure described in the CSO Decision COST 134/14.

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TECHNICAL ANNEX

OVERVIEW

Summary

This Action is a programme for establishing a network of BioImage Analysts (BIAlysts), in order to maximize the impact of advances in imaging technology on the Life-Sciences (LSc), and to boost the productivity of bioimaging-based research projects in Europe. BIAlysts have recently emerged in various research institutions but these experts are still not well recognised in the LSc community. They are specialised in customising image analysis (IA) workflows by assembling and automating multiple computational tools, and by interacting with Software developers and Life Scientists to facilitate IA. The Action aims to provide a stronger identity to BIAlysts by organising a new type of meeting fostering interactions between all stakeholders including: Life scientists, BIAlysts, microscopists, developers and private sector. It will collaborate with European Imaging research infrastructures to set up best practice guidelines for IA. The Action plans to create an interactive database for BioImage analysis tools and workflows with annotated image sample datasets, to help matching practical needs in biological problems with software solutions. It will also implement a benchmarking platform for these tools. To increase the overall level of IA expertise in the LSc, the Action proposes a novel training programme with three levels of courses, releasing of open textbooks, and offering of a short term scientific missions programme to foster collaborations, IA-technology access, and knowledge transfer for scientists and specialists lacking these means. This Action will support the long-term scientific goals of European science and industry by bridging essential fields of scientific excellence.

Areas of Expertise Relevant for the Action	Keywords
● Biological sciences: Morphology and functional imaging of cells ● Biological sciences: Molecular biology and interactions ● Biological sciences: Cell biology and molecular transport mechanisms ● Electrical engineering, electronic engineering, Information engineering: Computer vision ● Electrical engineering, electronic engineering, Information engineering: Development of scientific computing, data processing, simulation and modelling tools	● BioImage Analysis ● Imaging ● Digital Image Processing ● Advanced Microscopy

Specific Objectives

To achieve the main objective described in this MoU, the following specific objectives shall be accomplished:

Research Coordination

- The establishment of a new network aims to provide a stronger identity for BioImage Analysts to play a well defined role in bridging the gap between Image Analysis technology and Life Sciences
- The network aims to undertake the task of safeguarding image data integrity in Life Sciences
- The network aims to conduct organised efforts to speed-up the process of Image Analysis
- The network aims to improve Image Analysis technology

Capacity Building

- To increase the speed of BioImage Analysis tool development, the Action mediates interdisciplinary communication between stakeholders, facilitates feedback and implementation, and promotes exchange of human resources within the public and private sectors of the network
- To increase the overall level of knowledge in the Life Science community, the Action offers courses ranging from the basics to the state-of-the-art Image Analysis theories and practices, provides access to innovative methods, and publishes open access textbooks for BioImage Analysis
- To boost the number of BioImage Analysts, the Action seeks to firmly establish their roles and positions.

● To augment the efficiency of knowledge transfer, the Action establishes and strengthens the network.

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DESCRIPTION OF THE COST ACTION

1. S&T EXCELLENCE

1.1. Challenge

1.1.1. Description of the Challenge (Main Aim)

The aim of this Action is to maximise the outputs of image-based research in Life Sciences by empowering the international network of image analysis (IA) experts. Imaging has become widely popular in the Life Sciences (LSc) owing to remarkable advances in commercially available digital microscope systems. Indeed, more than 70% of all high-impact bioscience publications rely on advanced microscopy techniques. In this regard, IA provides the key to boosting this innovative technology even further. IA is the final step in imaging-based research workflows and has become the narrowest bottleneck. A pilot survey in 2015 based on 1841 researchers from the European bioimaging community showed that only ca. 42% of captured images are quantitatively analysed, and that 95% of those surveyed considered IA as important-to-essential in their research. The survey also revealed that 68% of respondents considered support and training lacking rather than hardware capacity. Consequently, the huge investments made by research institutes in advanced microscopes, roughly 1-2 billion euros in Europe, are not well balanced by the capacity to analyse the data produced.

Numerous IA tools for conventional imaging techniques are already available through open source and commercial software packages. However, many labs are still struggling to analyse their images. There are several reasons for this: i) Combinations of specimen preparation techniques, microscopy methods, and experiments produce a huge number of possible IA, and off-the-shelf software has limited flexibility to cope with this variety. ii) The number of IA tools is increasing, which ironically further hinders the matching of tools to address specific biological questions. Moreover, an understanding of image processing algorithms is required for the selection and combination of the most appropriate tools. iii) Advances in capacity to capture multi-dimensional image data and the automation of microscope systems have resulted in an increase in the volume of image data in each experiment. Accordingly, the automation of IA has become a prerequisite; however, most life scientists (LSts) are not comfortable with computer programming. Consequently, this community of researchers is faced with the dilemma of access to rich resources for IA while lacking instruction on how to best use them for their specific needs, thus leading to a bottleneck in the imaging pipeline.

To resolve this bottleneck, a new type of expert, hereafter called **"BioImage Analysts" (BIAlysts)**, has recently emerged in various research institutions throughout Europe. These experts are specialised in customising IA **workflows** by assembling and automating multiple computational tools and by interacting with tool developers and LSts to facilitate IA. This new field of expertise is still not well recognised by the LSc community, and BIAlysts are often regarded as part of the software developer community. Consequently, communication among BIAlysts to establish their own network is largely missing, thereby hindering the exchange of experience, knowledge and techniques. The absence of such a network has impeded BIAlysts from reaching beyond their local environment and from pooling their expertise, and has thus resulted in a huge duplication of effort. A network of BIAlysts is required in order to readdress this need. This COST Action seeks to establish a network of BIAlysts, with the aim to maximise the impact of advances in imaging technology in the LSc and to boost the productivity of bioimaging-based research projects in Europe.

1.1.2. Relevance and timeliness

Rapid progress in imaging technology since the beginning of 21st century was achieved by developments in two major sectors, namely the genetic labelling of proteins with fluorescent markers, and advanced light microscopy [5]. Nobel Prizes in Chemistry were awarded for the discovery of fluorescent proteins (e.g. GFP, 2008) and the invention of Super-resolution (2014). Concomitantly, publications using ImageJ, a de facto standard IA software for the LSc, surged from 62 in 2003 to

7550 in 2013. While data resulting from these new imaging techniques provide the key to understanding biological systems, its increasing complexity demands professional digital IA techniques to fully exploit its scientific value. More specifically, these data are multi-dimensional, i.e. 3D space + 1-D time + n-D molecular species. Such complex data exceed the capacity of the human eye and brain to comprehend. Computational visualisation to reduce the complexity of the data and to focus on relevant features is essential. Moreover, digital IA enables precise and automatic measurements of various parameters of biological systems from complex image data, including temporal changes and spatial distributions. These results pave the way to understanding the mechanisms underlying systems, to screen for abnormalities and phenotypes to determine the specific role of genes and proteins, and to model the systems to assess hypotheses. For the large image datasets generated by modern microscopy, computational approaches are often necessary. Thus, computational analysis of BioImage data is crucial for the application of advances in imaging technology to research into biological systems. Furthermore, LSts are not sufficiently trained for bioimage analysis. Such training will eventually be introduced into this community, but meanwhile the needs of the LSc community are now pressing and must be addressed. Strong support to establish a network of BIAlysts is now required to increase the capacity of the LSc community to deal with increasingly complex image data.

1.2. Specific Objectives

1.2.1. Research Coordination Objectives

LSts perceive IA as the most difficult step in a typical bioimaging workflow, but consider it an essential step and therefore strongly demand support. Initiatives to increase access to the expertise of BIAlysts have started only recently, and a more powerful coordination at the European level is urgently needed. This Action leverages current initiatives in order to establish a stronger network of BIAlysts with the following research coordination objectives.

Firstly, the network per se aims to provide BIAlysts with a well-defined role in bridging the gap between IA technology and the LSc. This goal will be reinforced through various types of meetings with explicitly defined interactions between the groups of stakeholders, including developers, LSts, BIAlysts, microscopists, and companies (WG1).

Secondly, the network aims to undertake the task of safeguarding image data integrity in the LSc by collaborating with international and European research infrastructures in microscopy and biological data management, contributing to standardisation efforts, and establishing best practices for IA in biology in order to avoid falsification and ensure the reproducibility of IA in publications (WG3).

Thirdly, the network aims to conduct organised efforts to speed-up IA by: a) creating an interactive database of bio-image analysis (BIAS) tools with an unprecedented level of detail, as well as a collective repository of annotated image datasets for sample use; and b) providing LSts with more direct support for IA and helping them find relevant processing tools that match practical BIAS problems (WG4, WG5).

Fourthly, the network aims to improve IA technology by: a) coordinating the benchmarking of tools (WG5); b) creating synergies with industry and SMEs in image software development through benchmarking tests; c) mediating access to off-the-shelf solutions, as well as pointing out the most challenging biological problems requiring IA innovation (WG3); d) interacting with both LSts and software developer communities to provide workflow examples designed by BIAlysts (WG4); and e) providing a publication channel for application-oriented IA tools (WG6).

These objectives require consensus between all stakeholders, and therefore a critical mass. Intensive discussions and coordination are to be prioritised. The challenge is ambitious and can be achieved only by means of regular meetings, which require sustained financial support.

1.2.2. Capacity-building Objectives

The capacity of IA in the European bioimaging community is determined by the following major parameters:

A) the speed of development of innovative IA tools for LSc research,
B) the overall level of IA knowledge & expertise of LSts and microscopists,
C) the efficiency of knowledge transfer among BIAlysts, and from BIAlysts to LSts and microscopists.
D) the number of BIAlysts, and
E) the number of developers.

The network of BIAlysts aims to boost the first four parameters to enhance the capacity of IA in Europe. Firstly, the network will increase **A)** the speed of BIAS tool development by mediating interdisciplinary communication between stakeholders in order to facilitate feedback and implementation (WG1, WG5), and by promoting exchange of human resources with the business sector (WG7). Secondly, the network will increase **B)** the overall level of knowledge by offering courses ranging from the basics to state-of-the-art IA theories and practices (WG2), providing access to innovative IA methods (WG7), and publishing an open access textbook for BIAS (WG6). Thirdly, the network will boost **D)** the number of BIAlysts by firmly establishing their roles and positions. Fourthly, the network will augment **C)** the efficiency of knowledge transfer (WG1, WG3, WG7).

1.3. Progress beyond the state-of-the-art and Innovation Potential

1.3.1. Description of the state-of-the-art

IA in the LSc has been shown to exceed human ability in some aspects, such as the detection of subtle phenotypes in complex multi-dimensional data. In more detail, IA allows LSts to do the following:

Explore: Reduce the complexity of modern microscopy datasets to facilitate understanding. Some ad-hoc representation can reveal hidden information.
Quantify: Extract quantitative information objectively.
Automate: Automatic analysis is unavoidable with big data derived from high content screening microscopy and recent high resolution imaging. Smaller assays can also be scaled up by means of automation.
Model: Raw data require model-based post-processing in some imaging techniques (*e.g.* super-resolution, tomography) or the extraction of indirect measurements (*e.g.* tension from retraction profiles).

General IA activity in current LSc laboratories does not always embrace all these aspects. The potential of IA is often underestimated, and even when it is fully perceived, most laboratories lack the technical means to perform advanced analysis. This is because IA is generally performed by LSts themselves or by self-taught image analysts running the microscopes of imaging facilities. At best an expert from a nearby imaging facility handles IA, but an individual is often involved in many projects and has to find quick solutions for several researchers at a time. Additionally, many researchers involved in IA acknowledge a partial lack of knowledge regarding:

Methodology: What information can be extracted?
Theoretical information: Am I doing it right?
Existing tools: Is there a way to get there simply?

The information provided in traditional IA textbooks or introductory programming IA courses is often theoretical. There are no, or very few, dedicated IA sessions in generic LSc conferences, and IA is only marginally represented in applied microscopy conferences (e.g. ELMI). These sessions are held mostly in conferences for algorithm developers (e.g. ISBI [9]), but they are very technical.

1.3.2. Progress beyond the state-of-the-art

The dissemination of IA knowledge through this Action will increase access to state-of-the-art IA for the wider LSc community and lead to a significant increase in current average standards, and hence in the quality and speed of findings in fields using high-end imaging.

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Various events organised by the network of BIAlysts will afford forums to discuss and exchange knowledge and techniques for IA applications in the LSc. Among these events, the Action will provide a new training strategy to strengthen knowledge in BIAS. The courses will focus on designing and programming IA workflows that tackle common biological problems. The courses will also provide self-teaching textbooks, a companion website with updates, supplementary information, and forums for interacting with the teachers. In addition, a new repository cataloguing relevant bioimage processing tools and workflows will be set up. Most of the state-of-the-art tools will be benchmarked and directly available for testing through this webtool, together with associated sample data sets. Tags, synonym dictionaries, and ontologies will allow experts and end-users to efficiently search the tools available. The tools will also be linked to technical articles describing them and articles describing examples of their applications. This information will greatly facilitate the use of these tools and encourage more researchers to test them.

Improved dissemination of IA knowledge will clearly stimulate a need for more BIAS tools by raising the overall standards. It is also likely to trigger discussions on the shortcomings of existing tools, new strategies to overcome these limitations, and the need to better integrate IA in research projects. Ultimately, beyond the classical IA framework, improved access to IA knowledge may enable Life Scientists to leverage the potential of computers to decipher the complex mechanisms of life.

1.3.3. Innovation in tackling the challenge

The Action will provide **innovative interactive activities and a new training strategy centred on practical applications**. This training will be innovative, as it will emphasise the difference between general image processing and BIAS. BIAS aims to extract the parameters of biological systems through collaborative work between microscopists, LSts, BIAlysts and software developers, and training on BIAS is largely absent in conventional bioimaging training courses.

In addition, the Action will organise events that bring all these types of expert together. To facilitate the transfer of knowledge, the events will be organised in an innovative style: parallel “showcase”, “webtool and webpage curation” and “course” activities will be undertaken in which the role of speakers, audience, teachers and students will be rotated among all attendee profiles. The Action will focus on solving BIAS problems in day-to-day datasets; however, a distinct field of expertise will be covered in each activity. For example, specific sessions will challenge software developers and BIAlysts with live interactions. This initiative is expected to trigger greater engagement of LSts in BIAS advances. Outside the meetings, this engagement will be encouraged by highly interactive discussion forums and a new publication channel for practical tools.

1.4. Added value of networking

1.4.1. In relation to the Challenge

The collaboration between LSts and software developers is currently sporadic and inefficient. This Action aims to establish a BIAlysts community, which is expected to have a broad impact on IA throughput across Europe by bridging the gap between LSts and developers. The COST framework is particularly suited to this aim because it enables expansion, thus avoiding duplicated efforts, by gathering forces working towards the same goals. Bottom-up by nature, this Action will ensure that countries and research centres that do not have access to integrated infrastructure initiatives because of a lack of resources will enter and benefit from a wider IA community. Unlike the trend in top-down approaches that aim to concentrate investments in centralised hotspots, this Action is designed in such a way to ensure that networking goes beyond political and national barriers. It will leverage existing resources and will not require a new infrastructure, although the networking itself will require limited support. Importantly, the targeted professional group (BIAlysts) is the least organised one in the BioImaging community.

Establishing a network for the BIAS community will bring about immediate results by maximising the use of important existing resources: instruments, software and scientists. National estimates of the current infrastructures **managed by the group of proposers** include 180 million euros of investment in instrumentation over the last 8 years and a pool of ca. 3500 microscopy users. Within

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this group, only 15% currently collaborate closely with analysts to perform IA, and the previous survey shows that over 40% of users in Europe lacked support. Therefore, despite large investments in infrastructure, end-users demand more extensive support from analysts. Networking could immediately address this issue using existing resources. A network would be highly cost-effective, as one can estimate that a yearly networking expenditure equal to ca. 0.1% of the value of the infrastructure could address 40% of its users' demand for IA support.

Networking has the additional advantage that it saves BIAlysts' time. Given that teaching is a part of their duties, the sharing of teaching material would accelerate research by releasing many BIAlysts from individually preparing it and by opening access to new tools and teaching modules for cutting-edge techniques that they are not yet experts in. The web-based material (WG2 & WG6) will be made immediately available to the whole LSc community in a cost-effective manner.

Networking provides a bridge between the LSc community and the software industry. BIAlysts in research centres are in a key position to assess, beta-test, and compare products available and report on their usefulness and efficiency, based on daily end-user feedback. Currently, such feedback is given mostly on an individual basis. The network of BIAlysts will accelerate the development of commercial innovations by disseminating state-of-the-art knowledge and by objective assessment, thereby increasing the potential for timely innovation, competitiveness, and returns to scientists and society. A central role is given to industry in almost all deliverables of the Action, especially by including them as active participants in meetings and webtool content generation.

1.4.2. In relation to existing efforts at European and/or international level

In Europe, LSts, microscopists, and DIP developers are already networking to combine the efforts of their individual communities. However, to date, the interaction between these groups is not well coordinated. Moreover, emerging and advanced IA experts (BIAlysts) are still not organised as a community. Strong support of their networking efforts is needed in order to establish and promote awareness of their profession and to increase the impact of their work on scientific developments. This new community will target a gap in the knowledge transfer between other communities, while being fully complementary to their activities.

The Action intends to **bridge the gap between European microscopists and software developers** by being represented or showcased in their community meetings: e.g. the ELMI meeting, which gathers facilities, instrument providers and scientists; the meetings of BIAS developers such as Bioimage Informatics, Quantitative BioImaging (QBI); and ISBI meetings, which predominantly stem from larger image processing communities (IEEE, or IAPR).

The Action will approach and synchronise with initiatives that have recently shown a strong need to gather analysis software tools and knowledge into web-based repositories and will collaborate to take these tools a step further by making fully interactive repositories which the community can test, benchmark, rate, and add content to (WG4, WG5).

The Action will **network with other parallel initiatives that combine efforts to build bridges between networks**, e.g. to facilitate standards and ontology on Biomedical Data, or to provide the community with a "Next Generation" Image Repository.

Finally, the Action will **actively interact with European initiatives involved in large-scale image acquisition, storage, and analysis** in a variety of fields in which many of the proposers of this Action are involved. These include Euro-Bioimaging, the pan-European Imaging infrastructure project under evaluation by ESFRI. The Action will support these infrastructure-oriented initiatives in order to maximise their impact. Given that COST offers an open, bottom-up and uniform participation framework, a BIAlyst network could be run in an agile manner, free of the complex international and governmental interactions that characterise infrastructure implementation. A new network of BIAlysts will help further attain the long-term scientific goals and achievements of European science and industry by bringing together three essential fields of scientific excellence.

2. IMPACT

2.1. Expected Impact

2.1.1. Short-term and long-term scientific, technological, and/or socioeconomic impacts

Firstly, carefully scheduled training sessions and the publication of open access textbooks will boost the IA knowledge of LSts in Europe. Importantly, both will focus on the applications of IA tools and the **design of practical workflows**. Training that meets the uncovered needs of the LSc community is expected to rapidly increase the efficiency of IA in Europe. The long-term impact will be an overall increase in successful studies using IA, and more scientific publications based on imaging.

Secondly, enhanced communication between software developers and BIAlysts through discussion-based interactions during the annual event will have a positive impact on software development. In the short term, this new communication channel will increase the usability of IA software for LSts and is likely to generate novel ideas for the implementation of image processing algorithms that are better suited to the practical needs of biomedical sciences. The long-term impact will be important advances and a much wider use of high-end IA technology in the LSc community.

Thirdly, the establishment of the community will stabilize the job role of BIAlysts in LSc research and provide a new career model. The short-term impact of the planned outreach activities is expected to attract more young scientists into IA in the LSc. A survey indicates that 40% of biomedical imaging researchers lack support from IA experts—a figure that reflects a huge unsatisfied demand. In the long term, an increase in the number of image analysts will fill this need and boost output in imaging-based research projects.

Finally, this Action will provide the essential BIAS infrastructure for European scientists to carry out cutting-edge research and positively impact societal challenges, especially in health care, such as assisting diagnostics, tailored medicine, and large-scale screening. It will increase Europe's knowledge-based industry and competitiveness and foster the development and leverage of intellectual property.

2.2. Measures to Maximise Impact

2.2.1. Plan for involving the most relevant stakeholders

The Action involves five major types of stakeholder: **life scientists (LSts), BIAlysts, software developers, microscopists, including imaging facility staff and software/microscope companies**. The Action will be organised mainly by **BIAlysts** and **microscopists**. These scientists are at the interface between all players and will directly benefit from the Action to promote IA, to gain access to new tools and publication channels, and to increase their network and knowledge. **LSts** will gain IA knowledge and techniques by participating in the courses offered by image analysts. The "Call for help" sessions will directly address some of their specific needs, and these scientists will also provide feedback on software usability and experiences to developers and BIAlysts. Overall, LSts will be constant references for the direction of this Action. **Software developers** will present their work in showcase meetings and teach in courses. These two occasions will not only be opportunities to directly interact with users, but may also provide the occasion to establish new collaborations. Overall, the Action will allow a better definition of the tools required in practice and an improvement in user experience. **Software companies** will also be invited to present their products in the showcase meetings. These gatherings will allow them to market their products to interdisciplinary audience and also to gather feedback on user experiences. At the same time, showcase meetings will allow them to see state-of-the-art IA in the LSc and to directly exchange valuable information with other developers, e.g. to plan inter-operability and standardisation. In addition, companies will be able to search for potential collaborators and launch testing or open development campaigns to empower their Software Development Kits. Lastly, they will be able to effectively promote their products through the webtool and take part in benchmarking. Overall, the

Action is expected to increase the competitiveness of software companies by bringing them abreast of the latest tool developments and increasing user literacy on the topic.

2.2.2. Dissemination and/or Exploitation Plan

The Action will disseminate **two major types of results**: newly acquired knowledge through activities such as **event reports, custom workflows, sample datasets, textbooks, tool benchmarks and survey results**; and organised knowledge such as **annotations or tags on image processing software and functions**. For the latter, a webtool will be specifically developed and maintained to gather the results. In both cases, Internet-based dissemination will be the major method through which to inform the LSc community, through multiple channels including: the Action's main webpage (where details will be reported), mailing lists, social networks such as Twitter, Linkedin, Github, Facebook, and web-portals managed by various biomedical societies. In addition, the results will be presented in annual Biomedical Imaging and BioInformatics meetings, such as FOM, ELMI, Seeing is Believing, FEBS, EMBO, and ISBI. Course manuals prepared for training sessions will be compiled as an open textbook after revisions based on feedback from students. Free access to the textbook via Internet download will be offered. The textbook is expected to circulate within the wider LSc community and its interactive website and forum will be an additional advertising tool to propagate the results of this Action, which plans to collaborate with an academic publisher to maintain this textbook webpage in a professional way to facilitate access. The results of wide-reaching surveys on the state of IA needs will be published in biology or bioinformatics journals, accompanied by expert analysis. The results of collaborative efforts with related research infrastructure (ELIXIR, EuroBioImaging, BioMedBridges and national microscopy and BIAS networks etc.) will be reported on the main website of the Action.

2.3. Potential for Innovation versus Risk Level

2.3.1. Potential for scientific, technological and/or socioeconomic innovation breakthroughs

The Action has three potential impacts: one for each of its scientific, technological and socioeconomic aspects.

Firstly, (**science**) successful networking between various fields of expertise will not only accelerate imaging-based research in the LSc, but also push a new field forward, namely multi-dimensional biology—a novel approach to study the nature of complex biological systems. Molecular biology is a powerful approach to reduce biological phenomena to simple regulatory pathways; however, it has partially failed in using this knowledge to explain how living systems operate. The power of cutting-edge microscopes to capture multidimensional molecular dynamics, when coupled with progress in IA, will produce critical data to understand the nature of biological systems. This attempt to unravel such systems as a whole might be overly ambitious, but by taking moderately complex subunits and processes, such as organelles or tissue dynamics, there is the potential to provide fruitful scientific outcomes as the primer for multi-dimensional biology.

Secondly (**technology**), one of the focuses of the Action is to describe complex IA protocols as standardised workflows or sequences of elementary image-processing operations with clearly identified input, output and function. The design of new workflows from existing material will be simplified by stressing the relationship of their components rather than their internal technical details. It will for instance be easier to design workflow variants by replacing some components by other compatible ones. This whole process, as well as the selection of parameters, could also be automated by benchmarking many workflow variants. Such automation would greatly simplify and speed up the task of exploring the combinations of components that give the best result. Even if this automation does not prove to be a useful innovation, the modularity of the workflows will contribute to their adaptation to varying biological problems.

Thirdly (**socioeconomic innovations**), LSts in the early 20th century conducted research projects mostly as single individuals. In contrast, ca. 6 authors on average currently collaborate for each project (pubmed). The LSc is now mid-science (compared to big science in physics), requiring many areas of expertise such as bioinformatics, microscopy, biochemistry, genetics and image analysis, to achieve scientific goals. Several technologies are typically used in a single project, and each is technically complex. Consequently, conventional single lab-based LSc projects need to be backed by a network of specialists free to collaborate with multiple projects. The Action pushes this trend forward, focusing on IA, to assert a new style of LSc research by strengthening an inter-disciplinary network. To achieve its aim, this Action must clearly underline the expected benefits and contributions for all the stakeholders involved.

3. IMPLEMENTATION

3.1. Description of the Work Plan

3.1.1. Description of Working Groups – Provide for each WG the Objectives, Tasks, Milestones and Deliverables

The WGs are exposed with the following nomenclature: **WG**: Working Group, **1.O.2**: Objective 2 of WG1, **1.D.2.3**: Deliverable 3 relative to Objective 2 of WG1. See Gantt in 3.1.2 for Milestones.

WG 1 Strategy & Scheduling for Events

The interdisciplinary nature of BIAS implies dealing with a multitude of advanced imaging techniques, large-scale datasets, and an increasing number of analysis tools. This inherently limits knowledge exchange, transfer of techniques and access to tools. To overcome these problems, WG1 will strategically coordinate various network activities, as described in the other WGs, aiming to promote interdisciplinary communication, synergies, knowledge exchange, and access to BIAS tools. The aim of WG1, through the annual Meeting of the Action, is to **act as a driving force for the network by gathering all stakeholders and scientists of the different communities into an innovative event format** (**1.O.1**). Accordingly, the outcome of the different WGs will be collected during the meeting and channelled into the initiatives underway, thereby building the network and setting forthcoming milestones. WG1 will also **ensure that knowledge exchange is promoted** (**1.O.2**) through the Action's events. To this end, WG1 will plan the Annual meeting (1.D1.1) by synchronising scientific sessions, WG meetings, courses, and user sessions. The impact of invitees will be maximised by enabling them to contribute to multiple sessions (e.g. speakers will also teach, teachers will also learn, users will also present). This format will also help keep costs under control. Representation of all stakeholders at the meeting will be decided by Policies (1.D1.2) and supervised by WG1. This task will be complemented by an online activity that WG1 will implement to keep the community active during event preparation: i.e. by running and moderating open online debate (1.D2.1, e.g. Forum, Surveys, screening for new content to be reported; tools, Software, etc.) WG1 will also work with the Management Committee (MC) to select candidates for local organisation of events (1.D1.3) and will write meeting reports.

Finally, WG1 will work on innovative ways (1.D2.2) to involve and connect LSts and software developers. New practical sessions will be arranged, where users and analysts will meet developers (commercial as well as academic). "Calls for Help" sessions will be organised so that users can explain problems they have been unable to solve, and analysts and developers will address them on screen and drive the debate with the audience.

WG 2 Training

Many Early Career Investigators (ECI) and Facility Personnel (FP) are not well prepared to extract quantitative data from images. Few of the higher education programmes in the LSc have included Digital Image Processing (DIP) courses. Biologists lack basic DIP knowledge, while Software developers also often lack domain knowledge (i.e. LSc, microscopy).

WG2 will **promote training for ECIs and FPs in DIP** (**2.O.1**) and **enhance communication of Software developers with BIAlysts** (**2.O.2**) **via training**. WG2 will provide the network with the infrastructure to build a three-level training programme (2.D.2.1):

- ECI Course: Dedicated to data producers (End-users), attendees will learn the basics, gain an overview of existing tools, and learn about the limits and ethics of DIP.
- FP Course: The everyday tasks of FP involve repeating individual complex tasks over several hundred images. This requires automation strategies, involving programming techniques covered by this "Facility Staff Course".
- IA Course: Software developers will upgrade the capacity of BIAlysts to programmatically use their software. They will also get feedback from BIAlysts, which in turn will be used to improve the usability of the packages.

WG2 will identify a team of instructors for each course and, with the help of other WGs, help them collect material, set up the teaching programme, and release course material online (2.D.1.1) in collaboration with WG6. WG2 will collaborate with WG1 to share human resources (teachers) during the Annual meeting, where at least one ECS course and 1 IA course will be given.

WG 3 Outreach and Inreach

The Action needs to reach a critical mass of participants and to ensure the involvement of all stakeholders. One of the objectives of WG3 will be to **build communication tools and initiatives to advertise and disseminate the Network Actions and outputs to the stakeholders (3.O1)**. To this end, WG3 will plan and schedule a communications strategy with the commercial and scientific communities (3.D1.1), including wide-reaching surveys. It will develop e-communication, such as quarterly newsletters (3.D1.2) and the Action website (3.D1.3), which will serve as an entry point to the network. It will also reference all the online deliverables of other WGs. It aims to reach wider microscopy, LSc and bio-image informatics communities by attendance at an identified list of events (3.D1.4). It will also ensure the presence of all stakeholders in the Action by designing dedicated sessions in the annual Meeting together with WG1 (3.D1.5) and promoting bridges with open software in collaboration with WG5 and WG4. WG3 also seeks to **promote collaboration with research infrastructure stakeholders, policy makers and biomedical imaging initiatives (3.O2).** In particular, this aim will involve helping to find sustainable funding for high-potential open source projects or resources lacking outside the framework of scientific publications. It will also promote standardisation and best practice within the BIAS field. WG3 will propose plans for effective collaboration with the other structural "bodies", institutions, and networks involved in Bio-Imaging (3.D2.1), and approach management teams and scientific boards to identify issues and catalyse beneficial collaborations and joint initiatives. In addition to these outreach objectives, WG3 will also be responsible for **creating an inclusive path for newcomers to this Action (3.O3)** by defining a list of minimal activity requirements (3.D.3.1).

WG 4 Webtool

Many tools for BIAS are already available. Information about these tools is non-uniform and often focuses on technicalities about the methods implemented rather than the problems the tools can actually solve. Since BIAlysts focus on applied problems, this information is often inadequate. To overcome this issue, the WG4 webtool (**4.O1**) will deliver **a web-based platform (BioImage Informatics Search Engine - BISE) that matches the problem with the relevant tools**. Learning from the success of community-based projects (e.g. Wikipedia) to achieve this goal, a **crowdsourcing technique fostering exchanges and collaboration** will be applied (**4.O2**).

In its initial phase and after reviewing existing technological solutions (4.D.1.2), WG4 will implement the first version of BISE with a web-based interface (webtool, 4.D.1.1). Once established, BISE will be incrementally updated. WG4 will deliver a proposal of ontology (4.D.1.3) for the organisation of data and implement a search engine (4.D.1.4) for the webtool. BISE provides a unification of views: problem-based (e.g. "find nuclei in cells"), method-based (e.g. "active contour-based segmentation") and tool-based (e.g. "CellProfiler"). Additionally, the webtool will include i) a community-edited rating of tools; ii) discussion forums (4.D.2.1) for both tools and problems; and iii) an interface to WG5-benchmarks' (4.D.1.5). The webpage will gather commented links on articles describing algorithms with high potential but without a usable source code (4.D.2.2). "Calls for implementation" will be launched to plan collaborative implementation through threads in the forum.

The database behind the search engine will be edited in a manner similar to Wikipedia: i.e. the community provides content that is managed by curators. Crowd-sourced database editing will be reinforced by strategic meetings (4.D.2.3) in order to ensure that a defined target number of entries (IA tools) is curated (4.D.2.4). These meetings will be events where bioimage analysts gather to boost the content (software, workflows, etc.). They are also aimed at reaching consensus on future directions and making sure the launch of the webtool (4.D.1.6) will meet the defined schedule. WG4 deliverables will be interconnected with other WGs. BISE will be promoted (WG3) and will aggregate workflow information from other WGs (e.g. WG1). WG4 will use the datasets provided by WG5 when connecting tools to problems. Tools, workflows, and datasets from WG6 will be integrated in BISE to make it an online companion for teaching.

WG 5 Benchmarking and Sample Datasets

WG5 aims to **identify common BIAS problems** (**5.O1**) and benchmark existing solutions. WG5 will create a framework that allows comparison of aspects of existing solutions by **running benchmarks** (**5.O3**) **on datasets** (**5.O2**). To guide the analysts' choice, the solutions referenced in WG4 will be tagged with the benchmark results. Users will be able to use the same framework to run the different IA solutions on a subset of their own image data and to explore the impact of different parameter values. This tool has the potential to boost the development of new and better solutions, and to trigger exchanges between open source and commercial solution providers. It can be used as a reference that helps to reproduce the IA used in scientific publications.

WG5 will define standards for the interoperability of IA software (5.D3.1) in order to be able to run the benchmark tests in different software packages. A standard way to define the expected results of tests (ground truth) must be defined. It will define standards for benchmarking (5.D3.2) of various aspects, such as correctness, robustness, efficiency, flexibility and usability. Another important step is the identification of BIAS problem classes (5.D1) and their association with solutions and compatible annotated images. The results from existing software competitions, for instance those organised within Grand-challenges.org, can be used as input. In order to obtain these results, meetings of the workgroup members will be organised.

A web-based platform that allows the running of benchmark tests and reports the results must be created (5.D3.3), based on existing solutions and similar initiatives. Cloud computing and storage solutions, adapted to issues related to Big Data formats, will be reviewed to implement the benchmarking platform, in collaboration with companies (5.D3.4). This tool will be interfaced with the webtool from WG4, populated with sample data gathered by WG5. The creation, implementation and maintenance of the software infrastructure will be supported during the WG5 meetings in close coordination with WG4. Comparisons of IA solutions will be published as scientific review articles.

WG5 also aims to gather supporting sample datasets. Real data will be sourced from existing sample data collections (5.D2.1), as well as new datasets submitted to open calls for data. Since one of the major applications of this collection will be benchmarking, synthetic datasets (5.D2.2) will be included and new synthetic datasets generated when necessary. Compatible licensing models for data sharing by will be devised (5.D2.3). Annotation of all data will be carried out collaboratively.

The final dataset collection will be made publicly available as part of the benchmarking webtool and as a stand-alone WG5 sample dataset repository. This resource will provide public access to a set of standard, annotated datasets reflecting common BIAS tasks. These will be critical for fair benchmarking of solutions and will produce a number of additional benefits, including use for illustrative purposes: i.e. to support teaching and knowledge dissemination (WG1 and WG6 in particular).

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WG 6 Open Publications

Most biological image processing textbooks focus on the inner workings of image processing algorithms, but the missing key to solve real biological problems is finding ways to combine these into practical **workflows**. WG6 will address this need by **publishing open access BIAS textbooks (6.O1).** They will feature chapters on image-processing basics, followed by more practical chapters on specific biological problems and how to solve them by BIAS techniques. Furthermore, WG6 will plan and integrate **highly interactive, continuously updated website with revision-tracked content (6.O2)** tightly coupled to the textbook. This will be an efficient instrument for collecting feedback, answering questions, and ensuring reproducibility of analysis results by archiving all updated history of texts and scripts. A large part of the content of the open textbooks will be based on teaching materials prepared for practical courses by WG2. WG6 will review workflows, manage cross-references and redundancies, and secure access to the learning material such as sample images (WG5), scripts and required add-ons. Both for the textbook and its website, WG6 will collaborate closely with an academic publisher. The content of the textbook as well as the workflows (WG4) will be indexed in the webtool. WG6 will publish the first Textbook edition by month 18 and add more chapters constantly during the Action period. The Textbook website (6.D2.1) will be launched by month 10, then moderated and constantly updated through m11-48. WG6 will prepare the release of a second Textbook edition by month 40. Lastly, WG6 evaluate the possibility to start up a **new open access journal** to publish practical IA tools for LSc, in tight collaboration with the web-tool (WG4) and sample data repository (WG5). A **report of feasibility (6.O3,** 6.D.3**)**, including possible overlaps with the scope of existing journals and actual deployment plans, will be delivered by month 33.

WG 7 Career Path and Short-Term Scientific Missions

Talented young scientists quickly move to the best international environments for their research. Creating a highly-visible and competitive BIAlyst community that continuously offers and supports the most needed cutting-edge IA tools and highest-quality services to LSts will allow Europe to attract outstanding international talent. WG7 will help BIAlysts gain more recognition and visibility by **fostering the opening of new positions in Europe** (**7.O1**) and by **strengthening relations with industry** (**7.O2**) to promote the transfer of talent and to push innovative developments. WG7 will devise best-practice guidelines (7.D1.1) for the career path of these experts, design surveys (7.D1.2) to scan existing curricula of BIAlysts, define a consensus Curriculum in Advanced BIAS (7.D1.3), and create job offer repository for positions available in the public and private sectors (7.D2.1).

In parallel, WG7 will **coordinate two innovative Short-Term Scientific Missions** (**STSMs**) programmes (**7.O3**) for individual i} Early Career Investigators (ECIs) and ii} experienced BIAlysts to visit a facility, company or laboratory across Europe. STSMs will strategically contribute to the Action’s scientific aim of maximising image-based research outputs by enabling 1) collaborations on innovative IA methods; 2) access to big data analysis technology and IA tools for scientists who do not have access to them locally; and 3) knowledge transfer to support careers and regional development.

STSMs for ECIs will focus on selecting outstanding projects where potential scientific breakthroughs and competitiveness are clearly impaired by the lack of BIAS means, while STSMs for BIAlysts will focus on the transfer of specific technology and skills between facilities and companies/SMEs. A **STSM committee** will be formed to coordinate both programmes, define the selection criteria (7.D3.1), and schedule a proof-of-concept call (7.D3.2, target: 20 STSMs, m12-16) and subsequent 5 STSMs Open Calls (7.D3.3. Total target: 100 STSMs, m24-45).

WG7 actions will help boost the career path of BIAlysts by detecting early career vocation and increasing their skills and know-how. International and multidisciplinary STSM projects will increase the potential for scientific breakthroughs, promote high-impact publications and new research fields, and create interdisciplinary collaborations that may not be considered by local imaging communities due to the current lack of means and know-how. Ultimately, WG7 will benefit the European economy and competitiveness by fostering new job opportunities of strategic benefit to economic growth.

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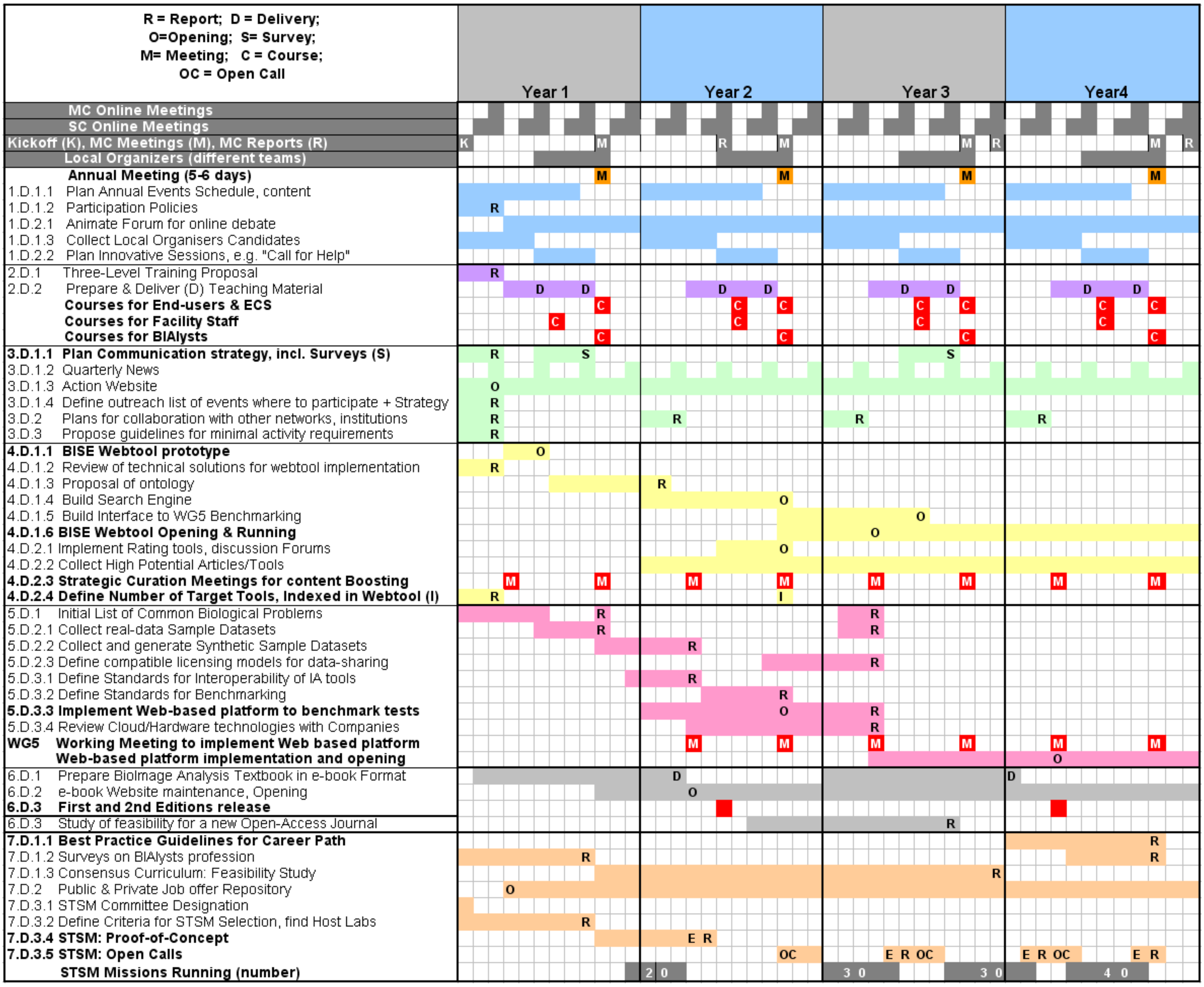
3.1.2. GANTT Diagram

Check Legend (top-Right) for Letters annotating the Milestones across the diagram.



3.1.3. PERT (optional)

The following PERT focuses only on the inter-relation between working groups in a schematic way.

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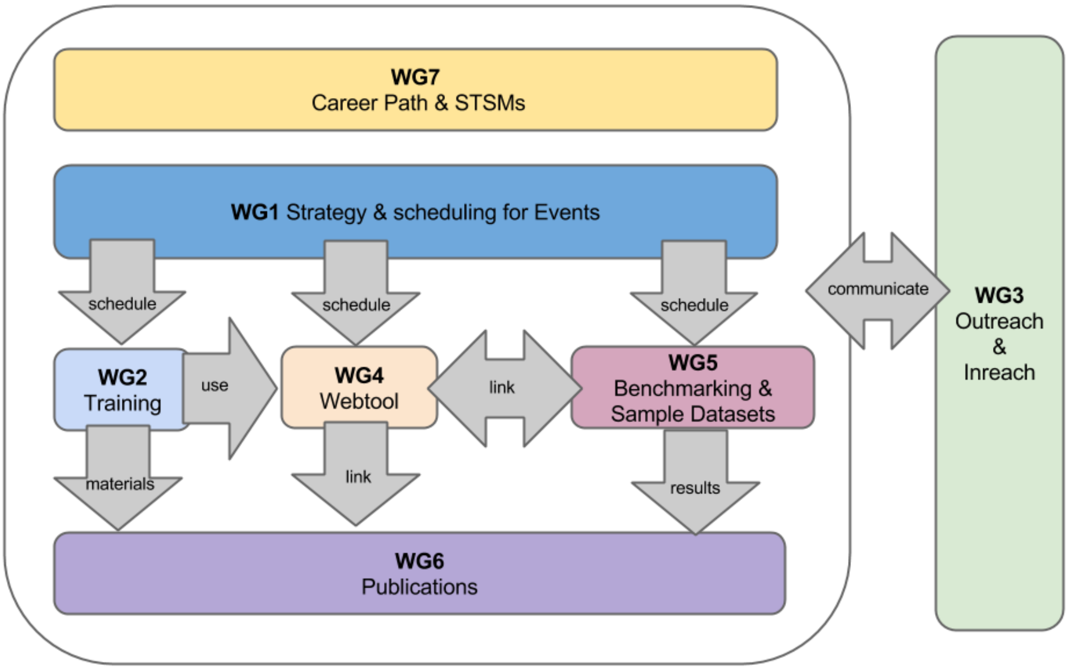

3.1.4. Risk and Contingency Plans

A list of the main identified risks of deliverables/activities, their probability, and contingency plan.

Risk relative to Action	Description	Proba	Contingency
General	Low activity of WGs outside scheduled events.	Med	Foster online tools, assign specific tasks, increase communication with WG chairs, rotate Chairs yearly. Transfer tasks to newcomers as a condition to participate.
General	Management Committee generating high costs due to numerous countries.	High	Limit meetings to one per year during the Annual meeting, complemented by quarterly online meetings.
General	Upon success, the total number of participants would increase continuously, making coordination more difficult.	High	Assign more participants to each task. Simplify decision-making. Push local activity, e.g. teaching.
WG1	Annual meeting too long due to excessive number of events (deliverables).	Med	Optimally design parallel sessions and courses.
WG1	Annual meeting too expensive.	Low	Focus on Academic Venues. Foster multiple roles for attendees: same participant teaches, speaks, learns. Seek minimal fee from participants. Reduce invited speakers. Seek industry and national/local sponsorship

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WG2	Low teacher availability with respect to the high number of courses delivered.	Med-Low	Rotate teachers: they teach only once per year. Train students and newcomers to become new teachers.
WG4	Poor uniformity in tagging and content.	Med-High	Increase the number of parameters, compulsory fields, track contributors by login (membership) to allow for post-editing of their contributions.
WG4+5	Implementation could be difficult technically.	Med (tools exist)	Recruit more people for WG4-5. Find an industry partner to sponsor and power the interface in the first 2-3 months.
WG5	Difficulty in involving industry in benchmarking/data standardisation due to IP and code secrecy.	Med	Offer industry partners the opportunity to build their own benchmarking modules following WG5 instructions and to participate in the standardisation process
WG6	The textbook website may experience low activity on the part of readers.	Low	Increase efforts to recommend the use of website in courses (WG2). Insist students & teachers conduct Q&A on the website.
WG7	Funds insufficient to achieve the target number of STSMs.	Med-High	Reduce the individual grant maximum allowance to prioritise the final number of STSMs. Look for complementary sponsors after proof-of-concept validation.
WG7	Access to instruments could be required during the STSMs in order to collect complementary data.	Med	Evaluate the risk before the project is accepted and deal with Facilities to ease access under special conditions (best: in-kind; expected: fee-based for the STSM visitor's lab with "internal" rates)

3.2. Management structures and procedures

The Action will be structured consistently with the description of the Working groups, i.e. centred on their activities.

The success of the Action greatly hinges on ensuring that all researchers and industry members can participate; however, due to many countries involved and the expected interest across Europe, the network could reach over a hundred participants in its first year in close to twenty countries. The MC will inevitably grow and need the support of a reduced group of core proposers, a Steering Committee (SC), in charge of preparing strategic suggestions for the MC to take decisions.

The workloads required to develop WG deliverables will be unequal and variable during the Action's calendar, as will the financial contribution to support their working meetings. Supervision of the activity of this large community of participants will also be a challenge for the MC. The mission of the SC, reporting continuously to the MC, will therefore be to analyse the progress of WGs in order to suggest the financial support of the Action to the specific WG missions according to the Action schedule (Preparatory phase vs. Running phase), and to supervise the activity of all members. For this latter task, a membership supervision tool will be created with the aim of setting up "participation guidelines" with minimum expected contribution level from all members to WG activities. This will also collect indicators, either through the WGs Chairs, or automatically, to ensure minimum activity in training (in the Action courses or locally in their institution/university), minimum contribution to outreach (e.g. advertising, collecting feedback and reporting to WG3), minimum contribution to WG4/5 web-based tools (e.g. filling content in the Webtool repository, providing rating on their tools), etc. For the geographic distribution of the Action's activities, the SC, WG3, and WG1 will screen and collect potential candidates for local organisers (for the Annual meeting and courses) and will report to the MC, which will coordinate the strategic deployment of the Action. An additional Committee, as described in WG7, will be nominated by the MC to coordinate the selection of STSM candidates and the operation of STSM programmes. This committee should include at least one member from the MC and SC.

The MC will meet yearly during the Annual meeting, and should as well organize online meetings every 3 months, together with the SC and WG Chairs or Vice-Chairs. The SC will work more closely with the WGs, every 1-2 months. All WGs will have the chance to organise WG meetings during the Annual meeting, while specific WGs, e.g. WG4 and 5, will be supported to meet more often to help with the more concrete tasks of web-based tool construction. Finally, one of the tasks of the MC, supported by regular WG reports, will be to screen for Intellectual Property rights and to ensure that licence policies are well defined in each WG. A 'state of IP' will be established at the beginning of the network. Open Source will be promoted but copyright correctness of all the Action's input will be monitored by WG Chairs (the MC will act as referee if needed).

3.3. Network as a whole

The starting group of proposers is composed of 44% Image analysts, 30% Microscopy Facility Staff, 17% Computer- and Life-Science investigators, and 9% companies. Overall, they form a group of relatively young, confirmed scientists with multi-disciplinary backgrounds (biologists, physicists, computer scientists, mathematicians) who have developed careers in Life Science Research Institutes (>85%). This will be central to address the challenge of the Action in that it will ensure the experience and scientific vision required to channel the efforts of the BIAS community towards scientific production in the LSc. The technical skills of this ensemble of professionals will allow them to achieve the Action's most challenging and technical objectives, e.g. the development of web-based tools and databases.

Over 65% of the proposers are involved in the activity or creation of their national Imaging Networks (Light Microscopy), and many of them in one or more of the aforementioned international initiatives (section 1.4.2). This broad presence will ensure proper exchange and synergy with the research BioImage infrastructure across Europe, which handles the production of most BioImage datasets, and will enable them to keep abreast of technological developments and scientific challenges in the LSc.

Over 80% of the proposers are involved in national and international courses, training sessions and workshops in BioImaging and analysis within the duties of their current positions. Such activities ensure the basis for the development of the Training programme of this Action (WG2).

Up to 40% of the surveyed LSts lack support in IA, but do have support to acquire Image data, in general. To change these figures, the strategy of the network will therefore be to stem from infrastructure Networks (e.g. Light Microscopy) with whom synergy is already ongoing in order to reach Life Scientists, the end-users.

Geographically, the Action has no specific limit as it aims to support all research institutes provided with imaging equipment. However, among the activities to be developed, WG7 STSM programmes will be able to orient the Action strategically to canvass countries with less organised imaging networks for talented scientists.

Collaborative efforts with the USA are an important aspect of this Action because many of the Open Software and tools currently available have been successfully developed there with extensive funding support (e.g. by NIH: ImageJ, MicroManager, CellProfiler) and because labs of reference in the USA are often the destination of choice for talented European scientists seeking a future in BIAS. Coordinating with the USA will therefore enable mutual knowledge exchange and avoid duplication in technology development, as well as improve the return of talented young scientists, engineers and leaders to Europe.

Last but not least, the competitiveness of existing commercial or new start-up companies will be boosted by joint methodology developments with this Action and its European partners (more representative of the market than individual labs), which may result in new inventions and improved access to the latest innovative imaging platforms.

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