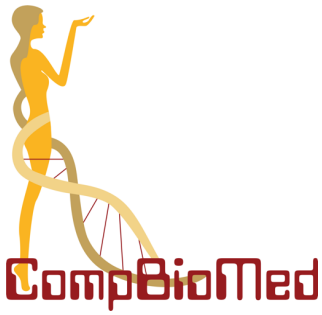

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D4.4 Final Report on Industrial and cPPP Collaboration

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Disclaimer

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1 Version Log

Version	Date	Released by	Nature of Change
V1.0	04/04/2019	Gavin J. Pringle	First Draft
V1.2	08/05/2019	Gavin J. Pringle	Update post internal review
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3 Acronyms and Definitions

Acronyms	Definitions
BAC	Binding Affinity Calculator
BoF	Birds of a Feather
BRD4	Bromodomain-containing protein 4
BSC	Barcelona Supercomputing Center
BTK	Bruton's tyrosine kinase
CADD	Computer-aided drug design
CFD	Computational Fluid Dynamics
CoE	Centre of Excellence
cPPP	contractual Public-Private Partnerships
EC	European Commission
EGFR	Epidermal Growth Factor Receptor
EMA	European Medical Association
ESMACS	European Society of Movement Analysis for Adults and Children
ETP4HPC	European Technology Platform for High Performance Computing
EuroHPC JU	European High-Performance Computing Joint Undertaking
FDA	Food and Drug Administration
FEP	Free Energy Perturbation
FMO-DFTB	Fragment Molecular Orbit – Density Functional Tight-Binding
FSI	Fluid-Structure Interaction
GDPR	General Data Protection Regulation
GPCR	G-protein coupled receptor
GROMACS	GROningen MAchine for Chemical Simulations
GSK	Glaxo Smith-Kleine
HGMP	Hierarchical GPCR modelling protocol
HPC	High Performance Computing
HPDA	High Performance Data Analytics
IAB	Innovation Advisory Board
IEP	Innovation Exchange Programme
IP	Intellectual Property
ISBA	In Silico Binding Assay
ISC	International Supercomputing Conference
ISUM	International Supercomputing Conference in Mexico
KPI	Key Performance Indicator
LDHA	Lactate dehydrogenase A
LES	Large Eddy Simulation
LTG	LifeTec Group
LUMC	Leiden University Medical Center
MD	Molecular Dynamics
MMPBSA	Molecular Mechanics Poisson–Boltzmann Surface Area method
MoU	Memorandum of Understanding
MRI	Magnetic Resonance Imaging
OLVG	Onze Lieve Vrouwe Gasthuis

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PaaS	Platform as a Service
PDE2	Phosphodiesterase 2
PLC	Public Limited Company
RANS	Reynolds-averaged Navier–Stokes
SME	Small and Medium Enterprise
STFC	Scientific and Technology Facilities Council
TAVI	Transcatheter Aortic Valve Placement
TIES	Thermodynamic Integration with Enhanced Sampling
UCL	University College London
UNIGE	University of Geneva
UPF	Universitat Pompeu Fabra
USFD	University of Sheffield
UvA	University of Amsterdam
VM	Virtual Machine
WP	Work Package

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4 Executive Summary

Our CompBioMed Centre of Excellence has around 30% of our Core Partners from Industry, and around 30% of our current 40 Associate Partners are also from Industry, and this report discusses our joint collaborations to further innovation in the field of personalised medicine. This report contains detailed discussion on the Core Partners' collaborative efforts within the Centre as a whole. Further, significant progress has been made in bringing in new Associate Partners; we currently have 40, with more expected over the coming months. Many new collaborations have been created between Core Partners, and between Core and Associate Partners, since the start of our CoE. We have established, revised and improved our Centre's 'incubation' activities, in collaboration with SMEs and other industrial stakeholders, to ensure our results are nurtured on the road to the marketplace. Our Centre has created strong links to the ETP4HPC Association, as part of the HPC cPPP, which established a mechanism for the HPC industry to interact with the computational biomedicine community, whether in academia, hospitals or SMEs. Our Innovation Exchange Programme has been created and is actively seeking to bring together individuals with visits to industrial companies to and from academic centres, with 37 visits to date. Finally, our Innovation Advisory Board contains 19 members from both hospitals and industry, particularly SMEs, predominantly from outwith CompBioMed.

5 Introduction

The importance of industrial collaboration to CompBioMed cannot be understated, given it is one of the key elements of success for our Centre of Excellence. We have closely collaborated with industry to create and implement a strong sense of innovation, thereby enabling the Centre to sustain itself well into the future. We have begun to provide a centre of information, a hub of ideas and a place where medical professionals can access both HPC computing resources and advice from HPC experts. To this end, CompBioMed works closely with its many and various industrial stakeholders, our current principal stakeholders being our Core or our Associate Partners.

In this report we describe not only this engagement with our principle stakeholder but also discuss our progress in developing our engagement with the wider community, via our work with the cPPP on High Performance Computing and the ETP4HPC Association, our Innovation Exchange Programme, and our Innovation Advisory Board.

This deliverable updates and therefore supersedes D4.2 *Interim Report on Industrial an cPPP Collaboration* [1].

Our Core Partners are funded by our Centre of Excellence and are the legal entities that sign the Grant Agreement and have the responsibility for the implementation of the action. They contribute directly to the execution of the research, transfer of knowledge and training activities by supervising, hosting, training and/or seconding staff members. The 30% of Core Partners from Industry are listed in detail below, where we describe the Partner, the official role in the project, and summarise their activities to date.

Of our 40 Associate Partners that have joined our Centre of Excellence, 30% are also from Industry. The benefits of being an Associate Partner are described in Section 0. Associate Partners are partners who have agreed to co-align themselves with CompBioMed and are listed at the following webpage: www.compbiomed.eu/associate-partners. Significant progress

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has been made, in this regard, as we have gathered many new Associate Partners throughout the CompBioMed project and expect the number to continue to increase substantially.

Many new collaborations have been created between Core Partner SMEs and between Core and Associate Partner SMEs, where companies have worked with CompBioMed, sought advice, provided data, use cases and end users, exploited CompBioMed resources, and/or attended our Workshops.

To bring in external industrial partners, we actively maintain tasks to promote, attract and involve them through the following activities.

We aim to coordinate the Centre's 'incubation' activities with SMEs and other industrial stakeholders, wherein we monitor novel ideas via our IP Register, determine suitable candidates for entry into the Innovation Management Process, then where appropriate, nurture them on the road to the marketplace. At the time of writing, our Incubator Service for Core Partners is maturing, and its final instantiation will be, in part, informed from the creation of our start-up ELEM Biotech and our spin-out EnsembleMD (see below).

The contractual Public Private Partnership on High Performance Computing (HPC cPPP) is part of the European HPC strategy which aims at optimising the national and European investments and addressing the entire HPC ecosystem. This strategy is based on three pillars defined as (a) developing the next generation of HPC technologies, applications and systems towards the exascale, (b) providing access to the best supercomputing facilities and services for both industry including SMEs and academia and (c) achieving excellence in HPC application delivery and use. The HPC cPPP entered into force in January 2014 to develop an ambitious research and innovation strategy for technologies usage and applications (pillars a & c) of the European HPC strategy along with training, education and skills development. The private partner in the cPPP is the industry association European Technology Platform for High Performance Computing (ETP4HPC).

The HPC cPPP brings together both the technology providers and the end users via the ETP4HPC Association and the Centres of Excellence. CompBioMed, as one of the Centres of Excellence, has created links to the ETP4HPC to establish a forum and mechanism for the HPC industry to interact with the computational biomedicine community, whether in academia, hospitals or SMEs. This is described in more detail below.

Our Innovation Exchange Programme, or IEP, actively seeks to bring together individuals with visits to industrial companies to and from academic centres. This is also presented in greater detail in Section 9.1.

The Innovation Advisory Board, or IAB, contains members from industry, particularly SMEs, which are not only from Core and Associate Partners, but also, and more importantly, from outwith CompBioMed altogether. This ensures a constant interrogation, discussion and flow of ideas into our Centre to help us learn, develop and remain at the forefront of our field.

CompBioMed online presence is guaranteed principally via a unique website created for the project by CBK (see section 6.1.1). The website has both external and internal access facilities and functions that facilitate the storage of key documents and dynamic interchange of project information to partners and to the public. All configurable documents are stored in their latest form in an "intranet" section of the website with viewing access enabled for the core partners.

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There is progressively less restricted access to facilitate the engagement of wider stakeholders in science and medicine, through to direct engagement with the public via news, events (& booking) and a knowledgebase. The project website was set up before the project started with the website release deliverable (D3.1) submitted at M3 detailing the public release of the website. The functionality of the website is regularly reviewed and developed as its use increases and the project output information builds. Specifically, the Software Hub is maintained within WP5, with applications from the Associate Partners being added as required and those from Core Partners being updated and maintained. The Training Repository holds a searchable list of training offered by various Core Partners and relevant to the CompBioMed community. In addition to this, on the main training page links to all our past training events and webinars are maintained with YouTube videos embedded or linked on the pages. The YouTube channel is updated regularly with videos from new training and workshop events that have taken place. The success of this shows in the regular increase of subscribers to the channel (now over 150).

A WP4 teleconference is held at least once per month, wherein the current and future industrial collaborations are discussed. The majority of Core Partners are represented, and actively engages with all aspects of the meetings, including the Innovation Panel wherein all novel news of the last month is discussed, ranging from any new IP to be recorded, to journal/conference articles to items reported in the Press. This ensures a nurturing sense of innovation is maintained and since March 2018 these Innovation Panels occur at all work package meetings.

Lastly, many industrial bodies also interact with CompBioMed via

- engagement with Core or Associate Partners,
- through companies employing CompBioMed HPC resources,
- companies participating in CompBioMed workshops,
- a company guest presenter at seminars/meetings.

The remainder of this Report describes each of our industrial Core Partners and the status of their involvement. It then describes the Associate Partners, our work with ETP4HPC, and the progress made by our IEP. Finally, we describe some ongoing efforts to improve industrial engagement, monitoring and suggests future improvements currently under consideration.

6 CompBioMed Industrial Partners

6.1 Core Partners

This section lists the Industrial CompBioMed Core Partners, first providing an overview of each company, second describing their role in the project and, thirdly, presenting their progress to date.

6.1.1 CBK Sci Con Limited

CBK's key contributions to the project include support for project management, where CBK works as an integral part of the project management team at UCL providing complementary experience from commercial industry perspectives alongside UCL's research management expertise. CBK is the lead partner co-ordinating the project's quality assurance planning, data management planning and the final public reporting. The project quality assurance system and its procedures were developed with all core partners under CBK's lead during the first 6

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months of the project, as was the project's approach to data management. Both areas were formally reported at this time.

As a partner in the team supporting the management of dissemination activities, CBK has developed the CompBioMed online presence, has a substantial presence in the overall dissemination and closely related training team. The company led the Centre in the development of the plan for dissemination, the public plan being published at the 3-month point. Subsequently CBK has led and continues to lead the co-ordination of the dissemination activities and produces all materials necessary in support of these activities. Public reports on all training and dissemination activities have been produced in September 2017 and in March 2018. This has resulted in substantial success in promulgating the results and knowhow to a wider scientific and public community. Where seen to be beneficial, CBK has co-ordinated the application of additional effort to achieve a significant boost to the dissemination of project information. A key example of this is the development of a film showing the state of the art of HPC use in biomedicine, [2], that formed the basis of an IMAX cinema showing to the public at the Science Museum in London in 2017, [3, 4]. This film and the material captured in recording the event has been further developed for wider distribution at science-orientated public events. In June 2018 the film was shown at the Cheltenham Science Festival and again a panel session was held with the public audience of over 200 people. The project training plan was developed early in the project and CBK is one of the core partners involved in the coordination of training activities, including help with workshop materials, facilities and organising events.

The management of innovation, led by the University of Edinburgh, includes CBK as a partner on the innovation management team and CBK also provides one of its directors to sit on the Innovation Advisory Board. CBK led the development of the plan for managing the processes within the project aimed at supporting the scientific research teams to best exploit the project results for maximum impact. The formal plan was issued 6 months into the project and encompasses the project's approach to identifying new knowhow and tools and then providing support in assessing their exploitation potential, whether this be academic, societal or commercial potential. To date this support has taken the form of advice for specific exploitation routes, enhanced dissemination to appropriate stakeholder groups, commercial advice for software commercialisation and early help in assessing how knowhow may be bundled to support provision of consultancy services. In addition, a specific new training module which serves to educate medical students in the use of HPC simulation is currently being assessed for its commercial potential. The project has a task which focuses on incubator coordination, namely T4.2 Incubator Coordination, which is led by SURFsara. Bringing its experience of university incubation and acceleration, CBK contributed to the development of the approach which aims to facilitate collaborations between research partners and commercialisation parties for results which have a high commercial growth potential.

6.1.2 LifeTec Group

LifeTec Group (LTG) has played a substantial role in our Innovation and Sustainability work package, particularly task T4.5 Pre-commercial Activities. The main tasks of LTG in this project are the development and application of cardiovascular *in silico* models and tools and to combine them with the models of other participants, to create workflows, pipelines and interfaces.

LTG is involved in business development for the CoE by working on the Innovation Plan, which established mechanisms to actively promote *in silico* methods to, for example, the

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cardiovascular devices and pharmaceutical industry. The Innovation Plan is a live document which is maintained throughout the lifetime of our Centre.

To date, LTG has developed a tool to provide clinical decision support as a Software as a Service. More specifically, discussions with clinicians have identified a challenge in the decision-making process to treat difficult coronary stenosis either by bypass surgery or by placing a stent. The simulation tool can predict the outcome of both interventions as well as present the accuracy of said prediction, which would be very helpful in the decision-making process and would reduce the cost of treating complications. The idea is that relatively (computationally) cheap 1D models with input from patient specific data will provide quick results of both interventional strategies, and that running many cases in parallel allows for a population of results that not only provides a result but also an assessment of the expected accuracy of the result. In the development of the tool, sensitivity analyses are performed in SURFsara facilities, and containers are in development that will facilitate the running of simulations without having to support local software installations in the SURFsara computing centres. Currently, the tool is being used as a local software in clinical practise on clinical data to obtain feedback on the accuracy of the predicted outcome.

The 1D models can also be used as a tool to provide inlet or outlet boundary conditions for more complex 3D cardiovascular models, such as to incorporate such 3D local simulations into a larger vascular computational environment. Coupling between 0D and 1D simulations and 3D CFD simulations have been achieved with ANSYS software, as well as FlowVision: CFD software developed in the collaboration of Capvidia (Belgium) and TESIS (Russia). The verification of 0D/1D model results with 3D CFD simulations will be performed on SURFsara infrastructure, where possible, using containers.

6.1.3 Acellera

Acellera is playing a substantial role in three work packages, namely Biomedical Research Activities (WP2), Innovation and Sustainability (WP4), and Empowering Biomedical Applications (WP6). Acellera provide technology and knowhow for large-scale molecular simulations and analysis. They participate in the following research activities within the Molecular-based Medicine theme: Molecular simulation of the transport properties and mechanism of gating, to decipher the key factors controlling selectivity; Fragment-based drug design for GPCR targets; rational antibody design for EGFR inhibitors.

Since the beginning of the project, Acellera participated in the dissemination of the project news and promoted the use of *in silico* methods in Industry and non-profit entities by participating and organising events, but especially by its effective marketing activity. This activity is illustrated by the organisation of workshops (10-11 Nov 2016, Barcelona, available at www.youtube.com/playlist?list=PLDYs662FgoLO-wPIerFTidunlj8uUIzZO; 24th October 2017, Slough; 10-11 May 2018, Cambridge), its participation in the winter schools (14-16 February 2018 and 13-15 February 2019, Barcelona in collaboration with partner BSC), and the organisation of webinars exclusively for CompBioMed partners, namely "Cloud based MD simulations with AceCloud", 21-22 February 2018, and "PlayMolecule - on demand discovery platform", 21 March 2018, “HTMD” 23 March 2018) for CompBioMed partners, as well as webinars tailored for our customers.

Strong in its expertise in biomolecular interactions, Acellera developed innovative methods to predict small molecule interaction with protein target, especially with GPCRs, in [5].

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Acellera's ISBA protocol, where ISBA stands for *In Silico* Binding Assay, has been optimized and is ready to initiate collaboration among CompBioMed partners. Moreover, they provide free access through its platform PlayMolecule.org to promote the use of *in silico* methods for drug discovery and molecular medicine projects. Contacts have been initiated with Evotec, Janssen and UPF as well as Microsoft Azure to discuss collaboration on the use of the computational methods.

Besides molecular dynamics simulations, Acellera embraced the use of machine learning applied to drug discovery and design. Started in 2016, the platform was released about a year after and shared with the scientific community for training and teaching purposes.

After two years of development, it covers early aspects of drug discovery such as structural studies (unlocking target behaviour knowledge) now being expanded to late aspects such as repurposing and free energy of lead binding. In order to validate the algorithms and protocols, Acellera has been able to collaborate closely within CompBioMed partner Janssen (JAN) and Universitat Pompeu Fabra (UPF). The development of the algorithms and protocols was initiated with UPF, taking advantage of their substantial expertise and efficient methodology in algorithm generation in the field. Since experimental validation for virtual methods is a critical requirement, JAN was an important partner within CompBioMed since they could provide their expertise and useful collaboration to validate the new algorithm. JAN is ideally positioned to validate the performance and value of the free energy of binding calculations as they have multiple internal projects (historical and active) in which the methods can be applied. The results of these validations are not yet public.

Another important aspect to CompBioMed is the scaling of simulations. Scaling allows complex and large system to be dealt with but also, provides access to a larger panel of users. As an SME, Acellera faced similar challenges to answer its internal R&D needs as well as to answer customers' requests. Acellera has benefited from allocated simulations time on the Archer supercomputer (www.archer.ac.uk). These simulation runs helped to develop and validate data for one of the applications available (Parameterize) on PlayMolecule. Note that PlayMolecule has been developed through a collaboration established as part of CompBioMed between UPF and Acellera

The arrival of new associate partners to CompBioMed offered a major opportunity to develop new relationships and approach other industries, potential stakeholders of Acellera. For example, a first contact has been established with Microsoft Azure to deploy and test PlayMolecule as a PaaS (Platform as a Service). The purpose and first advantage of offering a PaaS is to democratise the use of the platform. Since PaaS are deployed on cloud or on distributed resources, they also help users to control their budget. Acellera provides already its platform on distributed resources and continues exploring the possibility to deploy it on the cloud (e.g. Azure).

Finally, Acellera has produced a number of related publications since the start of our Centre [6, 7, 8, 9, 10]. All the publications reported here illustrate collaborations between Acellera, UPF and other entities (Pfizer, Novartis). While the first publications reported clear applications of the protocols designed for ligand binding studies, especially for GPCRs, the more recent ones witness how fruitful the collaboration was between Acellera and UPF during the transition to development of the platform, PlayMolecule.

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Others related articles are [11, 12, 13], which were produced before the start of CompBioMed, but are useful to understand the strategy chosen and the experience of the group.

6.1.4 Evotec (UK) Ltd

Evotec (UK) Ltd, as a leading industrial application partner, is responsible for four key objectives: adaptation of hierarchical GPCR modelling protocol (HGMP) to HPC platform, developing of the new HGMP-HPC based tools / plugins that require high scale calculations, testing and application of HGMP-HPC integrated technology in real drug discovery cases within the CoE and to make it available to third parties seeking assistance from the CoE and/or from Evotec, and dissemination of the results of this work to our partners in academia and in pharma & biotech companies in order to stimulate follow-on research. Evotec has also published the outcome of this work in peer-reviewed journals and at scientific conferences [14, 15, 16].

Evotec (UK) Ltd has established a close collaboration with UCL (group of Prof Andrea Townsend-Nicholson). In the framework of this collaboration, they developed computational methodology to rationalize the receptor-ligand binding and drug-candidates' residence time [17]. This methodology is based on integration between HGMP (Hierarchical GPCR modelling protocol) and FMO-DFTB (novel and rapid quantum mechanical method [16, 18]). The method was tested by Evotec (UK) Ltd and feedback provided (this is ongoing). Evotec will perform the testing and validation of the protocol in its real drug discovery projects [19].

Dissemination and training: Evotec has given keynote presentations at numerous high-profile international conferences: ACS Annual Conference Boston 2018, CBI Annual Meeting Tokyo 2018, RICT 2018 Strasburg (plenary speaker), ACS Annual Conference in Washington (August 2017) and 6th World Congress on Medicinal Chemistry in Milan (June 2017)

Evotec (Alex Heifetz) provided a training session in the CompBioMed & BioExcel Free-Energy Workshop, London, 31 May 2017; and at the CompBioMed winter school in Barcelona in February 2018 and in February 2019 on the subject of 'Introduction to Computer-Aided Drug Design (CADD) and GPCR Modelling' illustrated by examples from real drug discovery projects. Videos of both these sessions are available via the CompBioMed YouTube channel.

Publications: The translation of knowledge was performed by the following four publications, including a book 'Computational Methods for GPCR Drug Discovery' recently (2018) published by Springer [20].

6.1.5 Bull/Atos

Bull/Atos has been deeply involved in the Innovation and Sustainability work package coordinating the collaboration between CompBioMed and the cPPP on High Performance Computing, via the ETP4HPC. They have been active in the partnership and we have established connections with four individuals: Marcin Ostasz (BSC) business analyst, Hugo Falter (ParTec) secretary-administrator, Jean-Pierre Panziera (Atos) chairman, and Pascale Bernier-Bruna (Atos) communication leader. On top of regular exchanges with them, Hugo Falter made a presentation at our Kick-Off meeting in October 2016. Marcin Ostasz participated as a guest speaker at the CompBioMed Birds of a Feather (BoF) at ISC 2018 and will be part of the CompBioMed BoF at ISC 2019. Pascale Bernier-Bruna has helped disseminating information though ETP4HPC mailing list as well as social and professional

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media. Further, Bull/Atos is actively seeking to establish collaboration with at least two more ETP4HPC centres.

CompBioMed and ETP4HPC co-hosted a BoF at ISC18. Marcin Ostasz represented ETP4HPC there. CompBioMed and ETP4HPC plan to reiterate this event at ISC19. This work is described in more details below. The collaboration is also visible by the presence of one CompBioMed individual to all the cPPP Board Meetings since the beginning of the project. In collaboration with the other CoEs and via ETP4HPC, CompBioMed has provided comment and input to the text of the EC's 2018-20 calls during their development. Further, ETP4HPC is advertising CompBioMed events via their website. CompBioMed is featured in ETP4HPC 2018 Handbook of European HPC. Bull/Atos is seeking collaboration with other Industrial Partners out with ETP4HPC.

Lastly, Bull/Atos was heavily involved in Task 2.6 Upscaling of CompBioMed Production Applications for Future HPC Platforms (WP2) and continues to be heavily involved in Innovation and Sustainability (WP4). Bull/Atos intends to provide access to an "on-demand" HPC production infrastructure with dedicated portal and provide expertise. They contribute to best practice recommendations for efficient resource usage and solution upscaling toward the exascale.

6.1.6 Janssen Pharmaceutica NV

Janssen's interests are in developing and using advanced molecular simulation methods to optimize lead compounds in discovery programs. Such methods, if proven robust and accurate could have a profound impact on the way drug discovery is performed. They would permit reliable computational triaging of very close analogue molecules greatly improving efficiency. Also, this would lead to high-confidence design of synthetically more challenging molecules leading to better drugs in new chemical space. Also, we envisage the accurate prediction of compound binding for targets that have mutated residues. This latter application can be of value in diagnostics, by predicting the best possible compound for a patient clinically (personalised medicine), but is also of use in discovery, where mutated targets occur regularly in antibacterials, antivirals, and oncology compounds.

Janssen has been actively collaborating with UCL on calculation of free energies of binding on public and on Janssen internal compound sets (targets BRD4, LDHA and PDE2). A manuscript has been co-written and just accepted for publication on the BRD4 application. A second manuscript is under preparation describing the LDHA application. Both cases have led to learnings about the suitable application of MMPBSA, so called ESMACS approach, for the calculation of binding free energies. A third large and extensive study has been mostly completed and in the early stages of write up for publication. This study has involved the use of alchemical perturbation methods, the TIES approach was performed at the UCL group, and the FEP+ approach at Janssen. Results have been performed for multiple perturbations from various different protein targets. A particular focus has been to investigate the precision of both methods when submitted to extensive repeated trial calculations. The TIES work has also required new replica exchange methodology recently implemented for TIES in the Coveney group [21, 22, 23].

Within Janssen, they evaluated the use of GROMACS for Free Energy Perturbation. They streamlined the application of FEP with GROMACS with the help of HPC experts at SURFsara and ran calculations on the Cartesius system also at SURFsara. Calculations were performed and compared with Schrodinger's FEP+ software. We studied multiple datasets, generating lots

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of valuable insights on the strengths and limitations of GROMACS FEP. Parts of this work were included in our recent publication [24].

Janssen completed a study demonstrating the use of MD for understanding functional activity of allosteric modulators. This work is published online. It is part of their initiative to understand the value of MD simulations in computational drug discovery and was performed by their CompBioMed-funded postdoc at Janssen [25].

In addition, during the project Janssen has been a partner in two successful bids for HPC resources led by UCL: 32M core hours on SuperMUC in 2017-19, and on DoE Titan in an INCITE award worth around 100Mcore hours between 2018-2019. These grants will be used for work on binding affinity prediction. CompBioMed has advanced our understanding of the capabilities and limitations of binding affinity calculations, has enabled us to use new methods to do them, and allowed us to run them efficiently on at HPC centers. Without CompBioMed we would not have been able to do this.

6.2 Associate Partners

As noted earlier, CompBioMed has been very successful in attracting new collaborators, as represented by the current 40 Associate Partners, and their number is growing rapidly.

Associate Partners are encouraged to participate in CompBioMed meetings and events throughout the project, which gives them the opportunity to join our full network of partners and help steer the future of computational biomedicine through their influence on the actions of our Centre. Associate Partners also get complete access to the training provided by CompBioMed.

The list of benefits for Associate Partners includes:

- access to and provision of project resources including HPC facilities
- access to and provision of software
- access to and provision of training materials
- invitations to project meetings
- invitations to our workshops
- invitations to our training events
- listing as an associate partner on the CompBioMed website
- participation in our Innovation Exchange Programme
- participation in Incubator Coordination
- possible participation in our Innovation Advisory Board
- listing of software services on the CompBioMed Software Hub

CompBioMed Core Partners actively collaborate with companies/institutions outside the Core Partnership, often this collaboration will lead to them joining as an Associate Partner. Once such a company/institution has been identified, the project coordinator will send them an invitation email which outlines the benefits and opportunities that we offer to such entities [the list above]. We do not ask for any paperwork to be signed, unless they were to be involved in a meeting during which we would discuss confidential work from the partners. Once an agreement has been reached, we will add them to the Associate Partner page (www.compbiomed.eu/associate-partners), we announce them to the consortium (either through a dedicated email or in the monthly e-newsletter) and we add the inclusion of them on Twitter, the major contact is also added to our “all” and “associate” mailing lists. This way,

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we hope to inform all the major user groups within our consortium, and we keep the Associate Partner updated on the current work within the consortium, thereby encouraging further collaborations.

Our Associate Partners include institutions from industry, academia, medical hospitals and HPC Centres, and they benefit from their association with CompBioMed by either being engaged with a Core or another Associate Partner. Further, they may use CompBioMed resources or allow CompBioMed members to employ their resources, where these include HPC and HPDA resources or simply exploiting CompBioMed's growing information hub.

The list of Associate Partners includes the following partners from Industry; Avicenna Alliance, GSK, DNAnexus, Alces Software, Electric Ant Lab BV, Norton Straw Consultants, Pozlab (Poznan), Qatar Robotic Surgery Centre (Hamad Medical Corporation), Microsoft, DiaVita (Life Science), Dassault Systemes, Lightox, InSilicoTrials, ANSYS, Medtronic, Pie Medical Imaging, and AstraZeneca.

7 Details on Further Collaborations

The previous Section described our Industrial CompBioMed Core Partners progress to date. This Section now describes added value collaborations between SMEs and CompBioMed, which have arisen over and above what was initially planned.

7.1 Acellera's Collaborations

Since the beginning of the project, Acellera participated in the dissemination of the project news and promoted the use of *in silico* methods in industry and non-profit entities by participating and organising events, but especially by its effective marketing activity (during national and international events, such as congresses, and through their channels of digital marketing, such as Acellera website, LinkedIn and Twitter). This activity is illustrated by the organisation of workshops, its participation in workshops and its participation in various events and webinar (see Section 6.1.3).

Acellera's ISBA protocol has been optimized and is ready to initiate collaboration among CompBioMed partners. Discussions with CompBioMed partners Evotec and Janssen were started to define the systems to study, the approach to consider, and the legal aspects when sharing technological or scientific knowledge among partners. Since simulations depend on the choice of molecule, emphasis has been put on the development of the protocol, particularly the sampling protocol (e.g.: Adaptive sampling, Adaptive Goal sampling) and its deployment to scale-up the simulations (clusters and Cloud). Today, these protocols are implemented in the software provided by Acellera and used both for services and internal research projects at Acellera. They demonstrated their robustness when predicting ligand binding site and reproducing the binding pathway and have proved to be applicable to a wide range of biomolecules.

Moreover, Acellera provides free access through its platform PlayMolecule.org to promote the use of *in silico* methods for drug discovery and molecular medicine projects (see statistics shared elsewhere). This platform encountered a large success since its release in June 2017. Between June 2017 and March 2019, the number of visits reached 16000 distributed including some 85% of non-profit entities' users and 15% of industrial users, not only from large pharmaceutical companies but also SMEs. Several contacts were established with both large pharmaceutical companies and SMEs, showing a clear interest for the platform but also

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demonstrating the potential of the platform for visibility, testing and validating the interest for new applications or software in biomedicine.

In order to propose a larger offering and more power for Cloud Computing, Acellera contacted CompBioMed's Associate Partner Microsoft Azure. A recent (December 2018) collaboration has been set in order to promote Acellera software use in the Azure Cloud.

Acellera has a privileged relationship with UPF and both entities work closely. As the fruit of a recent collaboration and research activities of UPF, Acellera deployed several of their applications PathwayMap and DeltaDelta, an application to determine the free energy of binding of ligand on a chosen target. These applications are integrated in the PlayMolecule platform and proposed for non-profit and commercial use.

7.2 UPF and Janssen Collaboration

There's an ongoing collaboration between UPF and Janssen, focused on the development of a new biomedical application to predict free energy differences between molecules in congeneric series, based on deep learning methods. At the moment, the collaboration is still in an early stage, with early discussions on the development of such tool. The objective of the collaboration is to train and test the developed neural network using Janssen's internal datasets and compare and evaluate the outcoming results with previous experiments and predictions made inside the company. The method (still unnamed) will be made available through Acellera's PlayMolecule platform and results will be published in a joint paper between UPF and Janssen, as one of the outputs of this collaboration.

7.3 LifeTec Collaborations

LifeTec Group's efforts aim to exploit both the software and hardware infrastructure developed within and/or existing within the CoE. The hope is that the Centre can offer simulations that are beneficial to the daily practice of clinical teams, therefore, these solutions have to be accepted and practical in their use, fitting within current timescales of clinical work. As such, LifeTec has chosen to reach out to the Catharina Hospital to collaborate both on defining the need for assistance in the type of simulation as well as on collaborating in trying the software inside the clinical environment. Within this clinical environment there are restrictions and limitations at this moment in time, for the duration that such simulations can run as well as for the level of engineering skills that may be required to run such simulations. Therefore, a strategic choice has been made to gain clinical acceptance to apply relatively low-computational cost simulations that need a minimal amount of interaction. In light of exploitability and sustainability following CompBioMed, it is foreseen that such software may be exploited in the future on hardware infrastructure via licence agreement, or by consortium members such as LifeTec itself, as a simulation service. At this moment in time, the 1D predictive tool is taken into the Catharina Hospital to expose the clinicians to the simulations and to use real patient cases, both for obtaining clinical feedback on the tool itself and its applicability in standard practise as well as for verifying the results on actual clinical data. Plans are to introduce the coronary simulation tool also to the Amsterdam Medical Centre and OLVG hospitals in Amsterdam, the Erasmus Medical Centre in Rotterdam and the LUMC in Leiden.

Further collaborations have been initiated with device industries and hospitals. Discussions on collaboration with the Erasmus Medical Centre in Rotterdam for simulation on intra-coronary (pharmacological) interventions have begun, leading to the first simulation services expected to start towards the end of 2019.

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Besides clinical interest, the application of predicting interventional outcome within a certain degree of confidence would be a logical extension of existing software companies that are currently providing interventional planning and diagnostic tools, one of which is Pie Medical Imaging. LifeTec has started a collaboration with Pie Medical Imaging, such that their image pre-processing has become part of the LifeTec software toolchain. Depending on the success and accuracy of the simulation tool, one exit strategy may be that the toolchain be licensed to Pie Medical Imaging to be incorporated in their future software release. That would not only enable Pie Medical Imaging to diagnose the current patient condition, but also to predict the potential outcome of either bypass surgery or coronary stenting interventions. Meanwhile, Pie Medical Imaging has become an associate partner of the CompBioMed consortium.

A collaboration with SURFsara has been initiated to allow the simulation tools to run on HPC infrastructure, initially to perform a sensitivity analysis on the simulation tool and its input measures. In a later stage, a variation of input parameters may be used in multiple simulations for a single patient to identify how dependent the predicted outcome is on the accuracy of input values, supporting the accuracy of the prediction.

In the near future, the 1D simulation tools that are being implemented by LifeTec are planned to be connected to local 3D CFD simulations. The purpose of this effort is that the 1D simulation may serve as boundary conditions for such higher dimensional simulations. Interactions with the Core Partners USFD and BSC have started in order to define such forthcoming collaborations. Outside of the CompBioMed partners, connections have been made with the Living Heart project, where additional software are bundled for cardiac simulations. Early activities to connect 3D flow simulations to the 1D models are described above. Discussions with the Aarhus University Hospital in Denmark have taken place on setting up simulations to study the effect of transcatheter aortic valve placement (TAVI) on coronary flow, for which post-op measurements are available. There is an interest in future simulation services to predict interventional outcome in complex cases using this combination of modelling. Furthermore, discussions are ongoing with the Amsterdam Medical Center on 3D FSI simulations on biodegradable heart valve designs for children with congenital heart disease. Simulations on those valve designs should lead to better prototype geometries that may be tested in animal trials.

Discussions amongst LifeTec, BSC and ELEM Biotech (a start-up company described below) have initiated regarding experimental validation (4D MRI flow) of their Alya simulations for ventricular flow patterns.

It is envisioned that simulation capabilities will be offered to the many device companies currently visiting LifeTec Group for prototype device assessment in *ex vivo* organ platforms. From the physical results obtained in such platforms, simulations will provide direction for design and functional improvements prior to the manufacturing of the improved prototype versions.

7.4 Collaborations between Core Partners and SMEs

7.4.1 UCL and EnsembleMD

The company EnsembleMD has been created as a spin out at UCL, with the goal of exploiting tools to automate molecular simulations for use in the pharmaceutical industry. Under the umbrella of the CompBioMed project EnsembleMD has developed the BAC Pro software which provides a cloud interface allowing the execution of drug binding strength simulations on a

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variety of cloud platforms. Initial pilot projects, run since July 2017, have involved retrospective analyses conducted in collaboration with project partner Janssen, as well as GlaxoSmithKline and Pfizer. These exploratory projects were facilitated by business development contacts with associate partners and cloud providers Microsoft Azure and DNAnexus.

Work has begun to adapt our existing workflows to employ container formats that allow them to be executed in both cloud and HPC environments (primarily Singularity). Since EnsembleMD has become an Associate Partner, this work has been supported by EPCC and SURFsara. In response to feedback, both from the pilot project conducted with Janssen and interactions with SMEs in the molecular modelling and machine learning sectors, they are re-engineering their pipelines. The goal is to allow clients more fine-grained control of simulation execution and to make better use of preemptible VMs in the cloud. This work is forming the basis of tendering for fully commercial projects.

7.4.2 BSC and ELEM Biotech

ELEM Biotech is a biomedical company which develops a simulation environment for tissue and organ levels. ELEM Biotech is a start-up from Barcelona Supercomputing Center, co-founded by BSC's researchers Mariano Vázquez and Guillaume Houzeaux. ELEM Biotech was incorporated in mid-July 2018 and is now a PLC ("elem biotech s.l.") having an initial capital seed of 275K Euros from different international investors. The company is based in Barcelona, with a commercial office in Bristol after being selected for the 2nd Bristol Cohort of the Oracle's start-up ecosystem. ELEM Biotech is currently carrying on projects with Medtronic (cardiac mechanics and morphine pumps for spinal fluid) and iVascular (stent manufacturing and deployment).

ELEM Biotech is a successful demonstration of the research quality of CompBioMed partners and its projection towards a business development. It aims to provide a simulation environment deployed in HPC Cloud infrastructures with the Software-as-a-Service model. Since early stages of the company creation, CompBioMed's Core Partner CBK has discussed with the ELEM Biotech executives both business and financial issues, particularly in reference to raising capital. Elem Biotech is now an Associate Partner. During the last three months, ELEM biotech applied for three Torres Quevedo grants from the Spanish government to contract three Engineers in order to increase the development rate of the planned software solutions.

7.4.3 UNIGE and NUMECA International

NUMECA International, an SME with headquarters in Brussels, is a leading provider of software for computational fluid dynamics in many industrial areas. NUMECA offers a large panel of solvers, including finite-volume RANS, finite-volume LES, high-order methods, and particle-based methods, and has recently started offering a lattice Boltzmann fluid solver, which is developed in collaboration with core partner UNIGE. A knowledge transfer agreement has been established between UNIGE and NUMECA to allow industrial exposure of UNIGE research output. Computational biomedicine is one of the industries targeted by the lattice Boltzmann solver. In this field, UNIGE also acts as an expert partner to support NUMECA customer projects. NUMECA International will be an associate partner in CompBioMed2.

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7.4.4 Other SMEs

A large number of SMEs have also collaborated with CompBioMed Core Partners, who have worked with CompBioMed, or sought advice, donated data or use cases, exploited our resources and/or attended workshops, and these SMEs include, but are not limited to the following: Convergence Pharma, Norton Straw, Sardina Systems, Velocient, Tiara Solutions, Verne Global, Sygnature Discovery, iVascular, MedCity HQ, HiTs, Thoroughly modern media, Clyde Biosciences, QT Informatics, Vala Sciences, LumiraDX, Aridhia, Fios Genomics, PhysioMedics, MathResolutions, RSRCH BV, The Hyve, Base Clear, MicroLife Solutions, PacMed, Quaero Systems BV, Electric Ant Lab, Astrocyte, Lightox, Insilico Trials, and Pie Medical Imaging.

Of this long list of SMEs, the following have regularly engaged with and/or used CompBioMed services: Convergence Pharma, DNA Nexus, Alces Software, Norton Straw, iVascular, Thoroughly modern media, PhysioMedics, Lightox, Insilico Trials, Ensemble MD, and Pie Medical Imaging.

8 CompBioMed's Collaboration with the cPPP ETP4HPC

The cPPP on HPC brings together both the technology providers and the end users via the ETP4HPC Association and the Centres of Excellence. CompBioMed, as one of these Centres of Excellence, has created its own links to the ETP4HPC to establish a forum and mechanism for the HPC industry to interact with the computational biomedicine community, whether in academia, hospitals or SMEs.

ETP4HPC is the European Technology Platform (ETP) in the area of HPC. It is an industry-led think tank comprising of European HPC technology stakeholders: technology vendors, research centres and end users. The main task of ETP4HPC is to define research priorities and action plans in HPC technology provision (i.e. the provision of supercomputing systems). They issue and maintain a Strategic Research Agenda as a mechanism to help the European Commission define the contents of the HPC Technology Work Programmes. ETP4HPC also acts as the "one voice" of the European HPC industry in relation to the European Commission and national authorities. ETP4HPC was formed in October 2011.

Regarding general collaborative efforts, our Centre has attended all the HPC cPPP board meetings since CompBioMed started in October 2016. It was discussed at the last HPC cPPP Board meeting (October 23rd, 2018) that the cPPP will be terminating and the EuroHPC Join Undertaking (EuroHPC JU) will be taking over. EuroHPC will establish two Advisory groups: Infrastructure and Research and Innovation in which ETP4HPC can appoint four representatives. These Advisory groups may set up working groups to involve larger groups of stakeholders from Centres of Excellence, science and industry users. The EuroHPC fully supported and pushed for the "Extreme Scale Demonstrators". There is a strong focus on developing industrial HPC user organisations. Reciprocally, Hugo Falter, of the ParTec Cluster Competence Center and the ETP4HPC Association, gave a presentation at our Centre's kick-off meeting. Further, in response to requests from ETP4HPC, as the HPC cPPP coordinator, we have also made significant contributions to the EC's Work Programme 2018-2020 in the area of High-Performance Computing.

Regarding particular collaborative efforts, Bull/Atos has established a working relationship with four key contacts of ETP4HPC, namely Hugo Falter (ParTec) secretary-administrator, Marcin Ostasz (BSC) business analyst and research centre member of the Barcelona

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Supercomputer Center (BSC), and Jean-Pierre Panziera (ATOS) chairman and Pascale Bernier-Bruna (ATOS) who is in charge of ETP4HPC communication. On top of regular exchanges with them, Hugo Falter made a presentation at the CompBioMed Kick-Off meeting in October 2016. Marcin Ostasz participated as a guest speaker at the CompBioMed BoFs. Pascale Bernier-Bruna has helped in disseminating information though the ETP4HPC mailing list as well as social and professional media.

Bull/Atos is continually meeting new contacts and is planning to expand beyond the identified networks. Specifically, Bull/Atos plan to meet with Jesus Carretero, of the University Carlos III of Madrid – a member of ETP4HPC, and Sabri Pllana, of Linnaeus University, Sweden. Further, we are aiming to recruit various institutions associated with ETP4HPC to become Associate Partners.

To facilitate this, CompBioMed is featured in the 2018 Handbook of European HPC which is a summary of all European HPC Technology and Application projects. This link between CompBioMed and the ETP4HPC association allows the sharing of relevant news and events (Kick-offs, CompBioMed conferences, SC and ISC conferences, training sessions) with the ETP4HPC members and beyond. Such news and events already involve ETP4HPC members. Therefore, these mechanisms help exploiting interactions between CompBioMed Core Partners and ETP4HPC members and thus, attract and encourage additional ETP4HPC Partners to join as Associate members of CompBioMed.

Both CompBioMed and ETP4HPC have co-presented a Birds-of-a-Feather (BoF) session at ISC18 in Frankfurt, Germany on the 27th of June 2018. This BoF was entitled *The Computational Biomedicine Community and the HPC Industry: working together to advance personalized medicine*. This BoF was a very exciting opportunity that allowed a more open discussion between a wide range of participants, with focus on SMEs and other industrial and medical companies. This meeting was much less restrictive than an ISC workshop, and we succeeded in extending our reach and publicised CompBioMed, to attract new industrial collaborations through our many existing routes, i.e. by becoming Associate Members, membership of our IAB, attending our All Hands Meetings, workshops, presentations, and so on.

This BoF was organised by a CompBioMed Core Partner, namely Bull/Atos with strong support from members of the ETH4HPC themselves. Members of both ETP4HPC and six of CompBioMed's Core Partners were in attendance, including Bull/Atos, SURFsara, Barcelona Supercomputing Centre, LifeTec Group, Janssen Pharmaceutica, and EPCC of The University of Edinburgh. Our ISC18 BoF application is included in Annex A below.

Similarly, CompBioMed will reiterate its presence at ISC in 2019. The CompBioMed Core Partner Bull/Atos is again organising the BoF with the idea of bringing together the CompBioMed CoE stakeholders and other industrial stakeholders with the support of ETP4HPC. The ISC19 BoF is entitled *Personalised Medicine and the HPC Industry*. Our ISC19 BoF application is included in Annex B below. We intend to spend the maximum fraction of time on open discussions with questions/answers as it was appreciated during the previous BoF at ISC. As part of the dissemination process, we are investigating the possibility to video-record the BoF session and make it available to the members of the CompBioMed CoE though the relevant Work Packages for future development. The output of such events represents the key for application and system development and their use towards exascale.

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Similarly, thanks to the support of Core Partners, we have been able to interact with bio-scientists and other users from the medical community that exploit HPC services. We were able to demonstrate the use of HPC in this field. Using this information and the media available through the ETP4HPC network, we can encourage additional industrial stakeholders to join CompBioMed as Associate Partners.

Today, we have been able to engage with two institutions, namely the Queens University Belfast and the Bio-informatics Core Facility of the Luxembourg Centre for systems Biomedicine. Both groups are interested in the CompBioMed initiative and would like to build further expertise and projects.

Besides the ETP4HPC cPPP, Bull/Atos has been promoting intensively CompBioMed through seminars and webinars. Within Bull/Atos, the following events have been organised: Atos Tech Talks, webinar on October 3rd, 2018, *People in Motion*, webinar on October 11th, 2018 and the Scientific Community Meeting, seminar at Paris February 19-20th, 2019. Outside Bull/Atos, several seminars involving many industrial partners have been implemented. It is worth mentioning first the GSK Innovation workshop at Brussels on December 5th, 2018. This workshop gathered people from GSK, Siemens and Atos around the topic of precise development of vaccines. Roughly, 40 people attended this workshop, mainly from GSK and Siemens. Second, the STFC seminar series in Daresbury on February 13th, 2019 gathered a smaller audience of 10 to 15 people around the topic of genomics. Finally, the ISUM (International Supercomputing Conference in Mexico) on March 26-29th, 2018 hosted two talks and one round table about CompBioMed: the first talk gathered 50 people on Precision Medicine; the second talk discussed biotechnologies and had an audience of 30 people. During this last talk the CompBioMed video was displayed. Finally, this last talk was followed by a round table where the guests gave their views of the biotechnology area and answered questions from the audience.

Bull/Atos plans to continuously develop cPPP collaborations through seminars and round tables. Three other leads have been identified on this matter: the ELIXIR Bioinformatics Suppliers Forum in London on May 7th, 2019 where a talk will be given and one internal seminar Atos Tech Days at Paris, on May 16-17th, 2019. Finally, Atos will be meeting an audience from the HPC industry and the press at the TERATEC Forum in Paris on June 12th, 2019 where life science topics, among others CompBioMed, will be discussed.

Over the remaining months of CompBioMed, Bull/Atos aims to continuously identify further contacts within this community, establish a working relationship and determine potential synergies to be supported.

9 Innovation Exchange Programme and the Innovation Advisory Board

Industrial collaboration is strongly encouraged, fostered and extended via two of the Innovation and Sustainability WP4 activities, namely the Innovation Exchange Programme and the Innovation Advisory Board.

9.1 Innovation Exchange Programme

Our Centre's Innovation Exchange programme, or IEP, permits the technology transfer between academia, healthcare and industry in the field of biomedical computing by fostering a mentoring programme. In this programme experts from the research community spend time embedded within industrial organisations looking for assistance, applying the latest research

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techniques in their software. This mentoring programme is enabled via short internships within industrial organisations.

The associated work package, Innovation and Sustainability (WP4), and the sister work package, Training and Dissemination (WP3), work together to develop mentoring programme opportunities, which are posted on the CompBioMed website, and are open to both internal and external stakeholders. These visits nurture best practice in software development and techniques, and we anticipate that this will foster mentoring relationships and establish collaborations between the participating sites.

Our initial plan for visits were from academia to industry; however, after consultation within the associated work package, Innovation and Sustainability, we decided to extend the remit of the IEP: parties from industry can visit academia or other industrial institutions, and parties from academia can visit other academic institutions. Our only limitation is that one of the participants, either the visitor or the target institution, must be one of the CompBioMed core partners.

The IEP webpage, namely www.compbiomed.eu/innovation/visitor-programme, acts as a hub where visitors can publish their desire to visit a CompBioMed partner or various CompBioMed partners or hosts can publish their desire to host visitors. The objective of this is being an interaction match-making service between visitors and hosts.

Note that publicly we refer to the Innovation Exchange Programme as our Visitor Programme, to make it clear at a glance what the programme is.

Our plans include:

- holding conferences/seminars between academia and industry, in collaboration with CompBioMed Training and Dissemination;
- at least 5 participants in the IEP from European countries and regions with fewer HPC resources;

Clearly this programme requires extensive advertising, and, to this end, we advertise our IEP through the publicity channels of both CompBioMed and VPH, namely Newsletters, LinkedIn, and Twitter. Recently, we started a monthly Twitter post introducing a different visit with each post, with photographs and a general description of who was involved and what was achieved. It is worth noting that VPH advertises our IEP via their website, their monthly newsletter (which has over 8000 contacts), and via their VPH social media networks.

All past, current and future visitors are noted and displayed on our website at www.compbiomed.eu/innovation/visitor-programme/current-and-planned-exchanges. The table presented in Annex C is a snapshot of our IEP at the time of writing which currently lists 37 visits.

Our Centre has limited funds to support visitors. As such, we work closely with Core, Associate Partners and third parties who can provide financial support to the programme, such as the HPC-Europa3 project. To date, we have formed a Memorandum of Understanding, or MoU, between CompBioMed and the HPC-Europa3 Project. This MoU, shown in full in Section 0: *Annex D*, states that CompBioMed can apply to HPC-Europa3 travel grants, and visitors have already started to exploit this opportunity.

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For more information, please see the HPC-Europa3 website: www.hpc-europa.eu.

9.2 Innovation Advisory Board

Our Centre's Innovation Advisory Board, or IAB, has moved from strength to strength. We started with around 14 IAB members for the first meeting and currently have 19 IAB members. The members include academics specialising in HPC and professional sustainable software practices, practicing medics from hospitals and universities, alongside members from Industry, particularly SMEs. The members come from both our Core and Associate Partners but, most importantly, the majority are from outwith CompBioMed.

All IAB members sign NDAs upon attendance and present their own personal views which may be different to the views of their home intuitions.

IAB members from industry come from the following industrial companies, in no particular order: Microsoft Azure, Amazon AWS, Evotec (UK) Ltd, Vertex Pharmaceuticals, Merck, Neuravi Ltd, CADFEM Ireland Ltd, and Medtronic Plc.

9.2.1 First IAB meeting

The first IAB meeting was held at UCL in London on the 30th of May 2017. Six of the then fourteen members were in attendance, along with four CompBioMed staff members.

An outline of the 1st IAB Recommendations can be found in Section 0: *Annex E: First IAB Recommendations*.

We have addressed the proposals from the 1st IAB meeting and have adapted accordingly. Specifically, we are in the process of creating the User Forum, as outlined above. A Directory of Services is being created as part of a general, ongoing process to improve our website. CompBioMed Ambassadors may not exist in name, but our members attend a wide variety of conferences, armed with a relevant slide deck and dissemination material. Moreover, we organise booths at various conferences. We do not currently plan to help speed-up existing software, as this is within the domain of a sister CoE, namely POP: www.pop-coe.eu.

Regarding shifting our focus: we *are* introducing our concepts to medical students, and introducing ideas to clinicians; however, this is not our focus. We have several SMEs within our Associate Partners, and we focus on their needs. Further, we believe that CompBioMed has a very wide area of interest: i.e. we have had an HPC-related conference on Cloud and HPC, but equally we held a dedicated model-related workshop on Free-Energy considerations. We will consider model-related topics when we organise further workshops. Lastly, as our membership is very wide, we have members already working on both High Throughput Computing (HTC), as well as HPC.

Regarding offering Solutions as a Service: we acknowledge this is an area which requires more effort. To this end, we produced a public report which outlines our Solutions and End-users. Furthermore, we are actively collecting this information from our Associate Partners for the published deliverable D6.4 *Report on Selected Emerging Use Cases for Existing Solutions*.

Data security is already a key consideration both for user and the providers at CompBioMed's HPC Centres. As such, those that are handling sensitive/patient data have the necessary

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security in place, and we have ensured that they are aware of the GPDR requirements. Moreover, within our Associate Partner, DNAnexus cloud gives additional security for commercially sensitive and personal data, and we are working with them, alongside Birmingham City University who is also an expert in data security.

9.2.2 Second IAB meeting

The second IAB meeting was held at UvA in Amsterdam on the 30th of May 2017. Seven of the then nineteen members were in attendance, along with two CompBioMed staff members.

An outline of the 2nd IAB Recommendations can be found in Section0: *Annex F: Second IAB Recommendations*.

In general, we agreed with the recommendations from the 2nd IAB, and were pleased that their expectations are reflected in the work anticipated in CompBioMed2.

We are working hard to establish a large and useful network of collaborators with external communities. We have 40 Associate Partners, and we work with 17 related projects, by participating in joint meetings, sharing dissemination activities etc. We will continue to grow this network in the future and hope to grow this with clinical and medical institutions. However, there is a limit to how many such interactions a small finite CoE and management team can support, without further funding to grow the central team and services support.

We are looking at ways to improve scientific and medical understanding through our medical school course and attempting to integrate clinicians into the partnership. We acknowledge that we could do more here and will be working on this in the future.
We now have examples of commercialisation within the consortium, and this is a major focus going forward. We have recently produced our sustainability plan (D4.3), which was submitted in April 2019.

In terms of the teaching modules, we are investigating taking our HPC courses to other medical schools and acknowledge the need to consider the higher level of clinicians. We are also looking into the use of our simulations for teaching around medical device experimentation.

We are constantly working on the services that we offer; the software hub, and training repository are available to anyone to access and enables them to contact the relevant people for further information.

9.2.3 Third IAB meeting

The third IAB meeting was held in Oxford, UK, on the 29th of April 2019, where nine board members attended. The minutes, actions and recommendations from this meeting are still being finalised.

10 Further collaborative avenues

Many industrial bodies interact with CompBioMed not only via the mechanisms described above, but also through many other routes. These include engagement with Core or Associate Partners, or through companies employing HPC resources provided by Core or Associate Partners. We also interact with the wide community via invited attendance to our All-Hands meetings, and via our attendance to workshops, webinars, and seminars.

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Further, many individuals from several industrial bodies subscribe to the CompBioMed Newsletter including some from Pintail Services, HiTS, Genentech, HLRS and Oracle.

The following subsections describe two methods that we monitor that enable further collaborative avenues, specifically via a subset of our Key Performance Indicators, and various events we organise/attend where we have interacted with individuals representing industrial companies.

10.1 Key Performance Indicators

One method of monitoring our success in industrial collaboration fall under the management of our Key Performance Indicators, or KPIs. Of the thirteen KPIs, four of them relate to engagement with our industrial collaborators.

There are two KPIs regarding the impact on innovation, specifically: five of our industrial customers will report saving in development costs of ≥ €25K per annum, and our industrial customers will report saving in development costs of at least €200k per annum. We currently have a list of 7 companies that have reported a saving in development costs of over €25K per annum. At this stage, we have no reported savings for *in silico* trials; however, we are working with a number of projects that have data on this subject and are confident that this it is a viable achievement.

The KPI monitoring the IEP aims to include at least five participants from European countries and regions with fewer HPC resources. This KPI was surpassed in the first 18 months and, to date, we have had 20 participants from regions with fewer HPC resources both from within and outside Europe; and a total of 37 IEP visitors from 23 different institutions.

Finally, the KPI which monitors the engagements of industrial companies requires that at least 20 companies, where at last one third are SMEs, have accessed CompBioMed services. This too was surpassed in our first 18 months of operation and we now have over 90 companies engaged with 35% of these being SMEs. We predict our centre will continue to attract new companies and that the number of quality engagements will be far in excess of these numbers by the end of the project.

10.2 Events

Finally, for this Section, we list events which we have organised and participated in. Many have attracted attendance from individuals representing Industrial companies (the number of attendees from Industry at each event are given in square brackets).

Past Event

- 3-4 October 2016 – CompBioMed KO Meeting – UoL, London [9]
- 11-12 April 2017 – CompBioMed All-Hands Meeting – BSC, Barcelona [9]
- 27th April 2017 – Cloud & High Performance Computing in Biomedicine – UCL, London [37]
- 16th May 2017 – CompBioMed at PRACEdays 2017 – BSC, Barcelona [3]
- 31st May 2017 – CompBioMed & BioExcel Free-Energy Workshop – UCL, London [15]
- 27th September 2017 – “CompBioMed’s Cloud HPC Workshop”, Cristin Merritt, Alces Flight Ltd (UK), UCL, London [0]
- 27th September 2017 – “The Virtual Human” IMAX film at the Science Museum Lates event, Science Museum, London [20]

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- 22nd November 2017 – CompBioMed Webinar Series: HPC Simulations of Cardiac Electrophysiology [3]
- 30th January 2018 – CompBioMed Webinar Series: Introduction to cloud computing for the VPH. [0]
- 19 March 2018 – CompBioMed Webinar Series: Lattice Boltzmann method for CompBioMed (incl. Palabos) [4]
- 26-27 March 2018 – CompBioMed All-Hands Meeting, UvA, Amsterdam [16]
- 28 March 2018 – CompBioMed & VHeart Joint Workshop, UvA, Amsterdam [2]
- 19-20 June 2018 – CompBioMed exhibit at Teratec Forum 2018 – Palaiseau, France [1300 (total attendees at the event aimed at industry)]
- 27 June 2018 – CompBioMed/ETP4HPC BoF at ISC 2018 – Frankfurt, Germany [10]
- 4 September 2018 – CompBioMed training at VPH2018 – High Performance for the VPH – Zaragoza, Spain [0]
- 5-7 September 2018 – CompBioMed Booth at VPH2018 – Zaragoza, Spain [10]
- 15 November 2018 – CompBioMed BoF at SC18 Dallas, Texas, US [10]
- 13-15 February 2019 – PATC/CompBioMed Winter School 2019 on "HPC-based Computational Bio-Medicine" – BSC, Barcelona, Spain [0]
- 20 March 2019 – CompBioMed Webinar Series: Sensitivity analysis of a strongly coupled cardiac electro-mechanical model [3]
- 28-29 March 2019 - CompBioMed Containerisation Meeting: Container Technologies in Cloud and High Performance Computing Research and Commercial Applications, SURFsara, Amsterdam, [20]
- 29 April – 1 May 2019 - CompBioMed All-Hands Meeting, Oxford, UK. [15]

Future Events

- 29-30 May 2019 – UKCOMES/CompBioMed/VECMA meeting on "HemeLB: cardiovascular modelling and simulation in UKCOMES", London, UK.
- 19 June 2019 – CompBioMed/ETP4HPC BoF at ISC 2019 – Frankfurt, Germany.
- 25-27 September 2019 - CompBioMed Conference 2019, London, UK.

11 Conclusion

Industrial collaboration is a keystone to the success of our Centre of Excellence, and its importance cannot be understated.

This Deliverable has given an overview of the collaborations that CompBioMed has with industry in general, where we have shown an increased awareness of CompBioMed within Industry through our ever-expanding list of 40 Associate Partners, through to our Incubator services; the Innovation Exchange Service, which currently monitors 37 visits, to our Innovation Advisory Board which grew from 14 members at the 1st IAB, to 19 members for the 2nd IAB and has expanded to include members of the clinical profession. A total of 7 out of the possible 19 members attended the 3rd IAB meeting in Oxford. Furthermore, we had at least 79 attendees to our workshops and meetings from industrial bodies.

Moreover, within the HPC cPPP, our CompBioMed Centre of Excellence and the ETP4HPC Association, are collaborating well, both via Board Meeting attendance, and personal one-to-one collaborations, where early fruits from the latter has resulted in a successful joint ISC18 BoF and an upcoming joint ISC19 BoF.

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At this point, we have demonstrated that our Core Partners are fostering innovative advances throughout the Centre. Our strategy to introduce further industrial (as well as academic) Associate Partners into the Centre is ensuring that we can work on new innovations in the field, as well as to more effectively support the planned research of all our Partners. New Associate Partners (from all sectors) have often joined after collaborations with one of our Core Partners, indicating that our research and partnerships are strong ambassadors of the Centre. As our reputation grows, we will continue to actively seek further industrial partners to strengthen and build our Centre as we look ahead to CompBioMed2.

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Annex I: ISC18 BoF Application (accepted)

Title of the BoF session: The Computational Biomedicine Community and the HPC Industry: working together to advance personalised medicine

BoF organizer/speaker information: six of CompBioMed's Core Partners: Bull/Atos, SURFsara, Barcelona Supercomputing Centre, LifeTec Group, Janssen Pharmaceutica, and EPCC, of The University of Edinburgh, with close support from the ETP4HPC.
The persons quoted this after already have guaranteed their presence:
Peter Coveney from UCL (University College of London)
Cristin Merritt from Alces Flight
Marcin Ostasz from BSC (Barcelona Supercomputing Center), on behalf of ETP4HPC
Gavin Pringle from EPCC of the University of Edinburgh
Marco Verdicchio from SURFsara
Rush Aris (Barcelona Supercomputing Center)
Dieter Kranzlmüller from LRZ (Leibniz Supercomputing Centre)
Benjamin Pajot from Bull/Atos

Short abstract: How to bring HPC to medical SMEs, clinical researchers and hospitals? As we are nearing the exascale era, too few benefit from such computational power, and even fewer achieve excellence in HPC application delivery and use. By bringing together the biomedicine community and the HPC industry, we hope to help the community better embrace upcoming technologies, and help the industry better understand the needs: fault tolerance, data and compute resources, access mechanism (such as urgent computing, on-demand computing, advanced reservation…), computing power, code efficiency. Which feature is critical for Biomedicine? Is Industry aware of it, and what answers are planned in the future? Overall, how to bring these improvements to the people who diagnose, to the drug discoverer, or even to your doctor? As a Centre of Excellence working towards the advancement of computationally based modelling and simulation within biomedicine using large-scale and cloud computing resources, CompBioMed is a significant contributor to this debate, with experience to share, especially through its three exemplar research areas: cardiovascular, molecularly-based and neuro-musculoskeletal medicine. To complete the picture, we hope industry stakeholders will share their vision of a complex area involving so many different areas of expertise. To feed the debate, all interested parties are welcome to attend and help paving the way to excellence.

Topic area (as listed in the call for research papers):

- HPC Applications
- Exascale computing
- Domain-specific architectures
- Trends in the HPC chip market
- Job management
- Productivity improvement
- Data intensive applications
- Convergence of simulations and big data
- Workflow management
- Industrial simulations

One to five keywords: computational biomedicine, exascale, personalised medicine

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Maximum intended fraction of time spent for presentations: 15 minutes only: 5 minutes for introduction of CompBioMed, 5 minutes for introduction of ETP4HPC, 5 for the introduction of the BoF itself.

Description of approach to make the BoF interactive: gathering a panel of experts to lead the room-wide discussion and to collect details of interested parties.

Targeted audience: HPC industry stakeholders & the computational biomedicine community

Estimated number of attendees: 50

Annex II: ISC19 BoF Application (accepted)

Title of the BoF session: Personalised medicine and the HPC industry

BoF organizer/speaker information six of the CompBioMed's Core Partners: Bull/Atos, SURFsara, Barcelona Supercomputing Center, LifeTec Group, Janssen Pharmaceutica, EPCC of The University of Edinburgh, with close support from the ETP4HPC.

The persons quoted below are planning to attend:
Peter Coveney from UCL (University College of London)
Cristin Merritt from Alces Flight
Marcin Ostasz from BSC (Barcelona Supercomputing Center), on behalf of ETP4HPC
Gavin Pringle from EPCC of the University of Edinburgh
Marco Verdicchio from SURFsara
Dieter Kranzlmüller from LRZ (Leibniz Supercomputing Centre)
Cyril Mazauric From Bull/Atos
Tomas Karasek from IT4I
Marco Stijnen from LifeTec

Short abstract: How to bring HPC to medical SMEs, clinical researchers and hospitals? As we are nearing the exascale era, too few benefits from such computational power, and even fewer achieve excellence in HPC application delivery and use. By bringing together the biomedicine community and the HPC industry, we hope to help the community better embrace upcoming technologies, and help the industry better understand the needs: fault tolerance, data and compute resources, access mechanism (such as urgent computing, on-demand computing, advanced reservation…), computing power, code efficiency. Which feature is critical for biomedicine? Is Industry aware of it, and what answers are planned in the future? Overall, how to bring these improvements to the people who diagnose, to the drug discoverer, or even to your doctor? As a Centre of Excellence working towards the advancement of computationally based modelling and simulation within biomedicine using large-scale and cloud computing resources, CompBioMed is a significant contributor to this debate, with experience to share, especially through its three exemplar research areas: cardiovascular, molecularly-based and neuro-musculoskeletal medicine. To complete the picture, we hope industry stakeholders will share their vision of a complex area involving so many different areas of expertise. To feed the debate, all interested parties are welcome to attend and help paving the way to excellence.

Topic area (as listed in the call for research papers):

- HPC Applications

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- Exascale computing
- Domain-specific architectures
- Trends in the HPC chip market
- Job management
- Productivity improvement
- Data intensive applications
- Convergence of simulations and big data
- Workflow management
- Industrial simulations

One to five keywords: computational biomedicine; personalised medicine; exascale; HPC workflows.

Maximum intended fraction of time spent for presentations: 15 minutes only: 5 minutes for introduction of CompBioMed, 5 minutes for introduction of ETP4HPC, 5 for the introduction of the BoF itself.

Description of approach to make the BoF interactive: gathering a panel of experts to lead the room-wide discussion and to collect details of interested parties.

Targeted audience: HPC industry stakeholders and the computational biomedicine community.

Estimated number of attendees: 50

Annex III: Current List of Visitors promoted/monitored by IEP

This following table is a snapshot of our IEP at the time of writing, which currently lists 33 visits, where the possible nature of transfers can be Learning from Host, Learning from Visitor, Studentship, Undergraduate Training, Secondment, or Collaboration. Further, the level of visitor can be UG (Undergraduate), PhD, PD (Postdoc), Ac (Academic), or Ind (Industrial).

Host Institution	Visitor Institution	Dates	Nature of transfer	Level of visitor
Barcelona Supercomputing Centre (BSC)	BITS Pilani (India)	1st Oct 2016 – 5th Dec 2016	Studentship	UG
BSC	University of Oxford	1st Nov 2016 – 15th Nov 2016	Collaboration	PhD
University of Oxford	BSC	1st Nov 2016 – 15th Dec 2016	Collaboration	PD
Medtronic	BSC	2nd Jan 2017 – 1st Mar 2017	Collaboration	PhD
Flinders University (Australia)	University of Sheffield	1st Mar 2017 – 1st May 2017	Collaboration	PhD
University College	Evotec	1st Jan 2017 –	Secondment	Senior

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London (UCL)		31st Dec 2018		
Leiden University	Janssen	1st Jul 2017 – 31st Dec 2017		
UCL	Zayed University (ZU)	1st Oct 2017 (ongoing)	Studentship	PhD
UCL	Merck	Ongoing	Collaboration	PD
University of Alberta, Edmonton	University of Oxford	8th Nov 2017 – 22nd Nov 2017	Collaboration	PhD
University of Oxford	University of Bologna	15th Mar 2017 – 31st Jul 2017	Collaboration	PhD
University of Oxford	University of Bologna	15th Sep 2017 – 1st Mar 2018	Studentship	Masters
University of Oxford	BSC	29th May 2017 – 2nd Jun 2017	Collaboration	PhD
University of Oxford	Fraunhofer – Chalmers Research Centre	24th Apr 2017 – 30th Apr 2017	Collaboration	PhD
University of Oxford	Queensland University of Technology	24th Apr 2017 – 9th Jun 2017	Collaboration	Ac
University of Oxford	Queensland University of Technology	18th Sep 2017 – 15th Oct 2017	Collaboration	PhD
University of Oxford	Washington University in St. Louis	10th Sep 2017 – 15th Oct 2017	Collaboration	Ac
University of Oxford	Food and Drug Administration (FDA)	18th Sep 2017 – 22nd Sep 2017	Collaboration	PhD
University of Oxford	UCL	16th Oct 2017 – 21st Oct 2017	Collaboration	PhD
University of Oxford	Queensland University of Technology	6th Nov 2017 – 17th Dec 2017	Collaboration	Ac
UCL	Evotec	6th Nov 2017 –	Collaboration	Ac
BSC	BITS Pilani (India)	1st Feb 2018 – 30th Jun 2018	Studentship	UG
BSC	UPC	1st Feb 2018 – 6th Apr 2018	Studentship	UG
University of Oxford	Tampere University of Technology	1st Feb 2018 – 31st May 2018	Collaboration	PD
University of	ITMO	5th Feb 2018	Collaboration	PhD

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Sheffield		– 4th Mar 2018		
George Mason University	BSC	1st Feb 2018 – 2nd Feb 2018	Collaboration	PD, Ac
Medtronic	BSC	8th Feb 2018 – 10th Feb 2018	Collaboration	PD
Evotec	UCL	28th Feb 2018	Collaboration	PhD
Evotec	UCL	24th May 2018	Collaboration	PhD
Janssen	UCL	14th Jun 2018 – 15th Jun 2018	Collaboration	PhD
UPF	LifeTec Group	18th Jun 2018 – 22nd Jun 2018	Studentship	MSc
UPF/Acellera	Janssen	2nd Jul 2018 – 11th Jul 2018	Collaboration	PD
BSC	UvA	1st Oct 2018 – 27th Oct 2018	Secondment	PhD

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Annex IV: CompBioMed and HPC-Europa Memorandum of Understanding

Memorandum of Understanding

Between COMBIOMED and HPCE3
Version 0.2; 01 October 2017

1. Project Information

1.1. COMBIOMED

CompBioMed is a user-driven Centre of Excellence in Computational Biomedicine, to nurture and promote the uptake and exploitation of high performance computing within the biomedical modelling community. Its user communities come from academia, industry and clinical practice. CompBioMed has innovation at the forefront of its aims, promoting interdisciplinary entrepreneurial opportunities driven by our users' needs. Its industrial partners participate fully in the Centre's activities from the outset, with the number of associate partners expected to grow continuously over the lifetime of the Centre.

1.2. HPCE3

The HPCE3 project that run from May 1st 2017 to April 31st 2021 aims at maintaining the persistency of a high-quality service of transnational access to the most advanced HPC infrastructures available in Europe for European research. The project is based on a program of visits, in the form of traditional transnational access, with researchers visiting HPC centres and/or scientific hosts who mentor them scientifically and technically.
The visitors are:

1. Funded for travel, accommodation and subsistence, and
2. Provided with an amount of computing time suitable for the approved project.

The calls for applications are issued 4 times per year and published online at **www.hpc-europa.eu**

1.3. Common participants

SURFsara, BSC and EPCC are partners both of CompBioMed and HPCEuropa3 and can naturally act as liaisons between the two parties for administrative and technical collaboration.

2. Purpose

A close collaboration between CompBioMed and HPCE3 is very desirable as HPCE3 project is going to serve as a starting point for the applicants in their natural evolution towards future deployment of HPC exascale infrastructures, while ComBioMed promotes the uptake and exploitation of high performance compu-

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ting within the biomedical modelling community. The purpose of this MoU is to formalize the collaboration between the two parties.

3. Objectives

The high-level objectives of the collaboration are as follows:

- The HPCE3 Transitional Access programme visits could be used for collaboration with CompBioMed
- Both parties can actively disseminate the essential information and calls from each partner.
- Trainings - HPCE3 applicants can become CompBioMed training participants.

4. Joint Work Plan

The framework of the joint work plan is as follows:

1. Training **Parties involved:** CompBioMed: WP3 HPCE3: TA **Description of work:** CompBioMed organizes different training for use of HPC in biomedical modelling. HPCE3 TA can advertise and encourage the visitors to attend these events. **Milestones:** M1.1: CompBioMed to periodically communicate about the upcoming events with HPCE3
2. Dissemination **Parties involved:** CompBioMed: WP3 HPCE3: WP3 **Description of work:** HPCE3 will send dissemination material to CompBioMed as well as announcements of application calls. HPCE3 will also disseminate all the necessary information provided by CompBioMed. **Milestones:** M2.1: Disseminate the provided material M2.2: Disseminate the call announcements
3. Collaborative visits **Parties involved:** CompBioMed: WP4 HPCE3: WP3 **Description of work:** CompBioMed researchers can use the opportunities provided by HPCE3 for collaborative visits

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Milestones:
M3.1: Several visitors from CompBioMed to apply for HPCE3 programme

5. Schedule

Milestone	Time Due	Description
M1.1	30/04/2021	CompBioMed to communicate the upcoming event to HPCE3 on periodical bases
M2.1	31/10/2017	Start the dissemination of HPCE3
M2.2	31/10/2017	Start the dissemination of HPCE3 calls
M3.1	31/10/2021	Several applications from CompBioMed

6. Contacts

	CompBioMed	HPCE3
Main	Stefan Zasada UCL stefan.zasada@ucl.ac.uk +44-20 7679 5300	Debora Testi CINECA d.testi@cineca.it +39-3939761599
Secondary		Lilit Axner KTH lilit@kth.se +46 8 790 78 19

7. Signatures

The following agree to the terms and conditions of the MoU:

P. V. Coveney

Peter V. Coveney
CompBioMed project coordinator

Date:

Paola Alberigo

Paola Alberigo
HPCE3 project coordinator

05/10/17
Date:

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Annex V: First IAB Recommendations

What follows is a description of the 1st IAB Recommendations

Create a Forum:

- specialists/practitioners can learn what is out there
- provide translation/terminology service
    - clinicians don't understand biotech who, in turn, don't understand HPC
- Offer consultancy for
    - data management
        - storage/movement
    - connecting with other groups
    - FAQs
        - pre-clinical studies
        - how to get results quickly
- “ask an expert” button for real-time interaction

Provide a directory of services

- lists of contacts, groups, information, providers
- exhaustive list of CBM resources
    - codes, platforms, models, paradigms, etc.
    - list of associated experts
    - public domain
        - perhaps a second one is needed for internal use only

Create CompBioMed Ambassadors

- Informed and empowered members to attend conferences

Offer speed-up of existing software

- web browser app that looks like familiar UI
- front-end to cloud HTC/HPC
- Time to solution reduced by 50% is not good enough
    - Reduce from hours to minutes

Shift focus

- More on SMEs, less on practitioners
    - Focus on early results
    - Clinicians will be slow to employ CompBioMed results
- More on Models, less on HTC/HPC
    - General workshops are simply too general
    - Model-specific workshops
        - Speed of compute is key, however
        - Underlying code not of interest
- More on HTC, less on HPC

Miscellaneous

- Offer Solutions as a Service
    - Not “Software as a Service” or “HPC as a Service”

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  - Create pictorial representations for end-users
  - Then align representations with our CoE's objectives
- Need clear statement of data security
  - Critical to Business Model
  - All centres signed up to GDPR
- Consider expanding CoE's range of interest
  - Virtual reality for training purposes?
  - Machine learning plus medicinal chemistry for post-simulation validation

Annex VI: Second IAB Recommendations

What follows is a description of the 2nd IAB Recommendations

Medical Practice

- Consider more demos for awareness
  - Links with current imaging technologies
    - EOS for spine injuries, where EOS are a company offering image-based solutions for musculoskeletal pathologies
    - Clinical decision software
    - Low Dose X-ray (for videos)
  - Links with clinical decision software
- Patient engagement as a route to medical adoption
  - Public influence on their clinicians
    - Patients accept and implement treatments/medication when they understand the processes involved
    - Patient commitment through simulation exemplars
    - Extend definition of CompBioMed end users to include patients.
    - Self-investigation using medical avatar
      - Specific example given: 80% of bone fractures die within first year and changing the patient's gait can prolong life. Produce an app with an avatar which is given the same fractures as patient, then avatar displays where to expect pain when walking as normal, and where to expect pain when walking with a more beneficial gait.
- Public health/E-healthcare
  - Wearable devices
    - Current issue: unregulated
  - Home health apps
    - Unspecified issues (security?) with data storage and cloud
  - Determine the CoE's place in the public health landscape
- Look to online delivery & cloud solutions
  - Opportunity to share simulations and achieve belief in results
  - It may not be enough just to open eyes
- There is an issue with professional medics' adoption of simulation
  - Medics act within three timespans
    - Real time - now
    - Decision span – very soon
    - Long term – as long as it takes to get right answer

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    - Equipment manufacturers do run courses on "Simulation for Medics" and timescale to results is critical
    - Should investigate links with clinical simulation communities in US and EU
        - Mark Palmer to circulate information on some US communities
- Better focus on SMEs already active with medics

Teaching

- Look to more engagement with established medical training
    - Examples
        - Epicardio 4D simulation
        - ECGSIM
- Consider new training module to drop into lecture series "Modelling & Simulation using HPC" for medical schools
    - pretty simulation pictures do not relate to medics' life experience
    - teach medics to interpret these pictures
- Target early stage medical training – "they are used to it from the start"
- Simulators to aid clinical training - doctors like the idea of flight simulators

Research

- Sources of funding
    - Board view that biomedical simulation funding is far harder to get than experimental funding
    - Seek funding for modelling as part of experimental bids
    - Develop exemplar for future funding proposals
    - Cost benefit of modelling vs physical testing
- Better dissemination needed to Medical research
    - Medical Research Groups are mostly not aware of CompBioMed
- Foster better collaboration between computer scientists and practitioners
- Computer scientists learn from practitioners & practitioners learn from computer scientists
    - Route into research in clinical use

Regulatory

- Consider CoE role in regulation
    - In US some central services have approval from FDA
    - Drug development beginning to accept/mandate modelling & simulation in path to approval
    - CoE as "approved" provider

Industry

- Consider expand focus on medical equipment manufacturers as a route to acceptance
- Associate partners as a route to test the validity of the potential revenue streams
- Introduce service offerings in relation to
    - Pay per use
    - Pay per month
    - Pay more for urgent computing

Networks

- **Should be better engaged with community networks, target them to bring them into the CoE**

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- Biomedical research
- Manufacturers
- Patient groups

Future innovations the Board would like to see

- Achieving wide collaboration is a key innovation – seek more collaborations with established communities external to CompBioMed
  - CoE as a partner in other programmes
  - CoE as an entity not just individual partners
- Improve scientific and medical understanding through simulation
  - To push the design of better experiments
  - Trial application in clinical contexts
- Clear examples of commercialisation of services and products
  - People will pay for good results if they believe in its value
- Consider a new teaching module: "Benefits of modelling & simulation for medics"
  - Higher level to our existing "HPC for medics"
- Service provision of a "certified" toolkit, containing aspects on the following
  - Research – complex & multiscale
  - Teaching – collection of teaching modules
- Consider possible income streams
  - charging non-Core Partners (APs, 3rd parties) for HPC access
    - per use, per month, urgent computing, etc.
  - selling mobile apps for patient engagement
- Restrict focus on medics to those actively working with SMEs
- Longer term – Extend beyond servicing manufacturers to servicing clinicians

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