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Topic: Centres of Excellence for Computing Applications

D6.6 Final report on end-user solutions

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Lead beneficiary for this deliverable: USFD

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CI	Classified, as referred to in Commission Decision 2001/844/EC	

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1 Version Log

Version	Date	Released by	Nature of Change
V0.1			First Draft
V0.6			Final version before revision
V0.7			Pre-final version, to address internal reviewer comments
V0.9			Pre-final version, revised by all contributors
V1.0	19/09/2019	Emily Lumley	Final version for submission

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3 Definition and Acronyms

Acronyms	Definitions
1D/3D	1 Dimensional/3 Dimensional
AWS	Amazon Web Service
APDL	ANSYS Parametric Design Language
API	Application Programming Interface
BME	Budapest University of Technology and Economics
BMI	Body Mass Index
BSC	Barcelona Supercomputing Center

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CAAS	Magnetic Resonance Quantitative Analysis
CFD	Computational Fluid Dynamics
CoE	Centre of Excellence
CRyPTIC	Comprehensive Resistance Prediction for Tuberculosis: an International Consortium
CT (microCT/CT scan	Computerised Tomography
CT2S	Computed Tomography to Strength
DEM	Digital Elevation Model
DICOM	Digital Imaging & Communications in Medicine
DVC	Digital Volume Correlation
EOSC-hub	European Open Science Cloud Hub
EPCC	Edinburgh Parallel Computing Centre
ESRF	European Synchrotron Radiation Facility
EPFL	École Polytechnique fédérale de Lausanne
EPSRC	Engineering and Physical Sciences Research Council
FEM/FEA	Finite Element Method/Analysis
FFR	Fractional Flow Reserve
FPGA	Field Programmable Gate Arrays
GEC	Genetic Engineering of Cells
GPU	Graphics Processing Units
GROMACS	GROningen Machine for Chemical Simulations
HPC	High Performance Computing
HTBAC	High Throughput Binding Affinity Calculator
HTMD	High Throughput Molecular Dynamics
HTML	Hypertext Markup Language
ICEM	Integrated Computer Engineering and Manufacturing
ID	Identification
IST	In Silico Trials
ITK	Insight Toolkit
KACST	King Abdulaziz City for Science and Technology
LBM	Lattice Boltzmann Method
LBS	Language for Biochemical Systems
LHHM	Living Heart Human Model

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LIMA	Left Internal Mammary Artery
LRZ	Leibniz Supercomputing Centre
MSU	Moscow State University
MPI	Message Passing Interface
MQ	Message Queuing
MRI	Magnetic Resonance Imaging
MUSCLE	Multiscale Simulation Coupling Library & Environment
NA	Not Applicable
NCSA	National Center for Supercomputing Applications
NHS	National Health Service
NTU	Nanhang Technological University
ORNL	Oak Ridge National Laboratory
PaaS	Platform-as-a-Service
PACS	Picture Archiving and Communication System
PETSc	Portable, Extensible Toolkit for Scientific Computation
pFIRE	Parallel Framework for Image REgistration
PSNC	Poznan Supercomputing and Networking Center
RF	Radio Frequency
SAR	Specific Absorption Rate
ShARC	Sheffield Advanced Research Computer
STH	Sheffield Teaching Hospitals
STL	Standard Template Library
UCL	University College London
UEDIN	University of Edinburgh
UNIGE	University of Geneva
UOXF	University of Oxford
UPF	Universitat Pompeu Fabra
USFD	University of Sheffield
UvA	University of Amsterdam
VTK	The Visualization Toolkit
XNAT	The Extensible Neuroimaging Archive Toolkit

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4 HPC system definition

The following table provides a summary of all the HPC systems mentioned in this document. Detailed information (system specs or website) of these HPC systems are provided in D5.6 [1].

HPC System	Provider
ARCHER	EPCC
AWS	Amazon
Azure	Microsoft
Baobab	UNIGE
Blue Waters	NCSA
CADMOS	UNIGE
Cartesius	SURFsara
Cirrus	EPCC
Eagle	PSNC
JADE	UOXF
Lisa	SURFsara
Lomonosov	MSU
MareNostrum	BSC
Prometheus	PSNC
SANAM	KACST
ShARC	USFD
SuperMUC	LRZ
Titan	ORNL

5 Executive Summary

The main purpose of this deliverable is to provide an update to existing end-user applications previously described in deliverable D6.4, in order to include the further developments and implementations made up to M36 in the project. A secondary purpose of this document is that of providing a final update on the WP6 tasks that continued until the end of the project. The deliverable includes an introduction, a summary report for all applications and a description of the deployment of two new workflows based on applications: the CT2S and Alya workflows. The last four sections of this deliverable contain an exhaustive list of all 26 (11 cardiovascular, 9 molecular, 2 musculoskeletal and 4 others) end-user solutions and their user profiles. Note that information on impact activities including publications generated with each solution was reported in detail in D3.5 and WP2

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deliverables. The reader can refer to those documents for more detail; only a brief description is included here for each solution.

6 Introduction

Deliverable D6.6 provides a summary on the end use cases for all existing solutions, including those previously reported in D6.4. While deliverable D6.4 provides a report on selected emerging use cases for existing solutions at M24, and D6.1 reported on the solutions that were already available at the project's outset, the current report provides an update on user uptake since D6.4 at M24, and a history of user engagement since the beginning of the CompBioMed Centre of Excellence, with user numbers reported at three time points within the project (M0, M24 and M36). The expansion of the application users pool also prompted further development of the CompBioMed applications based on emerging and new end-users requirements. These are detailed, for each application, in the additional user uptake information. This report also includes additional applications that have been developed/exposed between M24 and M36.

The activity reported here relates to work carried out in WP6, in particular the following tasks as detailed in the Description Of the Action:

Task 6.2: Emerging Use Cases for Existing Solutions (M12-M36) [Deep Track]

Leader: USFD (6 PM), Partners: UPF (5 PM), UvA (5), UNIGE (5), LTG (5)

It should be noted that due to a clerical error D6.4 was originally marked as D.6.2.1 in the task description, whereas D6.6 was marked as D.6.2. Hereinafter we shall refer to these deliverables with the correct numbering, D6.4 and D6.6.

As D6.6 is an update to D6.4 and D6.1, we will only present changes since the last report. A fully extended end-users taxonomy was described in detail in D6.4, section 6.

Task 6.3: Adaptation to Commodity HPC Infrastructures (M12-M36) [Deep Track]

Leader: ACE (6 PM), Partners: BSC (3 PM), USFD (3), UEDIN (3), UCL (3), UPF (3), UOXF (3)

Task 6.5: Workflow Infrastructure Deployment (M1-M36) [Fast Track]

Leader: USFD (8 PM), Partners: UvA (5 PM), UNIGE (5), UPF (5), SARA (2)

7 End user report for each application

Based on the use cases described in D6.4 (M24), all application owners were asked to provide information on engagement with their end-users over the entire duration of the project (M01-M36). The CompBioMed Centre of Excellence currently covers a total of 26 biomedical applications: 11 in the cardiovascular domain, 9 in the molecular medicine domain, 2 in the musculoskeletal domain, and 4 other solutions in the more general biomedical domain. Five solutions have become inactive since M24, with some of these being merged with other applications to provide a more complete simulation

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suite. In the latest period of activities in WP6, particular emphasis has been placed on the trajectory of user engagement throughout the duration of the project and the role of users in the continuous improvement of the applications. User uptake is illustrated in Figures 1-5, starting with the total number of users across all solutions throughout the duration of the project (Figure 1), followed by a breakdown of users for each category of solutions (Figures 2-5). The breakdown of users across four categories of solutions is illustrated in Figure 6. These graphs show that user numbers have increased steadily and substantially throughout the duration of the project, with the largest increase seen in molecular medicine applications. A possible explanation for this is that compare with other categories, molecular medicine solutions are relatively mature down their development pipeline, with strong uptakes from pharmaceutical companies who attract a large number of users. In contrast, most cardiovascular and musculoskeletal applications are based on a personalised approach, and require some manual interactions with the workflow that limit the adoption of the technology to specialised users.

Each application has provided detailed information about their major user groups, the improvements they implemented in the application, as well as the impact generated by each user. This information is described in detail in Sections 9-12 under broad application categories.

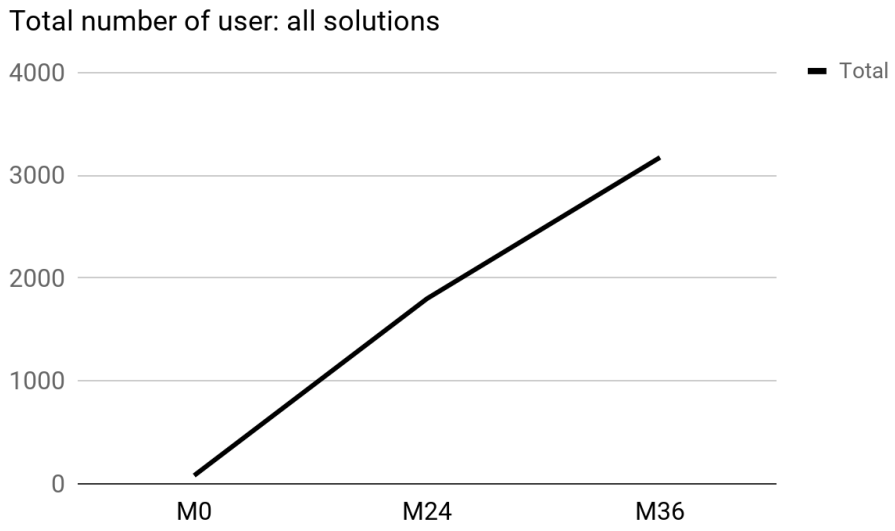

Figure 1: *Total number of users across all solutions throughout the duration of the project*

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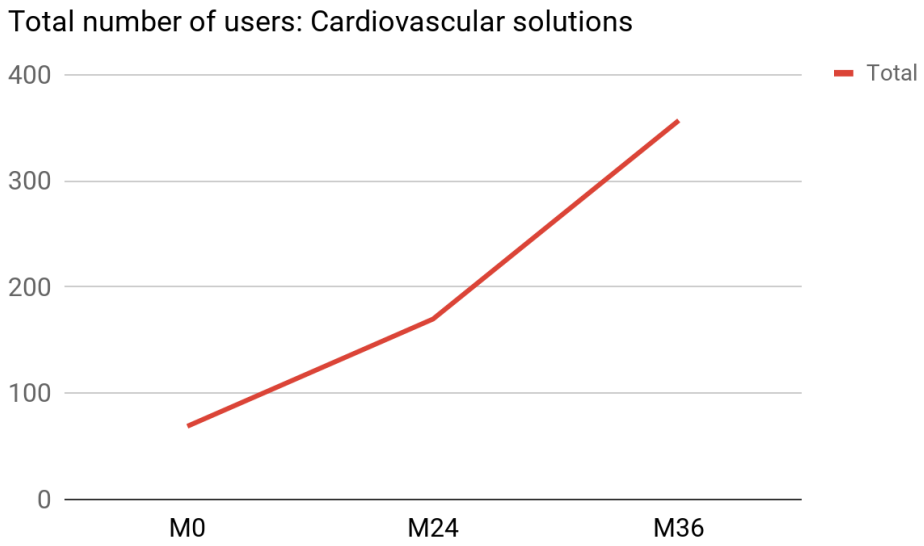

Figure 2: *Total number of users for cardiovascular solutions throughout the duration of the project*

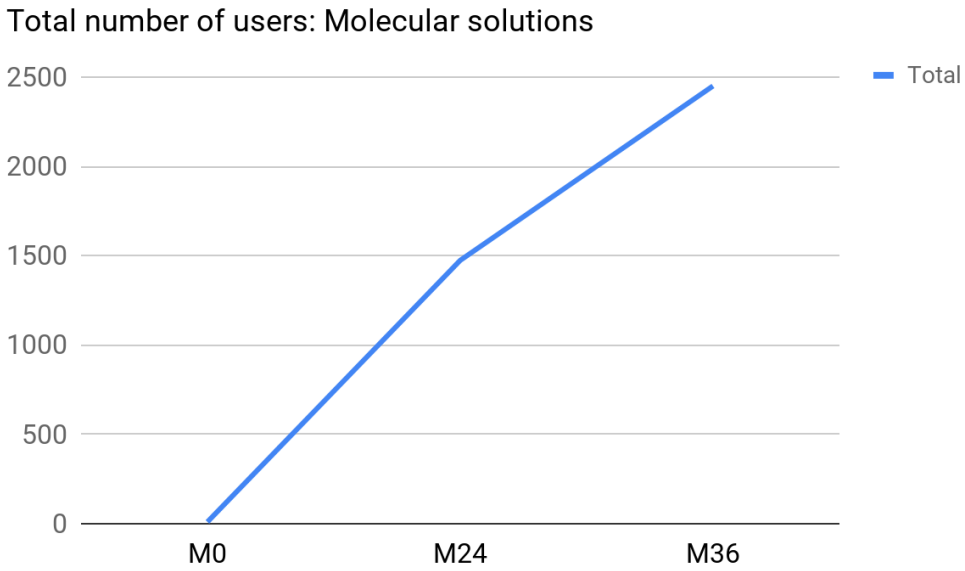

Figure 3: *Total number of users for molecular solutions throughout the duration of the project*

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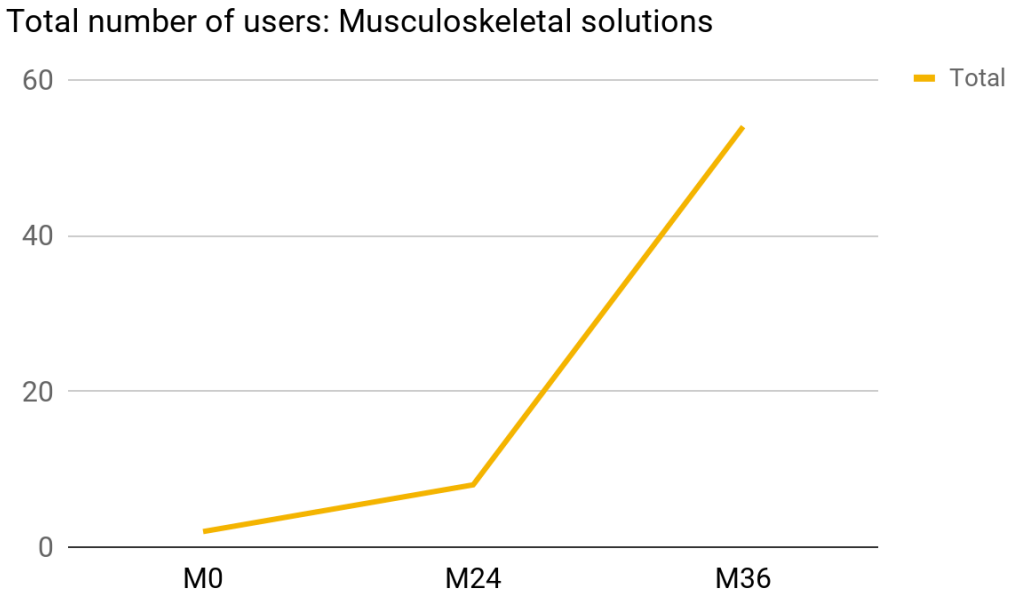

Figure 4: *Total number of users for musculoskeletal solutions throughout the duration of the project*

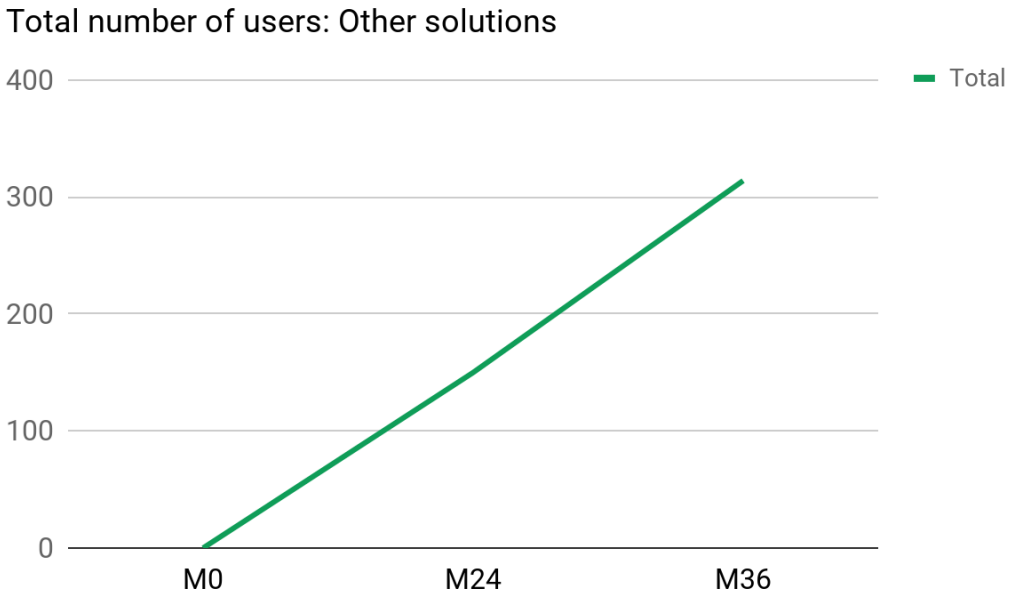

Figure 5: *Total number of users for other solutions throughout the duration of the project*

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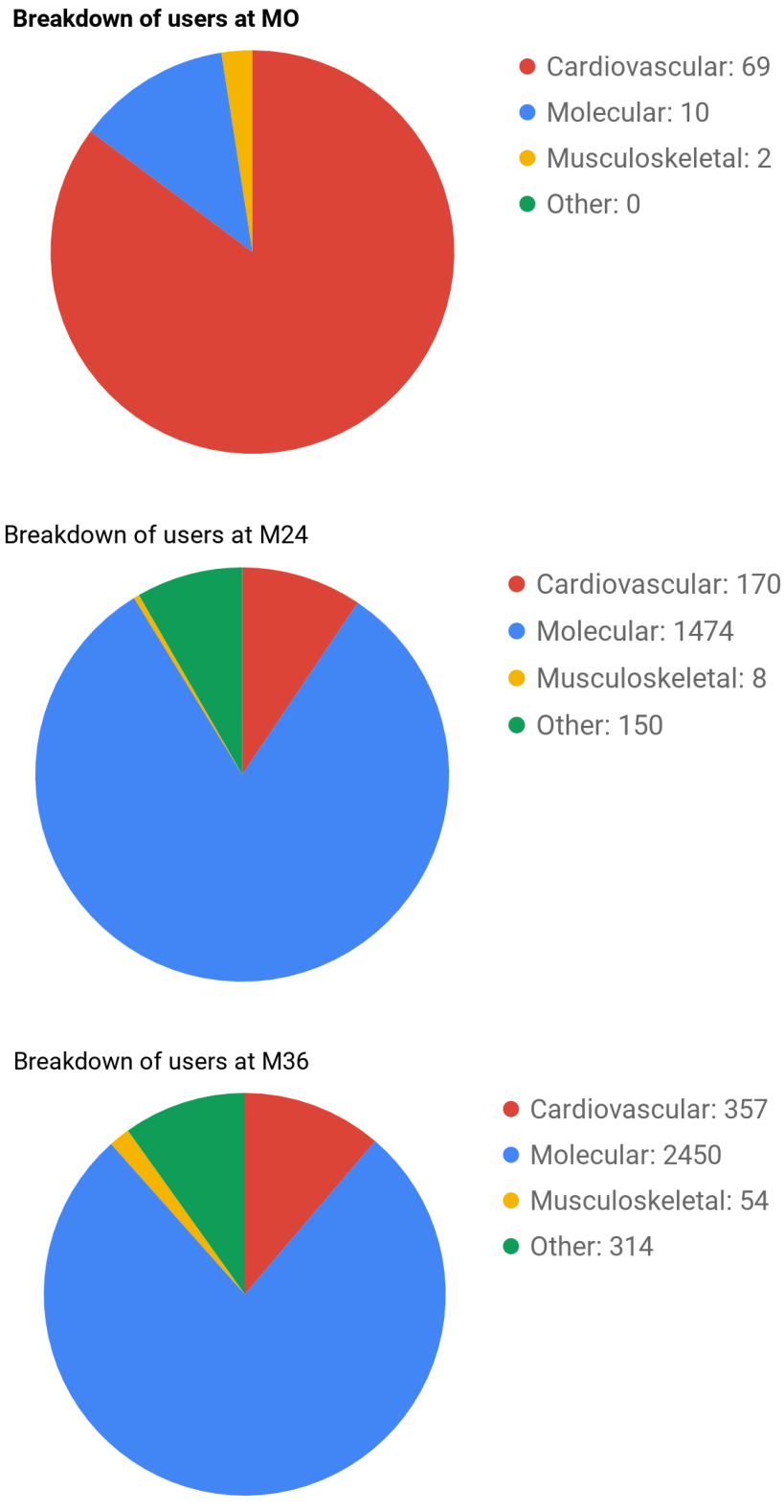

Figure 6: *Distribution of the end-users across the CompBioMed biomedical domains at M0 (top), M24 (middle) and M36 (bottom) of the project.*

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It should be noted that due to commercial sensitivity, some applications did not report detailed user information. These are indicated as "commercial sensitivity" towards the end of each relevant end solution. In such cases, the WP leader proposed an alternative way for collecting user data, which consisted in identifying users through the number of publications and citations related to those applications. The numbers gathered were then communicated with the application owners. However, it was not accepted as a viable way of tracking users due to legal implications as the commercial partners are legally obliged not to provide any information related to users (such as areas of research, publication domains) and are thus unable to confirm any indicative user numbers.

Based on the data on user type provided by each solution owner, a radar plot has been generated (Figure 7) to illustrate the user type composition within each CompBioMed domain. Overall, the largest user groups are clinical and non-clinical research, followed by clinical decision support and drug discovery, with few solutions currently targeted towards *in silico* preclinical trials or design & optimisation. The cardiovascular solutions seem to capture most of the user categories. The molecular solutions mostly target drug discovery and non-clinical research.

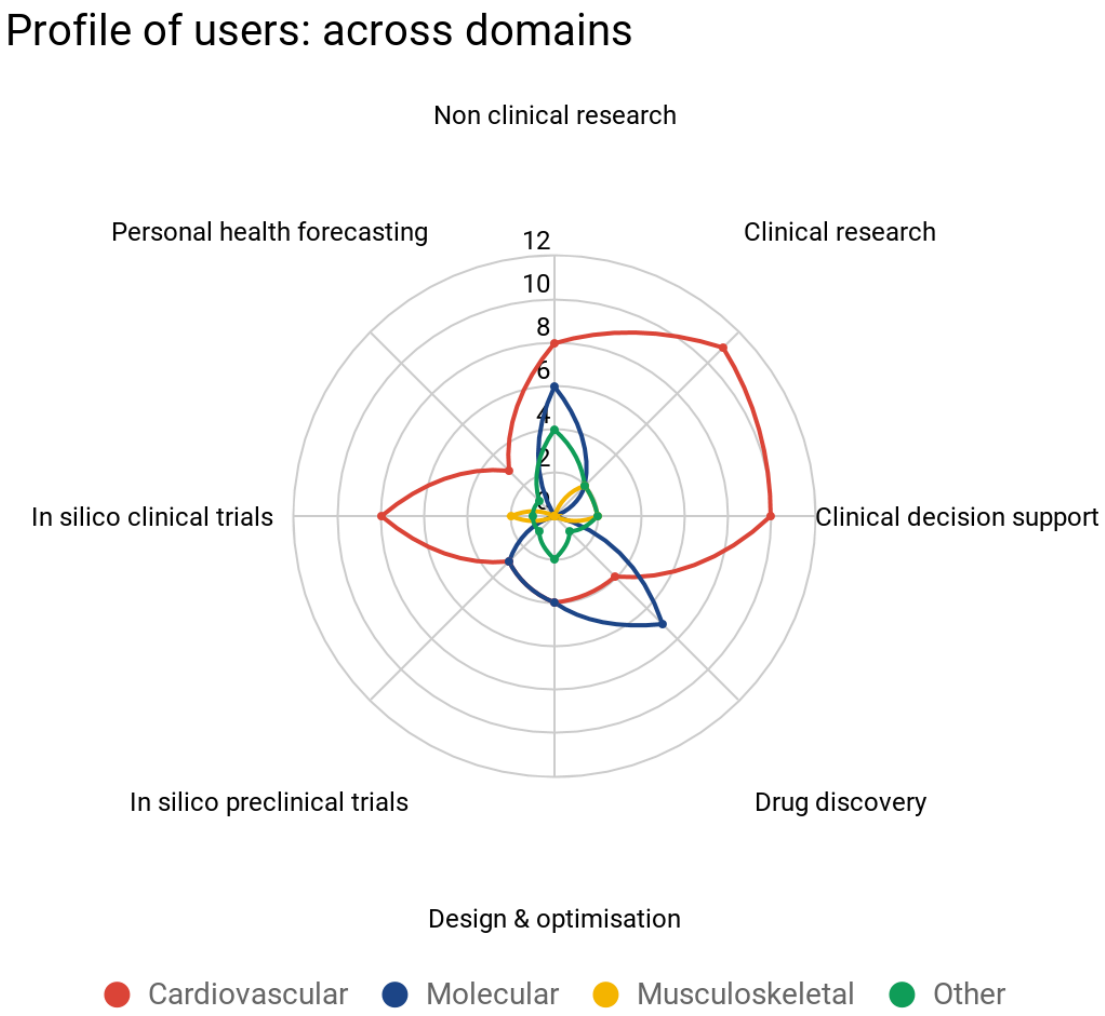

Figure 7: *User profile across all application domains as reported by solution owners.*

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8 Selected workflow infrastructure deployment

Workflow development and deployment within CompBioMed has been reported previously in D6.3: *Report on Workflow system provision* at M18 [2]. This section provides an update on the status of this activity for the period M18-36, focusing on two specific areas of workflow infrastructure development: (1) the CT2S hospital workflow, which targets delivering access to HPC workflows directly within a typical clinical environment in the UK; and (2) the data replication workflow to facilitate Alya analyses for which the technical developments have been reported in D5.5 [3].

8.1 CT2S hospital based workflow

This section summarises developments of the CT2S hospital-facing workflow implementation, reported in a recent conference abstract for the CompBioMed conference 2019 [4].

To improve clinical uptake of HPC technology there is a need to provide direct access to HPC workflows to clinical end-users without exposing the complexity of the underlying HPC environment. The Computed Tomography to Strength (CT2S) use case (further details are provided in Section 11.2 below) uses HPC approaches to provide quantitative metrics of bone strength based on CT images. This provides an opportunity to adapt an existing software framework developed to expose the CT2S workflow using a web service approach, in order to deliver the workflow directly to the clinical end-users. The request to perform a computational analysis and the return of an analysis report is made directly from the clinical environment by either the requesting clinician or a nominated representative. The hospital and university infrastructures of the workflow have been developed to specifically be deployed in a typical clinical/university setting. However, in collaboration with WP5 we are working towards a detailed description of the data transfer requirements and metadata scheme that will provide a solid basis for the re-creation of the same workflow in other non-UK settings (for example using EUDAT services). The engineering elements of the workflow consist of semi-automated segmentation of bones from CT images in DICOM format, 3D mesh generation, local material property definition based on CT attenuation, solution of the model over several loading conditions using FEM through the estimation of bone strength.

The FEA (typically 300k elements) uses ANSYS Mechanical APDL [5] with run times of around 90 minutes per load case for contact mechanics models and 8 minutes for the Multiple Point Constraint models [6] using the ShARC Tier 3 HPC hosted at the University of Sheffield (2016 processors and 8832 GB RAM). In order to deliver this workflow to clinical end-users, a software framework has been developed to automate the workflow from a clinical perspective, from the point of data entry to results reporting. This framework includes several elements, some of which are common to other computational workflows developed as part of the EPSRC MultiSim project [7], which are listed below:

- CT2SWebApp: provides the CT2S web site [8] allowing clinical users to initiate a request to perform a CT2S analysis and provides functionality to enter the structured data fields required to inform the finite element analysis (age, BMI, etc.)
- django-multisim: provides common web app functionality to multiple web services and includes DICOM file submission using the XNAT [9] API.
- AMQPClient: provides common RabbitMQ [10] messaging functionality to multiple apps.
- DataExchange: provides XNAT file transfer functionality to multiple apps.

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The operation of the workflow is illustrated schematically in Figure 8.

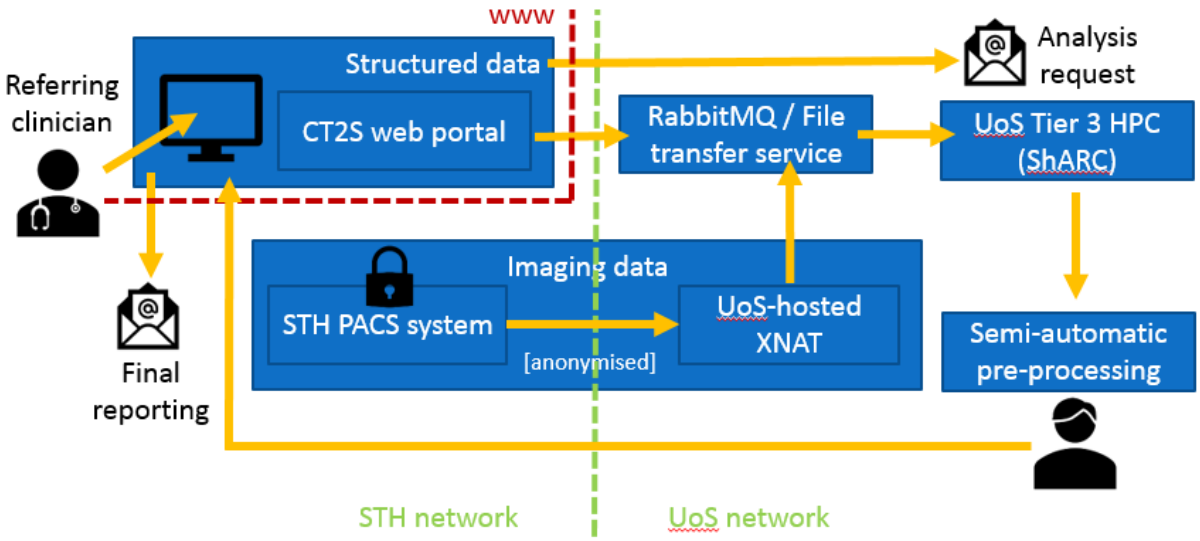

Figure 8: *Operation of CT2S workflow from initial clinician request to final reporting of bone strength assessment*

In addition to data entry within the CT2S web portal, the clinical team can directly transfer patient DICOM images from the Sheffield Teaching Hospitals (STH) NHS Foundation Trust PACS system to a University of Sheffield hosted XNAT database. This transfer process is facilitated by the Scientific Computing team at STH using the pix web service and incorporates their own in-house anonymisation step to remove all personal data from the DICOM images. Consequently, all information identifying the patient remains within the STH network, and the referring clinician assigns an independent, anonymous, patient ID within the CT2S web portal when the analysis is requested. This ID is common to that assigned during transfer of images to the XNAT database.

The django-multisim, AMQPClient and DataExchange services are used to orchestrate processes within the University of Sheffield network, which includes an automated request for analysis to a designated email account. Due to the semi-automated nature of the image segmentation, some manual intervention is required during pre-processing stages. The mesh is then generated automatically using ANSYS ICEM [11], subsequent load definition and finite element solutions are automated using software-specific scripting mechanisms, which have been used to generate results as described in a previous publication [6]

The simulation outputs are uploaded by a workflow operator to the corresponding job ID's web page using a HTML form. Once all the required fields have been supplied, an option to download a PDF report in a standardised format appears on the job's page. At this point, the requesting clinician is automatically sent an email with a link to this page. Email notifications are also sent whenever the job is updated to track progress with the analysis request.

This implementation has been tested with retrospective data obtained as part of the MultiSim project. Indicative timescales for individual elements of the workflow are reported as follows:

- Initialisation of workflow, including log onto CT2S web portal and transfer of imaging data from PACS to XNAT ~ 10 minutes

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- Image download and segmentation of femur from volumetric image data ~ 120 minutes
- Meshing of femur and assignment of material property data including initial set-up of ANSYS model ~ 10 minutes
- Finite Element Model solution step ~ 10 minutes for single load case
- Results export, post-processing and final report preparation ~ 10 minutes

This results in an overall workflow timescale of 180 minutes, majority of this process being dominated by the image segmentation step required to define the anatomy of the femur. A significant advantage of porting the CT2S workflow to HPC is the potential to expand the FEM analysis from a single load case to multiple load cases, to assess the sensitivity of fracture risk to the loading conditions on the femur.

8.2 Alya workflow

General use of Alya is described below in Section 9.1, this section focuses on the development of workflow processes to facilitate Alya analyses using large datasets, similar to the process described previously for the DVC workflow in D6.3 [2]. This workflow aims to explore the capabilities and challenges towards the use of Alya for Exascale simulations.

Within CompBioMed, Alya simulations focus on an FEM-based electro-mechanical coupling solver, optimised for HPC infrastructures. In order to apply Alya to large scale input data, a test scenario has been developed as reported in D5.5 [3] using the B2SAFE [12] data replication tools arising from the EUDAT project [13] and facilitated by EOSC-hub to exchange data between three HPC facilities (BSC, SURFsara and EPCC).

The data workflow for this scenario starts with the acquisition of raw data at the European Synchrotron Radiation Facility (ESRF) (similar to acquisition at the Diamond Light Source in the UK described in D6.3) and a second dataset acquired using microCT at the University of Manchester [14].

In the case of the data acquired at the ESRF, the data was initially locally stored on tape and then transferred to BSC using 8TB hard disk drives that the researchers carried to the site during the experiments. Data was then pre-processed at BSC using both manual and automated steps for image stitching, segmentation and meshing.

In the case of the microCT data from the University of Manchester, the data was uploaded to an unlimited capacity Google drive account. The compressed segmented data with labels occupied 173MB and the reconstructed volume of the data occupies 28GB (image with labels).

In order to address this large data transfer problem, a data replication service is then provided for the resulting 3D FE mesh files used as input for Alya analyses (maximum file size 1.2TB, total data volume 24TB). This allows researchers to leverage compute resources hosted at all three participating centres. Replicated data is provided both as a direct download for researchers and collaborators to exploit the simulation results and/or replicate the simulations or workflows. Use of B2SAFE allows tight integration of a transparent data policy within the replication process, as described in D5.5. Each centre plays a distinct role in the replication process with BSC providing pre-processing and compute services, EPCC providing compute service and SURFsara providing an archiving service.

The feasibility of this approach, and that of the DVC pilot reported in D6.3, supports the maturity of such technologies to robustly support data management aspects associated with the large-scale input

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data required for HPC simulations using CompBioMed tools. A more general assessment of the ease-of-use and uptake of these approaches within the target domains (cardiovascular and musculoskeletal research in these exemplars) is now required which can be achieved through engagement with end-user groups detailed in the following sections for Alya and CT2S.

8.3 Exascale Alya workflow

In the case of the microCT data provided by the University of Manchester, a preliminary setup of a full workflow has been implemented. This workflow unveiled new challenges that should be addressed to create exascale, high resolution and relevant cardiovascular simulations.

Researchers at BSC along with their collaborators want to create high fidelity simulations of the human cardiac conduction system along with the full biventricular description of the cardiac muscle. This is a multi-disciplinary collaborative work that aims to reproduce the human anatomy as closely as possible. For this purpose, the cardiac conduction system was stained in order to extract its exact morphology, as can be seen in Figure 9.

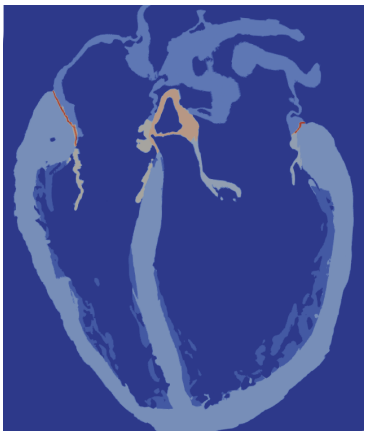

Figure 9: *The image acquired has a 45µm isotropic voxel size, with all 5 cardiac chambers labelled, including the mitral and tricuspid valve, cardiac conduction system, atrio-ventricular (AV) and sino-atrial (SA) nodes.*

The image is 3108 x 2508 x 3749 pixels in size. The hexahedral mesh corresponding to that image would have 5.5 billion elements. The aim was to solve this problem using 50K cores, since BSC launched an internal challenge to solve exascale problems using MareNostrum IV. Given the scalability of Alya, an approximate amount of 5 billion elements would be most efficiently run on 50K cores.

The mesh itself includes the fiber information and additional labels required for electrophysiology simulations, which is expected to occupy 697GB of space. This amount of memory is required at the initial problem setup within Alya in order to do the mesh partitioning and other mesh preparation steps. Mesh generation and fiber calculation could pose a potential problem. A high memory node within MareNostrum IV has a total of 380GB capacity; 7.9GB per core. MareNostrum has a total of 216 high memory nodes with 48 cores each (10,368 cores in total). Currently, it is impossible to deal with a 697GB input problem. However, given a manageable sized input to a high memory node, the mesh division can be performed in each partition. Alya is capable of solving a problem of 5.5 billion elements, just not fully exploiting high resolution (≈697GB) input data.

Detailed simulation requirements are broken down below:

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- Image subsampling: The currently estimated mesh size is too large to fit into one node of MareNostrum IV; therfore downsampling the image twice along each dimension (increasing the voxel size to 90µm) provides a more feasible mesh size of around 700 million elements and 90GB in size. This, however, reduces the resolution of the data, which goes against the aim of an exascale application.
- Hexahedral mesh generation from an image: An ITK [15]/VTK [16] based program has been developed to convert the image into a hexahedral mesh, where every voxel is transformed into a hexahedron and the voxel value (label) is assigned to it. Additional model information needs to be included in the future.
- Fiber orientation: A rule-based algorithm [17] with a corrected left ventricular outflow tract and right ventricular outflow tract orientation is being used, but currently it is not parallelised.
- Cell model: Ventricular myocardial tissue has different electrophysiology properties to the purkinje fibers, therefore labels indicating this have to be included, along with the apex-to-base normal heterogeneity.

Further work is required to launch the Exascale workflow with ultra high-resolution data using Alya. A new input strategy should be explored, along with optimisation of the pre-processing tools to handle the large amount of data.

9 Cardiovascular solutions

9.1 Alya

The purpose of Alya is to perform Cardiac Computational Mechanics simulations, from tissue to organ level. FEM-based fluid-electro-mechanical coupling solver, specifically designed for the efficient use of supercomputing resources.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	✓
Clinical decision support	✓
Drug discovery	
Design & optimisation	✓
In silico preclinical trials	
In silico clinical trials	✓
Personal health forecasting	

Provider: BSC

Contact email: mariano.vazquez@bsc.es

Number of user organisations (list the top 5): University of Oxford, Universitat Pompeu Fabra, Universitat de Valencia, George Mason University, ELEM Biotech, Medtronic

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Estimated users at M0: 30 internal and 20 external

Estimated users at M24: 35 internal and 30 external

Estimated users at M36: 40 internal and 40 external

(IMPORTANT NOTE: as Alya is used in different domains, the number of users is the grand total)

Access mode: Direct

URL: https://www.bcs.es/research-and-development/software-and-apps/software-list/alya

User manual: mariano.vazquez@bsc.es

HPC Systems: MareNostrum (BSC), ARCHER (EPCC), Cartesius (SURFsara), Blue Waters (NCSA), SuperMUC (LRZ)

HPC motivation: Solve unreducible model; Multiscale model; Strongly coupled multiphysics model.

Additional user information:

End user name	Blanca Rodriguez's group	Oscar Camara's group	JR Cebral's group	ELEM Biotech	**Dr. Asimina Kazakidi's group**
Affiliation	UOXF	Universitat Pompeu Fabra	George Mason University	-	**University of Strathclyde**
Application area	Cardiac modelling	Cardiac modelling	Vascular simulations (aneurisms)	Cardiovascular modelling, respiratory system, cerebro-spinal fluid	**Cardiovascular modelling of the right side of the heart**
No. of associated users	6	5	2	3	**1**
Target use	Research	Research / educational	Research	Commercial, research	**Research**
Improvements implemented	New models, efficiency, etc.	N/A	Efficiency	Efficiency, models, deployment, etc.	**N/A**
Impact	Papers	Papers	Papers	Product design, media release, papers	**N/A yet**
Use of any e-infrastructure available via CompBioMed	BSC and EPCC	BSC	BSC	BSC	**BSC**

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9.2 HemeLB

This code simulates the blood flow through a stent (or other flow diverting device) inserted in a patient's brain. The aim is to discover how different stent designs (surface patterns) affect the stress the blood applies to the blood vessel, in particular in the region of the aneurysm being treated. The pipeline also allows the motion of magnetically steered particles, for example coated with drugs, to be simulated and estimates made as to where they might statistically end up. More technically, the pipeline takes as input an STL file of the surface geometry of the patient, generally obtained via segmentation of DICOM images from a CT-scan. Also required is the (peak) velocity-time profile of fluid flow at each of the inlets to the simulated region. If inserting a stent, the start and end points of the stent in the vessel must be specified, as well as an image file containing a black and white representation of the surface pattern (black signifying 'solid'). The HemeLB setup tool voxelizes the geometry bounded by the input STL at the given resolution, and HemeLB (lattice-Boltzmann CFD solver) then simulates the fluid flow within that geometry, using the given velocity-time profiles for each inlet. Once complete, the simulation output is analysed using the hemeXtract utility, which can produce images of cross-sectional flow, or 3D shots of wall shear stress distribution in the geometry using ParaView visualisation software.

End-user solution type	**Please tick one or more**
Non-clinical research	
Clinical research	✓
Clinical decision support	✓
Drug discovery	
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	✓
Personal health forecasting	

Provider: UCL

Contact email: robin.richardson@ucl.ac.uk

Number of user organisations (list the top 5): UCL, Hamad Medical Corporation, Qatar University

Estimated users at M0: 9

Estimated users at M24: 40 (mostly academia)

Estimated users at M36: 40

Access mode: Direct

URL: https://github.com/UCL/hemelb

HPC Systems: ARCHER (EPCC), SuperMUC (LRZ), Prometheus (PSNC), Blue Waters (NCSA)

HPC motivation: Solve unreducible models

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Additional user information:

End user name	Peter Coveney's group	Julien Abinahed's group	Abbes Amira's group
Affiliation	UCL	Hamed Medical Corporation, Qatar	Qatar University
Application area	Cardiovascular	Cardiovascular	Cardiovascular
No. of associated users	4	3	3
Target use	Research	Research / clinical	Research
Improvements implemented	Fully automated input file generation pipeline	Integrated clinical pipeline with image segmentation	Real time visualisation with GPU, FPGA implementation
Impact			Papers
Use of any e-infrastructure available via CompBioMed	EPCC		

9.3 PolNet

PolNet is a software tool for the computer simulation of blood flow in realistic microvascular networks imaged with a wide variety of microscopy and clinical imaging techniques. To date, PolNet has contributed to, a) uncovering the relationship between blood flow and blood vessel biology and its importance for correct vascularisation of tissues, and b) developing ways of predicting retinal vascular damage in diabetic retinopathy patients. PolNet facilitates the adoption of cutting-edge computer simulation technology by non-experts in the Biosciences. PolNet provides a complete workflow for image processing, three-dimensional vascular network reconstruction, and blood flow simulation with the HemeLB software. In addition, it provides tools for studying the relationship between the flow simulated and cellular/molecular readouts quantified in the same images. To date, PolNet has contributed to establishing the relationship between blood flow and endothelial cell polarisation and migration during vascular development. In addition, PolNet is being used to develop novel methods for the prediction of sight-threatening complications in diabetic retinopathy. PolNet uses the Docker platform to facilitate deployment in experimental biology laboratories and hospitals. PolNet allows execution of HemeLB simulations in both commodity software and High Performance Computing resources. Ongoing work is aimed at enabling HemeLB execution in Cloud resources.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	✓

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Clinical decision support	
Drug discovery	
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	
Personal health forecasting	

Provider: UEDIN

Contact email: miguel.bernabeu@ed.ac.uk

Number of user organisations (list the top 5): University of Lisbon, Max Delbruck Center for Molecular Medicine, Harvard University

Estimated users at M0: 0

Estimated users at M24: 0

Estimated users at M36: 9

Access mode: Source

URL: https://github.com/mobernabeu/polnet

HPC Systems: ARCHER (EPCC)

HPC motivation: Solve unreducible model

Additional user information:

End user name	Claudio A. Franco's group	Holger Gerhardt's group	Jennifer K. Sun's group
Affiliation	Instituto de Medicine Molecular, University of Lisbon	Max Delbruck Center for Molecular Medicine, Berlin	Joslin Diabetes Center, Harvard University
Application area	Developmental vascular biology	Developmental vascular biology	Ophthalmology research
No. of associated users	3	3	3
Target use	Research	Research	Research
Improvements implemented	Remote cloud execution	Remote cloud execution	

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Impact	Papers	Papers	Papers
Use of any e-infrastructure available via CompBioMed	EPCC	EPCC	EPCC

9.4 Flow Diverter Simulator

Palabos – Flow Diverter Simulator: This solution, currently in its final stage of development, uses Palabos to provide a vertical solution for the pre-operative planning for the insertion of flow diverters. CT scan images of blood vessels with aneurysms or other anomalies are converted into a Lattice Boltzmann Method (LBM) model. Different types of flow diverters are numerically inserted to test their impact on the blood flow pattern. Simulation output includes wall shear stress distribution in the aneurysm to predict the rate of blood clotting.

End-user solution type	**Please tick one or more**
Non-clinical research	
Clinical research	✓
Clinical decision support	✓
Drug discovery	
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	✓
Personal health forecasting	

Provider: UNIGE

Contact email: jonas.latt@unige.ch muscle

Number of user organisations (list the top 5): University of Geneva, Université libre de Bruxelles, CHU-Charleroi, Hopitaux de Lyon, Cardiatis, Numeca International,

Estimated users at M0: 0

Estimated users at M24: 0

Estimated users at M36: 54

Access mode: Source

HPC Systems: Baobab (UNIGE), CADMOS (UNIGE)

HPC motivation: Solve unreducible model; Multiscale model; Strongly coupled model.

Additional user information:
Due to commercial sensitivity, some information below has been anonymised. However, detailed

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user numbers have been accounted for in the overall statistics reported in Section 6.

End user name	NDA	NDA	NDA	NDA	NDA
Affiliation	NDA	NDA	NDA	NDA	NDA
Application area	Biomedical	Medical	Medical	Biomedical	Computational fluid dynamics
No. of associated users	NDA	NDA	NDA	NDA	NDA
Target use	Research / patient treatment	Research / patient treatment	Research / patient treatment	Research / commercial	Commercial
Improvements implemented					
Impact					
Use of any e-infrastructure available via CompBioMed					

9.5 Palabos

Palabos is a lattice-Boltzmann Method (LBM) solver, available as open source, and massively parallel. The team of Prof Bastien Chopard at University of Geneva (Switzerland) has specialised it to solve a number of relevant biomedical problems, including simulation of blood flow, and bone cement penetration during vertebroplasty. The software has specific features to deal with biomedical problems including tools to read medical images. Palabos was tested on CADMOS BlueGene/Q (EPFL), Baobab (UNIGE).

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	✓
Clinical decision support	✓
Drug discovery	✓
Design & optimisation	✓
In silico preclinical trials	✓
In silico clinical trials	✓
Personal health forecasting	✓

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Provider: UNIGE

Contact email: jonas.latt@unige.ch

Number of user organisations (list the top 5):

Estimated users at M0: 0

Estimated users at M24: 0

Estimated users at M36: General user base (the software is free for download, users are not tracked individually). Estimated around 100.

Access mode: source

URL: http://www.palabos.org

HPC Systems: Baobab (UNIGE), CADMOS (UNIGE), ARCHER (EPCC), MareNostrum (BSC)

HPC motivation: Solve unreducible model, validate reduced-order model, Test model convergence, Larger space-time regions, Uncertainty quantification, Inform surrogate model, Multiscale models, Strongly coupled models.

Additional user information:

No detailed information available as users are not individually tracked.

9.6 OpenBF

OpenBF is a whole-circulation 1D cardiovascular model that describes the physics of pulse wave propagation throughout the main vessels of the arterial system, including the Circle of Willis. The model has been previously quantitatively validated with predictions from other models and experimental data. In a recently published study driven by our clinical end-users and collaborators [18, 19, 20] we have used the code to identify more effective biomarkers of a cardiovascular condition affecting patients after stroke (cerebral vasospasm), and more recently have started developing the code towards clinical utility as a computational platform to explore what-if clinical scenarios to support clinical decision in treatment of ischaemic stroke and mechanical removal of blood clots.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	✓
Clinical decision support	✓
Drug discovery	
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	
Personal health forecasting	✓

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Provider: USFD

Contact email: a.marzo@sheffield.ac.uk

Number of user organisations (list the top 5): USFD, University Hospital of Tours, Federal University of ABC (Santo Andre', Brazil)

Estimated users at M0: 1

Estimated users at M24: 6

Estimated users at M36: 6

Access mode: Source

URL: https://INSIGNEO.github.io/openBF

User manual: https://insigneo.github.io/openBF/Docs/index.html

HPC Systems: ShARC (USFD), HPC Cloud (SURFsara)

HPC motivation: Uncertainty quantification; sensitivity analysis; embarrassingly parallel simulation

Additional user information:

End user name	Alessandro Melis	Ana Paula Narata's group	Ahmed Mustafa
Affiliation	Vivacity Labs, London, UK	University Hospital of Tours, France	USFD
Application area	Transportation and machine learning	Diagnosis of cerebral vasospasm, management of ischaemic stroke	Treatment of ischaemic stroke
No. of associated users	1	3	2
Target use	Commercial	Clinical	Research / clinical
Improvements implemented	openBF formed the theoretical basis for the development of a model aimed at a more effective management of traffic at national level in the UK	The code was extended to allow simulation of blood clot removal and the influence of the medical device used for this treatment on blood flow	Code was further developed to allow prediction of influence of the medical device used in procedure (thrombectomy) on haemodynamics and the blood clot being removed.

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Impact	N/A	Papers [19, 21] and conference presentations[1]	Conference presentations[2]
Use of any e-infrastructure available via CompBioMed	HPC Cloud (SURFsara), ShARC (USFD)	HPC Cloud (SURFsara), ShARC (USFD)	HPC Cloud (SURFsara), ShARC (USFD)

9.7 HemoCell

High-performance library to simulate the transport properties of dense cellular suspensions, such as blood. It contains validated material models for red blood cells and additional support for further cell types (white blood cells, platelets). The blood plasma is represented as a continuous fluid simulated with an open-source LBM solver (Palabos). The cells are represented as DEM membranes coupled to the plasma flow through a tested in-house immersed-boundary implementation. HemoCell is computationally capable of handling a large domain size with high number of cells (10^4-10^6 cells).

End-user solution type	**Please tick one or more**
Non-clinical research	
Clinical research	✓
Clinical decision support	✓
Drug discovery	
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	✓
Personal health forecasting	

Provider: UvA

Contact email: g.zavodsky@uva.nl

Number of user organisations (list the top 5): UvA, NTU, BME, UOXF

Estimated users at M0: 0

Estimated users at M24: 12

Estimated users at M36: 12

[1] Work presented at meeting on EU project INSIST, Milan (Italy, April 2019)
Work to be presented at CompBioMed conference in London, September 2019

[2] Work presented at meeting on EU project INSIST, Milan (Italy, April 2019)
Work to be presented at CompBioMed conference in London, September 2019

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Access mode: Source

URL: https://www.hemocell.eu

HPC Systems: Cartesius (SURFsara), Lisa (SURFsara), SuperMUC (LRZ), MareNostrum (BSC), Eagle (PSNC), Sanam (KACST), Lomonosov (MSU)

HPC motivation: Solve unreducible model; Multiscale model; Strongly coupled model.

Additional user information:

End user name	UvA	NTU	BME	Department of Engineering Science
Affiliation	UvA	NTU	BME	UOXF
Application area	Microfluidic blood flows	Malaria research	Microfluidic research in white blood cell transport	microfluidics (red blood cell flows in capillaries)
No. of associated users	7	2	2	1
Target use	Research	Research	Research	Research
Improvements implemented	Several technical improvements in the implementation and various new features added (new boundary conditions, modelled cell types)	Added new features to model the malaria parasite in blood flow	Added new cell type (white blood cell)	N/A
Impact	Journal papers, local institutional media news, ERCIM article	Papers	Local news item	N/A
Use of any e-infrastructure available via CompBioMed	SURFsara	None	None	None

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9.8 Virtual Assay

The Virtual Assay predicts a variety of responses of human cardiac behaviour under pharmacological drug treatment to help with drug safety and efficacy. Virtual Assay starts with well-understood human cellular biology models and modulates the variables to generate a range, or population, of models, which will respond differently to the same inputs. These populations are then calibrated against experimental data, retaining only those models in Calibrated Model Populations within the range of experimental observations. Once calibrated, these populations can be used to analyse the effects of different pharmaceutical agents on cellular response at the population level.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	✓
Clinical decision support	✓
Drug discovery	✓
Design & optimisation	
In silico preclinical trials	✓
In silico clinical trials	✓
Personal health forecasting	

Provider: UOXF

Contact: elisa.passini@cs.ox.ac.uk

Number of user organisations (list the top 5): Janssen Pharmaceutica, UCB Pharma, Merck MSD, Amgen Inc

Estimated users at M0: 5

Estimated users at M24: 14

Estimated users at M36: 20

Access mode: Source, Indirect

URL: http://www.cs.ox.ac.uk/ccs/virtual-assay

User manual: elisa.passini@cs.ox.ac.uk

HPC Systems: NA

HPC motivation: Multiscale models

Additional user information:

End user name	Janssen	UCB Pharma	Merck MSD	Amgen Inc

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	Pharmaceutica			
Affiliation	Janssen Pharmaceutica	UCB Pharma	Merck MSD	Amgen Inc
Application area	Pharma	Pharma	Pharma	Pharma
No. of associated users	3	2	5	4
Target use	Commercial / research	Commercial / research	Commercial / research	Commerical / research
Improvements implemented	User feedback guided the development of V2 and V3 of the software	User feedback guided the development of V2 and V3 of the software	User feedback guided the development of V3 of the software	User feedback guided the development of V3 of the software
Impact	Journal papers, media release	Conference presentations	Papers, conference presentations	Conference presentations
Use of any e-infrastructure available via CompBioMed	None	None	None	None

9.9 SIMULIA LHHM

The SIMULIA Living Heart Human Model (LHHM) is a high-fidelity multi-physics model of a healthy, 4-chamber adult human heart and proximal vasculature. The LHHM was developed within The Living Heart Project, a translational initiative to advance the use of simulation in the delivery of safe and effective cardiovascular devices and clinical treatments. This is a finite element model of a human heart backed by the power of Abaqus within the SIMULIA Realistic Simulation software suite. The response of the LHHM is governed by realistic electrical, structural and fluid-flow physics. The model comprises a ready-to-execute dynamic, electro-mechanical simulation; refined geometry; a blood flow model, and a complete characterisation of cardiac tissues including passive and active behaviours, its fibrous nature and the electrical pathways.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	✓
Clinical decision support	✓
Drug discovery	✓
Design & optimisation	✓

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In silico preclinical trials	
In silico clinical trials	✓
Personal health forecasting	

Provider: Dassault Systemes

Contact email: clint.davies-taylor@3ds.com, steve.levine@3ds.com

Number of user organisations (list the top 5):

Estimated users at PM36: Academia, Industry, Clinicians and Regulatory Authorities

Access mode: Source, Direct

URL: https://www.3ds.com/products-services/simulia/solutions/life-sciences/living-heart-human-model/

HPC Systems: ARCHER (EPCC), ShARC (USFD)

HPC motivation: Solve unreducible model; Multiscale model; Strongly coupled multiphysics model.

Additional user information:

Commercial sensitivity.

9.10 Chaste

Chaste supports Cardiac Computational Mechanics simulations, from tissue to organ level. It includes an FEM-based electromechanical coupling solver, specifically designed for the efficient use of supercomputing resources.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	✓
Clinical decision support	✓
Drug discovery	✓
Design & optimisation	✓
In silico preclinical trials	✓
In silico clinical trials	✓
Personal health forecasting	✓

Provider: UOXF

Contact email: blanca.rodriguez@cs.ox.ac.uk

Number of user organisations (list the top 5): 4

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Estimated users at M0: 4

Estimated users at M24: 23

Estimated users at M36: 23

Access mode: download package from website

URL: https://chaste.cs.ox.ac.uk/trac

User manual: https://chaste.cs.ox.ac/public-docs/

HPC Systems: MareNostrum (BSC), ARCHER (EPCC)

HPC motivation: Highly biophysically-detailed multiscale model of cardiac electrophysiology.

Additional user information:

End user name	Blanca Rodriguez's group	Rina Ariga, Stefan Neubauer and Hugh Watkins	Raffaele Coppini, Elisabetta Cerbai
Affiliation	UOXF	John Radcliffe Hospital, Radcliffe Department of Medicine	Department NEUROFARBA, University of Florence
Application area	- Whole-ventricular simulations of pharmacological action in human hypertrophic cardiomyopathy; - Impact of genetic disease on human cardiac function; - Simulation of the forward electrocardiographic problem in the human ventricles; - Investigation of ischemia-induced arrhythmogenesis in humans using computer simulations; - Research of novel mechanisms of conduction abnormalities in arrhythmogenic right ventricular cardiomyopathy; - Investigations of proarrhythmic mechanisms caused by ion channel mutations and acute myocardial ischaemia.	Impact of hypertrophic cardiomyopathy in human cardiac function	Whole-ventricular simulations of pharmacological action in human hypertrophic cardiomyopathy
No. of associated users	16	3	2

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Target use	Research	Research	Research
Improvements implemented	- Development of a simulation pipeline for the investigation of concurrent anatomical and electrophysiological alterations in human heart disease; - Development of a simulation pipeline of acute myocardial ischemia which allows the execution and postprocessing of large sets of simulations; - Optimisation of parallel input-output in Chaste; - Development of an LGE MRI based simulation pipeline for ARVC patients; - Development of a simulation pipeline for populations of tissue fibres.	N/A	N/A
Impact	Journal papers, conference talks and posters [22, 23, 24, 25, 26, 27]	Papers [25]	Papers, conference presentations [27, 28, 29, 30]
Use of any e-infrastructure available via CompBioMed	EPCC, BSC	EPCC, BSC	None

9.11 AngioSupport: 1D simulation tool for coronary disease and predicting outcome of an intervention

AngioSupport is based on existing 1D hemodynamic models (such as HemeLB) integrated in a user-friendly workflow interface. It targets simulation of the severity of coronary stenosis, based on the FFR method, from angiographic imaging. The simulated FFR can be compared to invasive FFR measurements and are displayed alongside stenotic regions detected from anatomical images. Subsequently, the effect of different stent interventions (stent size and location) can be compared to each other as well as to coronary bypass surgery from the LIMA. This tool comprises an easy-to-follow user interface that allows clinicians to run the simulations on their own in clinical practise and support them in their decision making process. 1D wave propagation analyses are undertaken which currently require CAAS software for image segmentation.

End-user solution type	**Please tick one or more**

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Non-clinical research	✓
Clinical research	✓
Clinical decision support	✓
Drug discovery	
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	
Personal health forecasting	

Provider: LifeTec

Contact email: m.stijnen@lifetecgroup.com

Number of user organisations (list the top 5):

Estimated users at M0: 0

Estimated users at M24: 0

Estimated users at M36: 13 (trial users)

Access mode: local installation

URL: https://www.lifetecgroup.com/cases-papers-products-services/case-angiosupport

User manual: not started yet

HPC Systems: Cartesius (SURFsara)

HPC motivation: sensitivity analysis and uncertainty quantification

Additional user information:

End user name	Marcel van het Veer	Frank Gijsen	PhD student to be defined
Affiliation	Catharina Hospital Eindhoven	ErasmusMC	Amsterdam Medical Center
Application area	Cardiovascular	Cardiovascular	Cardiovascular
No. of associated users	11	1	1
Target use	Research	Research	Research
Improvements implemented	None	None	None

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Impact	Clinical validation	Clinical validation	Clinical validation
Use of any e-infrastructure available via CompBioMed	None	None	None

10 Molecular medicine solutions

10.1 ACEMD

ACEMD is Molecular Dynamics simulation software that allows simulation of molecular biosystems at the atomic level. ACEMD is a production level molecular dynamics software specially optimized to run on NVIDIA graphics processing units (GPUs) and it is one of the world's fastest molecular dynamics engines.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	
Clinical decision support	
Drug discovery	✓
Design & optimisation	✓
In silico preclinical trials	✓
In silico clinical trials	
Personal health forecasting	

Provider: Acellera

Contact email: compbiomed@acellera.com

Number of user organisations (list the top 5):

Estimated users at M0: NDA

Estimated users at M24: >744 (>~15% industry)

Estimated users at M36: >1000 (>~15% industry)

Access mode: Download

URL: https://www.acellera.com/products/molecular-dynamics-software-gpu-acemd/

User manual: https://software.acellera.com/docs/latest/acemd/index.html

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HPC Systems: Clusters, AWS (Amazon), GPUGRID

HPC motivation: Solve unreducible model.

Additional user information:

Commercial sensitivity.

10.2 HTMD

HTMD is a programmable environment to prepare, execute, visualize and analyse Molecular Dynamic simulations. It uses a Python-based programmable environment to perform system preparation and building, execution of simulations with different MD codes using adaptive sampling schemes and generate Markov State models to analyse simulations.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	
Clinical decision support	
Drug discovery	✓
Design & optimisation	✓
In silico preclinical trials	✓
In silico clinical trials	
Personal health forecasting	

Provider: Acellera

Contact email: compbiomed@acellera.com

Number of user organisations (list the top 5): NDA

Estimated users at PM0: NDA

Estimated users at PM24: >500 registered academic users; >5 commercial users

Estimated users at PM36: >750 registered academic users; >8 commercial users

Access mode: Source

URL: https://www.acellera.com/products/high-throughput-molecular-dynamics/

User manual: https://software.acellera.com/docs/latest/htmd/index.html

HPC Systems: Clusters, AWS (Amazon)

HPC motivation: Solve unreducible model; Do uncertainty quantification.

Additional user information:

Commercial sensitivity.

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10.3 Playmolecule

Playmolecule is an intuitive platform providing access to a diverse set of web applications for molecular discovery. It includes a repository of free best-in-kind applications with a diverse set of solutions like molecular predictors and modelling tools.

End-user solution type	Please tick one or more
Non-clinical research	✓
Clinical research	
Clinical decision support	
Drug discovery	✓
Design & optimisation	✓
In silico preclinical trials	✓
In silico clinical trials	
Personal health forecasting	

Provider: Acellera

Contact email: compbiomed@acellera.com

Number of user organisations (list the top 5): NDA

Estimated users at M0: It did not exist then

Estimated users at M24: >180 registered users; >13 % from industry; >8,000 sessions

Estimated users at M36: >700 registered users; >15 % from industry; >31,000 sessions

Access mode: Service

URL: http://playmolecule.org

Support contact: http://support.acellera.com

HPC Systems: GPUGRID.net project, AWS (Amazon)

HPC motivation: Solve unreducible model; Do uncertainty quantification.

Additional user information:

Commercial sensitivity.

10.4 BAC

BAC is a workflow tool that runs and analyses simulations designed to assess how well drugs bind to their target proteins and the impact of changes to those proteins. It provides a collection of scripts, which wrap around common molecular dynamics codes to facilitate free energy calculations. BAC is

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being used as a clinical decision support tool with a clear aim of clinically driven research, and there is considerable hope to take this further in the future. BAC delivers the use of ensemble simulations to provide robust, accurate and precise free energy computations from both alchemical and end-point analysis methodologies. EnsembleMD [31] are commercially developing user friendly interfaces to replace existing prototypes produced at UCL.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	✓
Clinical decision support	✓
Drug discovery	✓
Design & optimisation	✓
In silico preclinical trials	
In silico clinical trials	
Personal health forecasting	

Provider: UCL and EnsembleMD

Contact email: dave.wright@ucl.ac.uk

Number of user organisations (list the top 5):

Estimated users at M0: 1 team, 10 users

Estimated users at M24: UCL, GSK, Janssen, 17 users

Estimated users at M36: UCL, GSK, Janssen, 17 users

Access mode: Service (Source available to academic collaborators only at present)

URL: No current website – DNAnexus app available only to UCL/GSK at present, Azure interface only available to UCL/EnsembleMD/Janssen.

HPC Systems: AWS (Amazon), ARCHER (EPCC), Cartesius (SURFsara)

HPC motivation: Solve unreducible model; performs uncertainty quantification.

Additional user information:

End user name	Ian Wall	Hermann van Vlijmen	Peter V. Coveney's group
Affiliation	GSK	Janssen	UCL
Application area	Drug discovery	Drug discovery	Clinical decision

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			support and drug design
No. of associated users	2	5	10
Target use	Commercial / research	Commercial	Research
Improvements implemented	Initial web interface (UF-BAC) developed to facilitate usage, workflow deployed on DNAnexus cloud	Azure deployment and extension of UF-BAC interface	None
Impact			Clinical validation
Use of any e-infrastructure available via CompBioMed	Compute time at BSC and Cirrus at EPCC (testing of container based solution)	Compute time at SURFsara	Compute time at SURFsara, BSC, EPCC

10.5 Antibiotic Resistance

The Fowler Lab has developed alchemical free energy computation techniques, using GROMACS, to predict the effect of individual protein mutations on the effectiveness of specific antibiotics.

End-user solution type	**Please tick one or more**
Non-clinical research	
Clinical research	✓
Clinical decision support	
Drug discovery	
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	
Personal health forecasting	

Provider: UOXF

Contact email: philip.fowler@ndm.ox.ac.uk

Number of user organisations (list the top 5): John Radcliffe Hospital

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Estimated users at M0: 0

Estimated users at M24: 12

Estimated users at M36: 12

Access mode: Service

URL: http://fowlerlab.org/

HPC Systems: ARCHER (EPCC), JADE (UOXF)

HPC motivation: Solve unreducible model

Additional user information:

End user name	Comprehensive Resistance Prediction for Tuberculosis: an International Consortium (CRyPTIC)
Affiliation	research project led by UOXF
Application area	Clinical microbiology
No. of associated users	12 partner laboratories
Target use	Research
Improvements implemented	Initial web interface (UF-BAC) developed to facilitate usage, workflow deployed on DNAnexus cloud
Impact	Various methodological improvements and streamlining, optimisation of resource allocation
Use of any e-infrastructure available via CompBioMed	None

10.6 Visual GEC

Visual GEC is a software tool for designing engineered cells and simulating biochemical interactions. The Genetic Engineering of Cells (GEC) software, developed by the Biological Computation team at Microsoft Research (Cambridge, UK), is a modelling tool that can be used to design and simulate synthetic genetic circuits. At the core is a domain-specific programming language for biochemical systems (LBS), originally developed at the University of Edinburgh. The tool supports stochastic and deterministic simulation of the temporal dynamics of chemical reaction networks, but also spatio-temporal dynamics via reaction-diffusion equations. Parameter inference can also be performed using Metropolis-Hastings Markov chain Monte Carlo with time-series data.

End-user solution type	**Please tick one or more**

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Non-clinical research	✓
Clinical research	
Clinical decision support	
Drug discovery	
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	
Personal health forecasting	

Provider: Microsoft

Contact email: ndalchau@microsoft.com

Number of user organisations (list the top 5): Not tracked

Estimated users at M0: Not tracked

Estimated users at M24: Not tracked

Estimated users at M36: Not tracked

Access mode: Direct

URL: https://www.microsoft.come/en-us/research/project/genetic-engineering-of-living-cells/

HPC Systems: Microsoft Azure Cloud Computing Platform & Services

HPC motivation: Solve unreducible model

Additional user information:

Commercial sensitivity

10.7 HTBAC

The High throughput binding affinity calculator (HTBAC) is a scalable solution for adaptive personalised drug discovery. It provides high level python object abstractions for defining simulations, physical systems and ensemble-based free energy protocols. The Runner class as part of the HTBAC abstraction uses underlying building blocks middleware developed by the RADICAL team to create and execute multiple concurrent executions of protocols on supercomputing cyberinfrastructures while abstracting and handling execution management, and data transfer.

End-user solution type	**Please tick one or more**
Non-clinical research	
Clinical research	
Clinical decision support	
Drug discovery	✓

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Design & optimisation	
In silico preclinical trials	
In silico clinical trials	
Personal health forecasting	

Provider: UCL and Rutgers

Contact email: dave.wright@ucl.ac.uk, jdakka@scarletmail.rutgers.edu, shantenu.jha@rutgers.edu, kristof.farkas-pall.14@ucl.ac.uk

Number of user organisations (list the top 5): UCL

Estimated users at M0: 0

Estimated users at M24: 10

Estimated users at M36: 10

Access mode: Source

URL: https://github.com/radical-cybertools/htbac

HPC Systems: Blue Waters (NCSA), Titan (ORNL)

HPC motivation: Test model convergence

Additional user information:

End user name	Peter Coveney's group
Affiliation	UCL
Application area	Drug discovery
No. of associated users	10
Target use	Research
Improvements implemented	None
Impact	None
Use of any e-infrastructure available via CompBioMed	None

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10.8 DNAnexus

DNAnexus is a data agnostic platform which allows one to store, manage, analyse and share data. DNAnexus is a cloud-based Platform-as-a-Service (PaaS) which supports the ingestion of any type of data and any type of Linux-based software (your own, commercial or open-source) for the analysis of said data. Most of the current applications are in the genomics space but do include a few in the Computational Chemistry space.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	✓
Clinical decision support	
Drug discovery	✓
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	
Personal health forecasting	

Provider: DNAnexus

Contact email: info@dnanexus.com, fiona@dnanexus.com

Number of user organisations (list the top 5): UCL

Estimated users at PM0: 0

Estimated users at PM24: 1

Estimated users at PM36: 1

Access mode: Source

URL: www.dnanexus.com

HPC Systems: Cloud-based

HPC motivation: Test model convergence

Additional user information:

Commercial sensitivity

10.9 General Janssen IP

Janssen employs a team of computational chemists involved in early phases of drug discovery. Their work in the compbiomed project has involved collaborating with several partners such as at UCL, UPF and Acellera. Part of their time in this project has been used to investigate the feasibility of free energy

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calculations for predicting drug protein target interactions and affinities. The work used open source software and is well known for its complexity to implement. This work required the development of protocols to streamline the application of existing theory and methodology for large numbers of protein-ligand systems and using parallel HPC. Computational scripts were developed allowing command line/expert-level of application of dozens of potential separate steps into 2 main scripts. The calculations were run at SURFsara with time allocated from the project HPC allocation service, and with the support of the experts there to help run and manage the jobs. These computational protocols were not developed to high quality for public release and still require expert level users.

End-user solution type	**Please tick one or more**
Non-clinical research	
Clinical research	
Clinical decision support	
Drug discovery	✓
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	
Personal health forecasting	

Provider: Janssen Pharmaceutica NV

Contact email: hvvlijme@its.jnj.com, gtresade@its.jnj.com, laurea.perez20@gmail.com

Number of user organisations (list the top 5): Janssen

Estimated users at M0: 0

Estimated users at M24: Internal use only ~ 5-10 computational chemists

Estimated users at M36: Internal use as above

Access mode: Command line, expert user

HPC Systems: Cartesius (SURFsara).

HPC motivation: Large scale computations run in parallel using HPC CPU plus GPU nodes

Additional user information:

End user name	Laura Perez Benito, Gary Tresadern, Christophe Meyer, Herman van Vlijmen
Affiliation	Janssen R&D
Application area	

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No. of associated users	5-10
Target use	Pre-competitive research. Tested for possible commercial application
Improvements implemented	None
Impact	Several publications resulted from our work in the project, this one specifically includes results of calculations enabled by the protocols developed here: J. Chem. Theory Comput., 2019, 15 (3), pp 1884–1895. DOI: 10.1021/acs.jctc.8b01290
Use of any e-infrastructure available via CompBioMed	SURFsara

11 Neuromusculoskeletal solutions

11.1 Vertebroplasty Simulator

Palabos – Vertebroplasty Simulator: This solution, currently in its final stage of development, uses Palabos to provide a vertical solution for the pre-operative planning of vertebroplasty. Micro CT images of the damaged vertebral body are converted into an LBM model, which simulates multiple cement injections with different access point and cement volume. The simulation results predict exact filling patterns of the injected cement. Plans for future developments include converting the results into a finite element model, which will predict the increase in biomechanical strength with respect to the untreated vertebra.

End-user solution type	**Please tick one or more**
Non-clinical research	
Clinical research	✓
Clinical decision support	✓
Drug discovery	
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	✓
Personal health forecasting	

Provider: UNIGE

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Contact email: jonas.latt@unige.ch

Number of user organisations (list the top 5): University of Geneva, Numeca International

Estimated users at M0: NA

Estimated users at M24: NA

Estimated users at M36: 46

Access mode: Source

HPC Systems: Baobab (UNIGE), CADMOS (UNIGE)

HPC motivation: Solve unreducible model; Multiscale model; Strongly coupled model.

Additional user information:

Due to commercial sensitivity, some information below has been anonymised. However, detailed user numbers have been accounted for in the overall statistics reported in Section 6.

End user name	NDA	NDA
Affiliation	NDA	NDA
Application area	Computational biology	Computational fluid dynamics
No. of associated users	NDA	NDA
Target use	Research	Commercial
Improvements implemented		
Impact		
Use of any e-infrastructure available via CompBioMed		

11.2 CT2S

This web-based service is provided by USFD. Details of the web service are described in Section 8.1 of this document. The modelling pipeline is used to predict the strength of a patient's bone from a CT scan of that bone. Stochastic FEA of subject-specific model can also be generated from CT data.

End-user solution type	**Please tick one or more**
Non-clinical research	

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Clinical research	✓
Clinical decision support	✓
Drug discovery	
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	✓
Personal health forecasting	

Provider: USFD

Contact email: ct2s-support@insigneo.org

Number of user organisations (list the top 5): STH, USFD, Sheffield Children's Hospital

Estimated users at M0: 2

Estimated users at M24: 8

Estimated users at M36: 8

Access mode: Via request

URL: https://ct2s.insigneo.org/ct2s/

User manual: Via request

HPC Systems: ShARC (USFD), ARCHER (EPCC)

HPC motivation: Multi-scale computation, sensitivity analysis, stochastic analysis

Additional User Information:

End user name	Eugene McCloskey's group	Richard Eastell's group	Amaka Offiah's group
Affiliation	STH	STH	Sheffield Children's Hospital
Application area	Diagnosis of osteoporotic fracture	Diagnosis of osteoporotic fracture	Diagnosis of child abuse and infant's musculoskeletal diseases
No. of associated users	3	2	3
Target use	Research / preclinical	Research / preclinical	Research / preclinical

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Improvements implemented	An intermediate process/tool needs to be set up in order for anonymised patients' imaging data to be sent from the Hospital Trust to the University for further analysis (detailed in Sec 8.1)	None	Some parameters within the pipeline were adjusted to suit the paediatric application.
Impact	Papers [32] [6]	Paper [33]	Papers [34, 35]
Use of any e-infrastructure available via CompBioMed	Computing time at EPCC	Compute time at EPCC	None

12 Other solutions

12.1 MUSCLE-HPC

Multiscale, multi-physics applications are central to solve the scientific challenges in CompBioMed. Computationally speaking, the difficulty is to combine high performance computing with the need to couple various codes or solvers, each representing a different scale or a different physical process. MUSCLE-HPC is a new HPC implementation of MUSCLE-2, a previously developed Multiscale Coupling Library and Environment. Using MUSCLE-HPC to couple sub-models within the same HPC cluster leads to better computing performance comparable to a native MPI execution and can, thus, reduce the coupling overhead.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	✓
Clinical decision support	✓
Drug discovery	✓
Design & optimisation	✓
In silico preclinical trials	✓
In silico clinical trials	✓
Personal health forecasting	✓

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Provider: UNIGE

Contact email: jonas.latt@unige.ch

Number of user organisations (list the top 5):

Estimated users at PM0: 0

Estimated users at PM24: 0

Estimated users at PM36: General user base, open-source software freely available. Estimated 10 users based on publications quoting the software.

Access mode: Source

URL: https://gitlab.com/benbelga/muscleHPC

HPC motivation: Solve unreducible model, Validate reduced-order model, Test model convergence, Larger space-time regions, Uncertainty quantification, Inform surrogate model, Multiscale models, Strongly coupled models.

12.2 pFIRE

pFIRE is an Image Registration Code, used to evaluate the difference between a pair of images and express them as a mapping field. This allows measurement of e.g. changes to organs over time, or how a bone changes shape when force is applied. Parallel Elastic Image Registration based on the method of Barber and Hose [36]. The PETSc framework (flexible library for parallel computing in C++) is used to distribute the problem over many nodes to allow registration of multi-gigabyte to terabyte images. Out-of-core execution is also supported to facilitate registration of large images on memory limited machines.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	✓
Clinical decision support	✓
Drug discovery	
Design & optimisation	
In silico preclinical trials	
In silico clinical trials	
Personal health forecasting	

Provider: USFD

Contact email: i.benemerito@sheffield.ac.uk

Number of user organisations (list the top 5): USFD (for potential users)

Estimated users at M0: 0

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Estimated users at M24: 0

Estimated users at M36: 4

Access mode: Source

URL: https://github.com/INSIGNEO/pFIRE

User manual: https://insigneo.github.io/pFIRE/

HPC Systems: ShARC (USFD), ARCHER (EPCC), Cirrus (EPCC), MareNostrum (BSC)

HPC motivation: Solve unreducible model.

Additional User Information:

End user name	Enrico Dall'Ara's team
Affiliation	USFD
Application area	Tissue-level modelling of bone mechanics
No. of associated users	4
Target use	Research
Improvements implemented	The original BoneDVC code has been developed to create pFIRE in order to fully utilise the code on HPC systems, especially for the processing of large images, such as those generated from the Diamond synchrotron facility.
Impact	Papers have been generated using BoneDVC. New impact using pFIRE has not been generated yet.
Use of any e-infrastructure available via CompBioMed	EPCC and BSC computing time

12.3 InSilicoMRI

InSilicoMRI predicts the overheating of a medical device during an MRI scan. Radiofrequency (RF) safety analysis of a passive device exposed to a 3T MRI birdcage coil field following the directives of ASTM F2182 [37, 38] standard. The simulation calculates the electromagnetic fields, SAR, and thermal heating after 900s of RF exposure.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	

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Clinical decision support	
Drug discovery	
Design & optimisation	✓
In silico preclinical trials	
In silico clinical trials	
Personal health forecasting	

Provider: InSilico Trials

Contact email: project@insilicotrials.com, elena.lucano@insilicotrials.com

Number of user organisations (list the top 5):

Estimated users at PM0: Not disclosed for commercial sensitivity

Estimated users at PM24: Not disclosed for commercial sensitivity

Estimated users at PM36: Not disclosed for commercial sensitivity

Access mode: Service

URL: https://insilicomri.com

HPC Systems: Azure (Microsoft)

HPC motivation: Solve unreducible model.

Additional User Information:

Commercial sensitivity

12.4 Training material for medical students

The training material comprises background information and an instruction set for the HPC-based computational analysis of microbiome data using the open source software programme Qiime (qiime.org). The material has been used to successfully introduce new users (undergraduates and medical students) to high performance computing and metagenomic analyses and for teaching computational biology to postgraduate and postdoctoral researchers in the computational sciences.

End-user solution type	**Please tick one or more**
Non-clinical research	✓
Clinical research	
Clinical decision support	
Drug discovery	
Design & optimisation	
In silico preclinical trials	

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In silico clinical trials	
Personal health forecasting	

Provider: UCL/EPCC training product

Contact email: a.townsend-nicholson@ucl.ac.uk

Number of user organisations (list the top 5): UCL, PRACE

Estimated users at PM0: 0

Estimated users at PM24: 150

Estimated users at PM36: 300

Access mode: Face to face training, service

HPC Systems: By request

Additional User Information:

End user name	Andrea Townsend-Nicholson
Affiliation	UCL
Application area	Education / non-clinical research
No. of associated users	Medical student and undergraduate science student education; academic and industrial researcher training
Target use	Educational, research
Improvements implemented	None
Impact	The work has led to the education of 60 pre-clinical medical students and 180 undergraduate science students as well as the training of 60 PRACE workshop registrants; Several publications are in preparation; The work is being used to inform the UKRI business case for exascale computing
Use of any e-infrastructure available via CompBioMed	EPCC, SURFsara, BSC

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