Early prototype software interface with atlas services based on initial versions of data models including DEMO1 of Showcases 1 and 2 (D1.1 - SGA3)

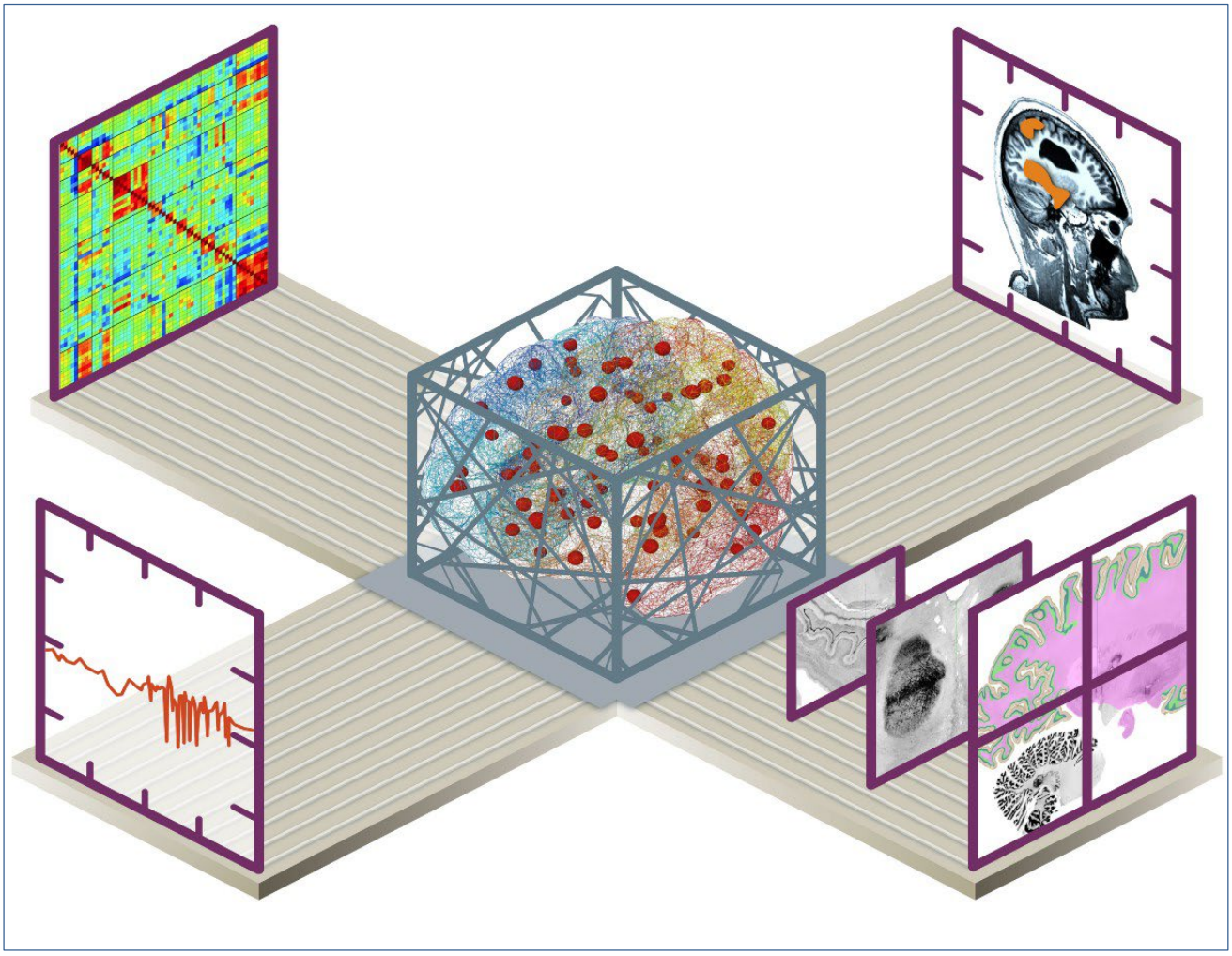

Figure 1: Showcase 1: Degeneracy in neuroscience - when is Big Data big enough?

The Virtual Big Brain is a personalised high-resolution virtual brain model, integrating network modelling with multiscale brain data from connectomics and region-variant architecture in the same reference frame.

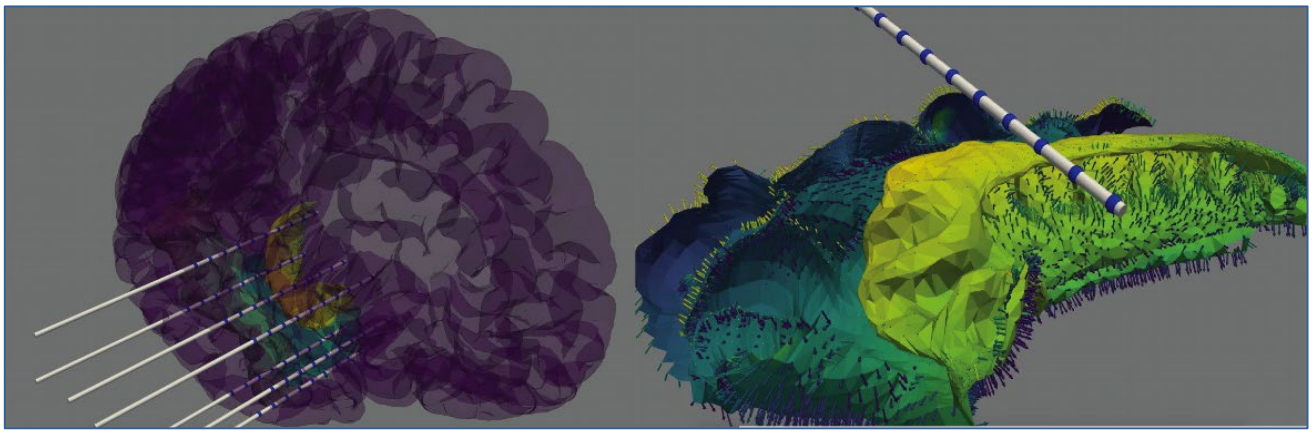

Figure 2: Showcase 2: Improving epilepsy surgery with the Virtual BigBrain

High-resolution cortical and subcortical surfaces in the Virtual Big Brain lead to better estimates of the epileptogenic zone through the integration of detailed connectivity, simulation of propagating neural fields and improved source-signal mapping. Left: Full brain model with implanted SEEG electrodes. Right: Human hippocampus model with dipolar neural sources (blue vectors).

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Description in GA:	A prototype implementation of the software interface between TVB and EBRAINS atlas services will be available. This prototype will first be based on incomplete versions of data and metadata models for the multiscale connectome data. It will demonstrate the principle of hosting the novel multiscale connectome and regional multimodal characteristics in EBRAINS, as well as linking of multiscale models to the atlas. Showcase demonstrators will comprise the prototype software interface and a video illustrating the influence of regional variability on seizure propagation through individual brain networks. Detailed specifications for DEMO2 are provided.
Abstract:	This report is the D1.1 Deliverable (M9) as stated in the DoA. It outlines an early and fundamental landmark in the development of WP1's Showcases 1 and 2. Showcase 1 establishes the link between EBRAINS' multilevel human brain atlas and The Virtual Brain (TVB) simulator and allows introduction of regionally variant structural markers into the modelling framework. The first prototype is available in EBRAINS and establishes the M9 Deliverable of Showcase 1. Showcase 2 demonstrates how EBRAINS enables advances in personalised medicine through the transition to high-resolution TVB. A video illustrates the progress and establishes the M9 Deliverable of Showcase 2. The existing functionalities of both demonstrators, including access to the showcases and a roadmap to the next Showcase Deliverable in M21 are also described.
Keywords:	Neuroscience, Big Data, Virtual Big Brain, Variability, Cohort, Personalisation, Epilepsy, Modelling
Target Users/Readers:	Clinicians, computational neuroscience community, computer scientists, consortium members, HPC community, neuroimaging community, neuroinformaticians, neuroscientific community, platform users, scientific community, students, funders, policymakers.

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History of Changes made to this Deliverable (post Submission)

Date	Change Requested / Change Made / Other Action
19 Jan 2021	Deliverable submitted to EC
03 Mar 2021	Resubmission with specified changes requested in Review Report Main changes requested: • Change 1 (Before publication, it would be valuable to add a preamble section explaining the positioning of these showcases and related demos in the context of SGA3 and HBP.) • Change 2 (The VBB should also be defined, compared to TVB)
31 Mar 2021	Revised draft sent by SP/CDP to PCO. Main changes made, with indication where each change was made: • Change 1 (see Section 1.1 PREAMBLE) • Change 2 (see Section 1.1 PREAMBLE, last sentence)
01 Apr 2021	Revised version resubmitted to EC by PCO via SyGMa

1. Preamble

Work Package 1 is creating two Showcases, which illustrate its capacity to build data-informed high-resolution brain models. These models can be personalised to human subjects through the use of individuals' anatomical and functional brain imaging data. Showcase 1 illustrates how the addition of detailed neuroscience data enhances our understanding and predictive power. For instance, through the integration of neurotransmitter distributions from *post-mortem* brains or individual brain images, we can better explain a patient's brain activity and provide more precise statements about his/her brain health status. Showcase 2 demonstrates how the transition to high-resolution brain models significantly improves the estimation of the epileptogenic zone in drug-resistant epilepsy patients. The Showcases highlight the two dimensions that exploit EBRAINS services and distinguish the Virtual Big Brain from preceding modelling efforts, that is the integration of detailed neuroscience data for regional specificity and high-resolution on the sub-mm scale.

2. Showcase 1: Degeneracy in neuroscience - when is Big Data big enough? Demo 1

2.1 Introduction

Showcase 1 addresses one of the oldest enigmas in neuroscience: the dichotomy of brain structure and function. Individual brains differ from each other, while maintaining full functionality within a range of normal variability. Outside of this range, brain function is diminished or lost. The functional loss, however, occurs for different conditions in each brain, and the same structural change may be functionally dramatic in one brain, but inconsequential in another. What applies to empirical data applies equally to mathematical models in neuroscience and is known as degeneracy, i.e. the propensity for different system configurations to support the same or similar functions. When validating models against data, increasingly large amounts of data are required to make meaningful statements about mechanisms in the models due to degeneracy. The objective of this showcase is to demonstrate that cutting edge datasets on structural variability can be used to drive whole-brain modelling and explain functional variability. Such a framework has the capacity to predict individual trajectories of brain health and their changes across age and disease. It directly addresses one of Europe's priorities, the active and healthy ageing of its population. Showcase 1 illustrates a concrete example of a workflow allowing the ageing brain to be tracked and the trajectories of its evolution to be explained. As degeneracy and variability having been recognized as some of the most daunting obstacles to progress in neuroscience, the efficient operationalisation of such workflows will empower the community to pursue higher quality research outputs, with a meaningful impact on brain health. The HBP's EBRAINS neuroscience research infrastructure is the instrument to realize and make accessible these workflows to the community.

The entry point of this showcase is via the creation of a virtual cohort of ageing brains, reflecting the variability and properties of the 1000BRAINS cohort made available by the Jülich Research Centre. Human brain ageing is a paradigm well-suited for this task, as it is well-described, both structurally (e.g. atrophies, micro-lesions and dysconnectivity) and functionally (e.g. network adaptations and hemispheric asymmetries). To this day, there is no established causality between structural and functional observations. To address this challenge, we choose the human brain's resting-state as the principal paradigm in Showcase 1. Resting-state activity is routinely imaged in basic and clinical research using fMRI and EEG/MEG; it is recognised as a fingerprint of an individual's brain, effectively reflecting the impact of drugs, disease, age and cognitive factors. To meaningfully explore ageing variability, large numbers of individuals are required, which implies the necessity of a cohort approach. This requirement imposes constraints in terms of cohort data, curation and storage, availability of compute resources, and the ability to perform multiscale modelling and validation. The only infrastructure supporting this range of connected services and workflows is EBRAINS. Previous efforts by the Human Brain Project (HBP) in SGA1 and SGA2 developed the EBRAINS technologies (mean field models, human brain atlas, model inversion and validation) and data

(including the Big Brain, cytoarchitectonic maps and multimodal data features, and high-resolution connectomics) needed to build a virtual cohort in SGA3. We believe that these achievements will prove instrumental in allowing the establishment of a causal hypothesis linking structural to functional variability. Specifically, we exploit the detailed high-resolution data (multi-scale brain connectome, region-specific data) to realise specialised virtual brain models, implement the hypothesized ageing mechanisms in the model, and simulate the functional resting-state brain imaging data of a large cohort of individual brains. A model inversion process for the resting-state (from imaging data to structure) will be developed during SGA3 and validate the model against the empirical cohort.

The M9 Deliverable is an early and fundamental step forward in the development of Showcase 1. It establishes a functional link between EBRAINS' multilevel human brain atlas and The Virtual Brain (TVB) simulator. It also introduces regionally variant structural markers of ageing into the modelling framework. This link has now been implemented and a first prototype made available through EBRAINS. It illustrates the manner in which data services can be connected to computing services, allowing exploitation of available data to inform simulation models in the Collaboratory. It provides the first use case for the automation of systematic access to data hosted within EBRAINS' atlases. Here, this is embodied in the release of a prototype Python client allowing interaction with the multilevel human atlas, "Brainscapes". While not all hosted datasets and functionalities are yet accessible through this client, it makes data formats, region specifications and access patterns explicit, thereby promoting co-design and greatly facilitating collaboration between the HBP's Work Packages WP1 and WP4. The work in this Deliverable underpins the activities of several Tasks in WP1 and will also generate use cases driving the elaboration of tools and capabilities in multiple EBRAINS Service Categories, being developed by WP4 and WP5. Such developments are instrumental in ensuring that the resulting EBRAINS workflows, co-designed with HBP researchers, address the neuroscience community's actual needs. Reciprocally, tailoring infrastructure developments to the use case herein is crucial to the success of the science tasks in WP1. This first prototype delivered in SGA3 Month 9 (M9 -December 2020), which constitutes a stepping stone towards the Virtual Big Brain, is the central building block of all subsequent work in Showcase 1 and in a meaningful number of tasks in WP1 and WP2.

The currently existing functionality of the prototype is described in Section 1.2 and constitutes the M9 Deliverable of Showcase 1. Section 1.3 details how to access the showcase. Ongoing work leading to the next Showcase Deliverable in SGA3 M21 is described in Section 1.4.

2.2 Technical Specification

The demonstrator for this Deliverable builds upon several software components, roughly divided into the atlas Python client (Brainscapes) and modelling software.

The atlas client gives direct programmatic access to typical patterns of interaction with EBRAINS' human brain atlas. It supports the multilevel character of this atlas, which defines cytoarchitectonic maps in multiple reference template spaces at different spatial resolutions (namely the MNI Colin, ICBM152 asymmetric, as well as the BigBrain microscopic space), and links them with complementary maps related to brain function, connectivity and fibre architecture. The functionality of the Python client matches common patterns known from browsing the interactive atlas viewer: Selecting a parcellation, browsing and searching brain region hierarchies, downloading maps, selecting regions, and requesting manifold information and features associated with brain regions.

A key feature of the atlas client, which is especially relevant for this showcase, is a streamlined implementation of performing data queries for selected brain regions, which gives access to multimodal regional "data features", which are mostly curated datasets from the EBRAINS Knowledge Graph (KG). The client implements a hierarchy of features, which currently models three different forms of atlas integration:

1) **Spatial data features** define a brain location by specifying a set of coordinates in one of the supported reference template spaces. They match to a query if their associated coordinates are located inside the brain region, as specified by its map in the corresponding reference space. An

example of spatial data features are gene expressions collected from small tissue blocks, or contact points of physiological electrodes.

2) **Regional data features** define a brain location by linking to a specific region defined in a supported parcellation. They match to a query if their associated brain region is part of the region that is selected in the atlas. Examples of regional data features are cell densities, and morphologies, neurotransmitter distributions and synapses or functional activations that were measured in a pre-specified region like e.g. CA1.

3) **Global data features** apply to the whole brain instead of a specific region. They can match to a query in different ways, e.g. by providing a whole-brain image defined in one of the supported reference spaces, or providing relationships between the regions of the selected brain parcellation. Examples of global features are functional activations maps or connectivity matrices.

As a result, all forms of data features can be queried using a single function of the atlas - *query_data()* - which takes as an argument a specification of the desired data modality, and uses the current selections made in the atlas for retrieval and filtering. For the current prototype, available data features include neurotransmitter densities, regional connectivity profiles, connectivity matrices, gene expressions, and spatial properties of brain regions. The focus is on data features defined in the MNI reference spaces for the Julich-Brain cytoarchitectonic maps. Some feature types provide only partial coverage of the brain regions to date. The further integration of data features from partners in inside the HBP, as well as external groups, is a continuous process.

As most of the multimodal data features are retrieved from the EBRAINS KG, each user of the Python client needs to provide an individual KG API token, which can be obtained on a dedicated page of the EBRAINS Knowledge Graph[1]. Besides EBRAINS, the client also implements access to other repositories, currently in particular the Allen Brain Atlas for retrieving gene expression data. By unifying access to different back end services, the client hides much of the complexity that would be required to interact with the individual services. Furthermore, by encapsulating many aspects of interacting with different maps and reference templates spaces, it also minimises common risks like misinterpretation of coordinates from different reference spaces, or utilisation of inconsistent versions of parcellation maps. The aim is to provide a safe way of using maps defined across multiple spatial scales. The atlas client also provides easily usable data structures for several data types that are relevant for modelling. For example, cortical profiles of different neurotransmitter receptors are exposed as dictionaries of named data vectors. Other data such as connectivities are available directly on a parcellation basis. The client will later enable access to cohorts of data and functional time series data, and ultimately customised big data queries, e.g. for extracting cell densities in certain brain regions. When a query is performed, the client stores downloaded items in a local cache to speed up later queries.

The modelling software used in the demonstrator is The Virtual Brain (TVB) software, a Python library and mathematical framework for simulating whole-brain network dynamics and neuroimaging data. Following the work done by the HBP's CDP8 in SGA2 (and continued by various Tasks in SGA3 - in particular, T1.8 and T5.4) this software is now available directly in the Collaboratory Jupyter notebook interface, as a Python package. TVB provides a Python API for constructing instances of classes, which represent the mathematical components of a large-scale brain simulation, of which two essential components are the connectivity, representing the white matter fibre bundles linking regions of interest together, as well as sets of neural mass models representing the dynamics of the regions of interest. These together form the minimal virtual brain model, built from any dataset wherein the parcellation is consistent, i.e. the spatial definition of the regions of interest is identical for the nodes in the connectivity and neural masses, which dovetails with the structural data provided by the Brainscapes atlas client detailed above, as it renders data features always in a format following the user-chosen parcellation. Specifically, in the current demonstrator we have focused on two data features: receptor densities and connectivities. The latter data feature contains one or more matrices of white matter tract measurements between regions. To ensure numerical stability of the simulation, a logarithmic transform is applied, and the result, along with the set of

[1] https://nexus-iam.humanbrainproject.org/v0/oauth2/authorize

region names and positions, is used to construct a TVB connectome object. Having the atlas-provided metadata passed on to the TVB objects enables further workflow steps such as computing forward solutions for EEG, MEG, or sEEG directly with TVB and allowing linking backwards from simulated activities to the region of interest in the atlas. Secondly, we incorporate the region-specific receptor densities, mapping their per-region values to parameters of the per-region neural mass model: in the current iteration this mapping is fixed, in which the excitation-inhibition ratio of AMPA and GABA receptors is mapped to the threshold parameter of the neural mass model Generic2D in TVB. To ensure that this ratio is evaluated in the same set of regions as the connectivity nodes, an iteration over connectivity nodes is performed, and the receptor density data feature is evaluated with the atlas client for each node. For the nodes, in which this data feature is available, the densities for AMPA and GABA are averaged over cortical depth, their ratio is retained and the mean over regions where the data is available is taken to fill in for the areas where data is not yet available. This results in a vector of values, one per region, which is then used to configure the TVB neural mass model. With the configured TVB connectivity and neural mass model, a TVB simulator is constructed, configured and run for a short amount of the time. The resulting simulation presents a typical transient from initial conditions to fixed point, ensuring a numerically stable simulation.

All the previous steps were accomplished entirely in the EBRAINS Collaboratory in Jupyter notebooks. The computational resources available to such notebooks are modest, which restricts the simulations. For large parameter sweeps, ICEI compute resources need to be used.

2.3 How to access the Showcase

The Showcase is implemented in the form of an interactive Jupyter notebook in a dedicated public EBRAINS collab. The collab can be found at:

https://wiki.ebrains.eu/bin/view/Collabs/sga3-d1-1-showcase-1

The notebook in this collab will load all required Python modules, including the ones for the EBRAINS human brain atlas (“Brainscapes”) and The Virtual Brain. It generates an instance of the brain atlas, demonstrates how a parcellation and brain regions are selected, and how data queries are performed. The retrieved data is then used right away to setup a simulation, run it, and assemble a brief summary of the simulation results.

Running the notebook requires a valid and recent EBRAINS authentication token with API permission. The steps required to generate and use the token are documented directly in the notebook.

2.4 Looking Forward

The following activities are ongoing and are expected to showcase their results in M21.

2.4.1 Model building

Showcase 1 will enable modelling of phenomena associated with inter-individual variability. Structural markers of ageing as a particular application are currently being implemented in virtual brain models integrating multilevel atlas information (Tasks T1.6 and T1.7). Mean field models (Task T1.5) will explicitly integrate receptor densities through the respective weights of excitatory and inhibitory inputs, as well as their variability (microscopic heterogeneity). This includes the AdEx mean-field models integrating AMPA/GABA receptor densities into synaptic weights (already integrated in TVB, see showcase 3). Target cohort data set for modelling is the 1000BRAINS data set. First simulations are being performed on EBRAINS for testing and refining established ageing theories about dedicated brain phenotypes.

2.4.2 Model inversion

Existing data fitting and parameter estimation technologies are currently being evaluated regarding their suitability for cohort level validation. Machine learning and AI approaches will be applied to the same data sets with the intent to be compared against the virtual brain-based modelling and causal inference.

2.4.3 Data availability

Brainscapes will add access to more data modalities with higher coverage of brain regions. In 2021, this will include (only items are listed that are relevant for showcase 1)

- layer-specific distributions of neuronal cells sampled from cortical patches in histological sections for a comprehensive set of cytoarchitectonic brain areas
- fMRI activation maps from different cohorts
- connectivity information extracted from different protocols and cohorts
- connectivity information based on *post-mortem* dMRI.

In 2022, the high-resolution connectivity will be further complemented by *post-mortem* measurements based on 3D PLI, and cell distributions will be complemented with type-specific measurements. The Brainscapes client will further allow queries to any data modality linked in the KG, even if they are not yet deeply supported as a structured data type. The HBP will concentrate on increasing the coverage of brain regions with the most strategically relevant data types, coordinating data acquisition and integration efforts between WP1 and WP4.

2.4.4 EBRAINS integration

The Python client will receive significant extensions during SGA3, support updated versions of brain parcellations, and be linked to more data sources. The list of supported reference spaces will be extended by the Freesurfer average template. Besides the Python client, an HTTP API and a command line client will be released which match its functionality. In the longer perspective, we aim to give access to Big Data queries that go beyond download of individual files, triggering custom extraction of cell densities and connectivity information from large datasets stored in EBRAINS, and allowing to conveniently crop regions of interest from BigBrain. In terms of simulations, it will be required to make use of ICEI resources in order to perform efficient parameter sweeps, allowing users to assess various scenarios of mapping data into TVB parameters. Much of the development for this is done but requires more integration efforts, such as creating intermediate API server on the ICEI cloud to enable seamless execution of workflows.

3. Showcase 2: Improving epilepsy surgery with the Virtual Big Brain. Demo 1

3.1 Introduction

Showcase 2 builds on a success story which started in the HBP's earlier SGA1 and SGA2 phases: the virtual brain epilepsy modelling and the associated clinical trial EPINOV (2019-2023), which aims at the confirmation of the modelling in 400 prospective epilepsy surgery patients. Worldwide, there are about 50 million medically refractory epilepsy patients. In those patients, medication does not provide relief and the surgical removal of the epileptogenic zone (EZ) remains the principal alternative treatment option. The success of this intervention is based on correctly identifying the EZ within the brain network. Current surgery success rates are about 60-70%, but going as low as 25% in extratemporal epilepsies. Previous modelling efforts during SGA1 and SGA2 have demonstrated an

improved capacity identifying the EZ through personalised brain network modelling in a cohort of 50 retrospective patients. So far, the personalisation of epilepsy patients' brain models has been limited to the use of individual connectomes and SEEG data, maintaining an otherwise fully generic (regionally invariant) network. The present showcase has two aims: firstly, to demonstrate that the integration of high-resolution and multi-scale atlas data in personalised brain models results in significant improvement of the models' predictive power; and secondly, to expand the use of virtual brain technology in epilepsy to other interventions such as neurostimulation, which has technically not been usable with the current resolutions in The Virtual Brain (TVB), but will become accessible with high-resolution TVB. As only about 20% of all patients initially considered as candidates for epilepsy surgery finally undergo this procedure, neurostimulation is an important alternative. Showcase 2 illustrates the application of high-resolution TVB to epilepsy, crucially requiring the integration of a large number of EBRAINS services. Its successful application will lead to an improved epilepsy patient management and novel technologies in personalized medicine.

In Showcase 2, we illustrate how EBRAINS enables the transition of TVB technology from discrete networks to spatially continuous cortical and subcortical surfaces. This step is imperative, otherwise the high-resolution connectivity cannot be meaningfully integrated. The price to pay is an increase in the computational demands by three orders of magnitude, so this approach relies heavily on EBRAINS simulation services and high-performance computing resources. Currently, a whole brain region, covering an area of 10-20 cm^2, is represented as a single network node, equipped with a neural population model. The neural field drastically increases the spatial resolution of the simulation to the mm^2 range. Instead of collapsing the brain area into a single point, we have a spatially continuous representation of the activity on the detailed cortical sheet. As a consequence, detailed multi-scale connectome features (up to the scale of 1µm) and regional variations informed by microscopic resolution data embedded in the EBRAINS atlas via the BigBrain model can now be integrated. Neural field modelling enables a more detailed forward solution, i.e. the projection of activity at the source level, electric activity from neural populations, to the sensor level, e.g. SEEG electrodes in epilepsy patients. The currently poor source-sensor link has been considered to be the most detrimental factor in epilepsy patient modelling. The scientific key challenge in these efforts is the development of a strategy to converge individual patient data with high-resolution *post-mortem* data, without the loss of predictive patient-specific data features.

The delivery of Showcase 2 at M9 is an HBP internal stepping stone, as it establishes the spatial basis for all subsequent integration efforts in Showcase 2. The existing functionality within Showcase 2 is described in Section 2.2 and in a video demonstrator, illustrating the steps leading to the neural field construction. The latter constitutes the M9 Deliverable. Section 2.3 describes how to access the demonstrator. Ongoing work leading to the next Showcase Deliverable in M21 is described in Section 2.4.

3.2 Technical Specification

The novel high-resolution TVB comprises a mesh of the cortical and subcortical surfaces, spanned in three-dimensional physical space, comprising intra- and corticocortical connectivity. At the time of writing, the implementation in EBRAINS had not yet been established and all existing software is distributed across various components. The key features of these components and their technical specifications are as follows.

- Data comprise T1 and diffusion-weighted MRI scanning, as well as SEEG electrode implantation and a post-implantation CT scan. From the structural T1 weighted MRI scan, the cortical surface and subcortical segmentation were reconstructed using the Freesurfer recon-all pipeline, resulting in one closed triangulated mesh per hemisphere with a total of ~260k vertices, with a vertex wise area in the range of 1 mm^2. For the current Deliverable, simulations do not run on EBRAINS yet, but on regular workstations and require a downsampling by a factor of ten to approximately 20k vertices, with vertex wise areas in the range of 5 to 10 mm^2.
- From the post-implantation image, we extracted the exact electrode positions and aligned them with the cortical mesh. To improve the source-sensor mapping via an improved forward model, we consider the dipole source orientation, which is generated by pyramidal neurons in grey

matter oriented orthogonally to the cortical surface. The high-resolution mesh allows this formulation and model the individual cortical folding pattern of a single subject.

- The improved pipeline considers more realistic important subcortical structures. We currently focus on the hippocampus. The hippocampus is a most commonly affected region in temporal lobe epilepsy. The detailed anatomical structure of the hippocampus is usually beyond the resolution of MRI used in routine clinical practice. We used the high-resolution microscopic data available in EBRAINS to extract the surface of the hippocampus and seamlessly connected it with the cortical mesh, such that the neural field continues from the cortical surface into the hippocampus.
- High-resolution connectivity information is integrated. We used the MRtrix3 software to pre-process and perform tractography in the diffusion-weighted MRI data. In the current state of the art, reconstructed fibre bundles were grouped according to the VEP brain atlas in 162 cortical and subcortical regions. With the neural field model, we now use the estimation of single fibre bundles to set the connectivity between vertices of the mesh, regardless of the chosen brain parcellation. This formulation provides the framework allowing the integration of the *post-mortem* high-resolution dMRI (2021) and PLI (2022) connectivities.
- The mathematical implementation of neural masses has been realised as follows: Each vertex point of the cortical mesh is represented by the 6-dimensional epileptor model, previously developed in SGA2 as a canonical computational model for seizure generation. Local connectivity between cortical vertices is estimated by a Laplace kernel, which decays exponentially with increasing distance along the surfaces. The long-range heterogeneous connectivity between cortical and subcortical regions is directly imported from the structural connectome. Signal transmission delays are estimated from the tract length. The system of differential equations is solved using a deterministic Heun integration scheme with a step size of 0.2 ms.

3.3 How to access the Showcase

The demonstrator is a video, and can be found under this link:

https://youtu.be/azat_LcN1Lc

3.4 Looking Forward

The following activities are ongoing and are expected to showcase their results in M21.

3.4.1 Model inversion

Currently, existing data fitting and parameter estimation technologies, in particular those used in the clinical trial EPINOV, cannot be applied to spatially continuous surfaces and need to be extended and adapted. Technical challenges include the application of Monte Carlo sampling techniques to neural fields and achieve convergence in finite time. Alternative methods are considered in parallel, including likelihood-free inference. This is part of the validation efforts in EBRAINS and we expect a functional prototype in M21.

3.4.2 Data availability

Brainscapes (Showcase 1 prototype) will add access to more data modalities with higher coverage of brain regions. In 2021, this will include (only items are listed that are relevant for Showcase 2)

- iEEG recordings behind a new GDPR-compliant authentication layer
- Layer-specific distributions of neuronal cells sampled from cortical patches in histological sections for a comprehensive set of cytoarchitectonic brain areas

- Connectivity information based on *post-mortem* dMRI.

Early in 2021, the metadata structures for this multiscale dataset will be prepared on the basis of the recently released openMINDS schemas, to allow for a timely integration into EBRAINS data services. In 2022, the high-resolution connectivity will be further complemented by *post-mortem* measurements based on 3D PLI, and cell distributions will be complemented with type-specific measurements.

3.4.3 Data fusion

Data from *post-mortem* brains need to be successfully integrated with data from individual patients. Strategies for doing so are being currently investigated, likely leading to a hierarchical Bayesian approach, in which patient-specific data (connectome, sodium imaging, PET) are used as a prior for model inversion using a high-resolution TVB (derived from *post-mortem* brains). As a minimum, we expect proof of concept in M21 demonstrating improved predictive power of the approach using simulation data.

3.4.4 Hippocampus modelling

An initial model of the CA1 region of the human hippocampus will be reconstructed as a region of interest, at a single neuron resolution, using the NEST simulator. Single neuron models, synaptic properties, and network connectivity, will be implemented using experimental data on cell densities and distributions, synaptic physiology, morphologies, and electrophysiology for pyramidal cells and interneurons as soon as they will become available. Missing data will be estimated or adapted from comparative studies on rodents. The model is expected to be continuously improved as more and more data become available.

3.4.5 EBRAINS integration

At the time of writing, the Demo 1 reconstructions and simulations were not yet available for execution in EBRAINS but are foreseen for Demo 2 in M21, making use of simulation, atlas and Knowledge Graph services. In addition, co-simulation technologies are being developed for TVB-NEST in WP1 and WP4, and shall be applied to the co-simulation of the CA1 subfield of the hippocampus with the high-resolution Virtual Big Brain.