DELIVERING PRACTICAL RESULTS FOR REVOLUTIONARY CLINICAL APPLICATIONS

THEVIRTUALBRAIN.

SWITCHING
TO THE FAST LANE

For over 20 years, bright minds and ambitious projects have attempted to emulate the human brain across various scales of organization. Despite impressive efforts to bring in the latest and greatest computing power of massively parallel hardware, success hasn t yielded practical applications yet.

To get practicality sooner, The Virtual Brain takes a network approach on the largest scale:

By manipulating network parameters, in particular the brain s connectivity, The Virtual Brain will simulate its behavior as it is commonly observed in clinical scanners (e.g. EEG, MEG, fMRI).

Though The Virtual Brain will incorporate the complex world of neuro-chemistry only to a small degree, it has lots to gain by not becoming as complex as the brain itself.

Instead, The Virtual Brain intends to embrace and extend novel concepts from computational, cognitive and clinical neuroscience in order to drastically reduce the model's complexity while still keeping it sufficiently realistic — and delivering the same output as clinical brain-scanners.

TRANSFORMING
CLINICAL THERAPY FOR BRAIN DISEASES

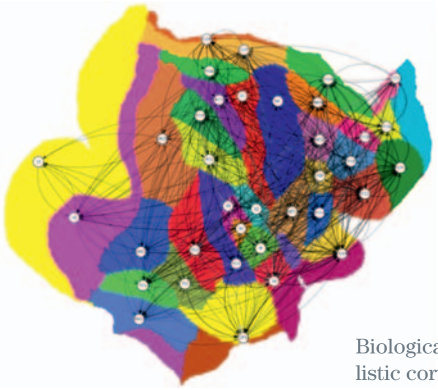
Prototypes of the system ultimately becoming The Virtual Brain already delivered unique insights into the functioning of the human brain s resting state network. Since the diseased brain shows different resting state behaviors in epilepsy and stroke, our connectivity based approach bears the promise to gain novel insights into the origins of network disorders.

Especially in the western world, epilepsy and stroke rank among the most common causes for death/disabilities and put a high socio-economic burden on society.

The Virtual Brain will be the first framework offering practical simulations to clinics treating epilepsy and stroke patients thanks to four unique features:

- The whole simulation system will be remotely accessible through a simple web browser, including a stunning 3D visualization. No need to have supercomputers or large databases on-site.
- The Virtual Brain will deliver the same neuro-imaging results as a patient's brain (EEG, MEG, BOLD). Its design will allow for complete customization and validation by uploading the patient's scanner readings into the simulation.
- The Virtual Brain is being tested and validated with data from clinical sites in Berlin, Irvine, London, Marseille and Toronto: Next up, this exhaustive and growing database of hundreds of brain scans from the past will serve as a wealthy source of normative constraints.
- By manipulating network parameters or intentionally damaging The Virtual Brain, predictions will be possible about the potential success of surgical or pharmaceutical interventions.

The participation of many clinics and research centers around the world is a beneficial feedback-loop, refining The Virtual Brain continuously with growing experimental data validated against refined models.



Biologically realistic cortical connectivity of brain areas

UNRAVELING THE KEYS TO THE BRAIN

What makes The Virtual Brain unique is a rather new way of addressing the inherent difficulties of simulating a large-scale network like the human brain:

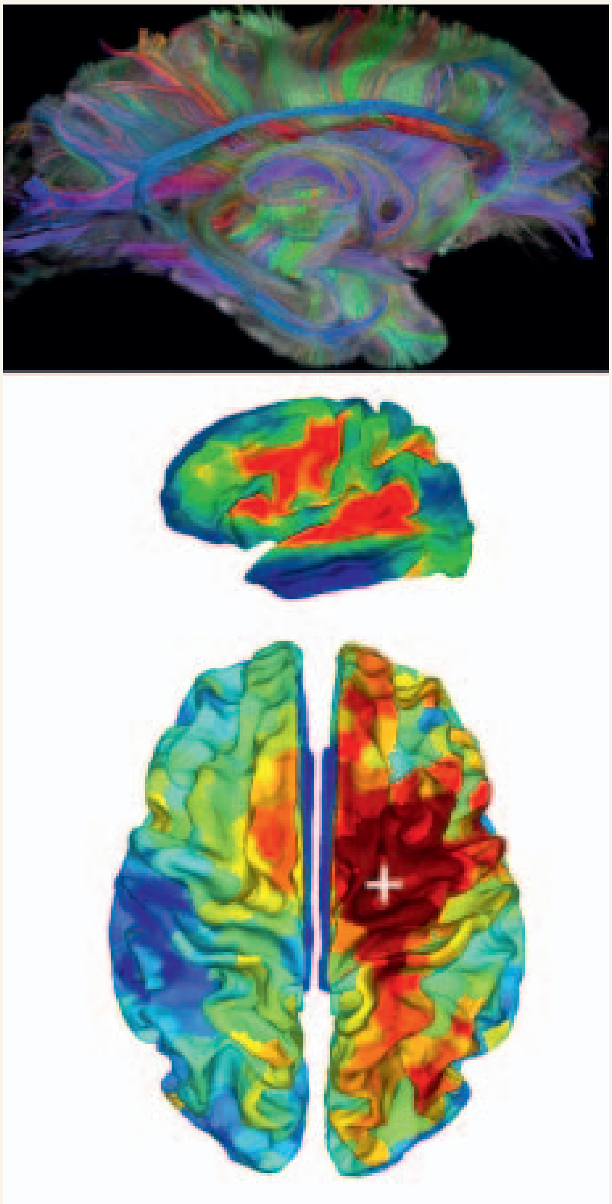
- Understanding the brain's behavior as a network's performance at all seems obvious but isn't so much in hindsight. The Virtual Brain builds upon the discovery of the critical network parameters of the human brain, their influence to functional processes and their proper tweaking to rectify a malfunctioning or damaged network.
- Rather than making simplifying assumptions about topology, density and range of large-scale connectivity (anatomical realism), The Virtual Brain will invoke the Connectome, simultaneously integrating multiple modes of network activity.
- The Virtual Brain purposes to include an array of new and useful measures for the brain's organization thanks to extensive use of graph theory: segregation, integration, efficiency and influence of subnetworks, nodes and their edges.
- For the first time, The Virtual Brain will provide the same qualities and quantifications of common neuro-imaging methods (EEG, MEG, fMRI) as a real brain, making it ideal for experimental validation and customization.

Realizing that network nodes in actual human beings are far from homogenous, The Virtual Brain captures the functioning of the sub-networks of the human brain through the novel concept of the space-time structure of the network couplings featuring means for quantifiable coupling matrices within and across regions.

Upcoming versions will constantly process these experimental results through machine learning methods, further refining The Virtual Brain to the best match for an individual clinical case.

While the responses of isolated brain regions are well studied today, The Virtual Brain overlays an elaborate map of functional pathways on and between these regions:

A robust mathematical core of anatomically realistic connection matrices (based on DTI/DSI scans) defines the network itself, a physiological model of neural populations captures the individual regions. This model is used to search for the crucial points in actual network damage scenarios in brain health.



Merging of structure & function in The Virtual Brain. Top: structural neuroimaging, below: functional neuroimaging

MATCHING BRAIN SCANS ACROSS MODALITIES

The Virtual Brain will produce virtual EEG, MEG and BOLD signals comparable to the same scanner readings of a real brain - both in quality and quantity as well as on multiple, realistic time-scales and anatomically accurate locations.

This feat will be achieved through a biologically realistic connectivity matrix (building on e.g. the COCO-MAC database and DTI/DSI scans) and by modeling The Virtual Brain's 3D voxels within a realistic skull-shape.

Speaking of 3D, current prototypes make headway towards a far more lofty goal: Watching, zooming and rotating The Virtual Brain while performing these scans — in a browser and in real-time.

Producing and comparing scanner results dynamically from the real and virtual brain and across imaging modalities paints a bright vision of revolutionary applications as well as a clear pathway to constant future enhancements:

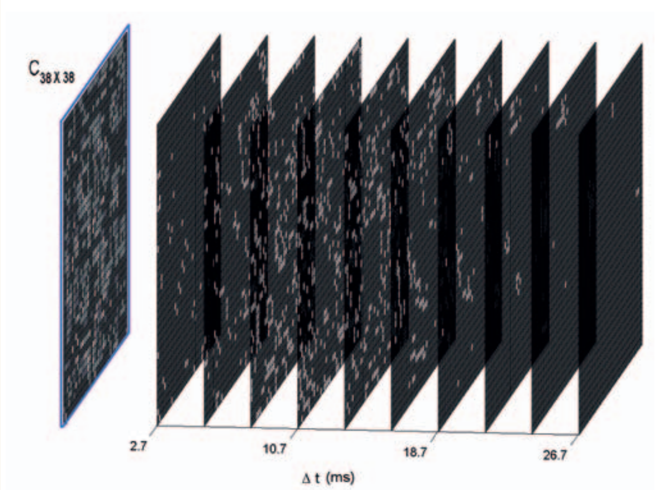
- The brain of a real patient can be scanned and subsequently will be modeled with The Virtual Brain by uploading the scanner results.
- Vice versa, the virtualized brain can be scanned and the readings compared back to the patient's in order to confirm the desired accuracy of the model.
- New modeling/network hypotheses could be applied to The Virtual Brain and realistically tested through virtual scans and comparison with experimental data.
- One could even "browse" through a shelf of different virtual brains until one finds the best match for preset experimental data.

ACCOUNTING FOR DIFFERING SPEEDS

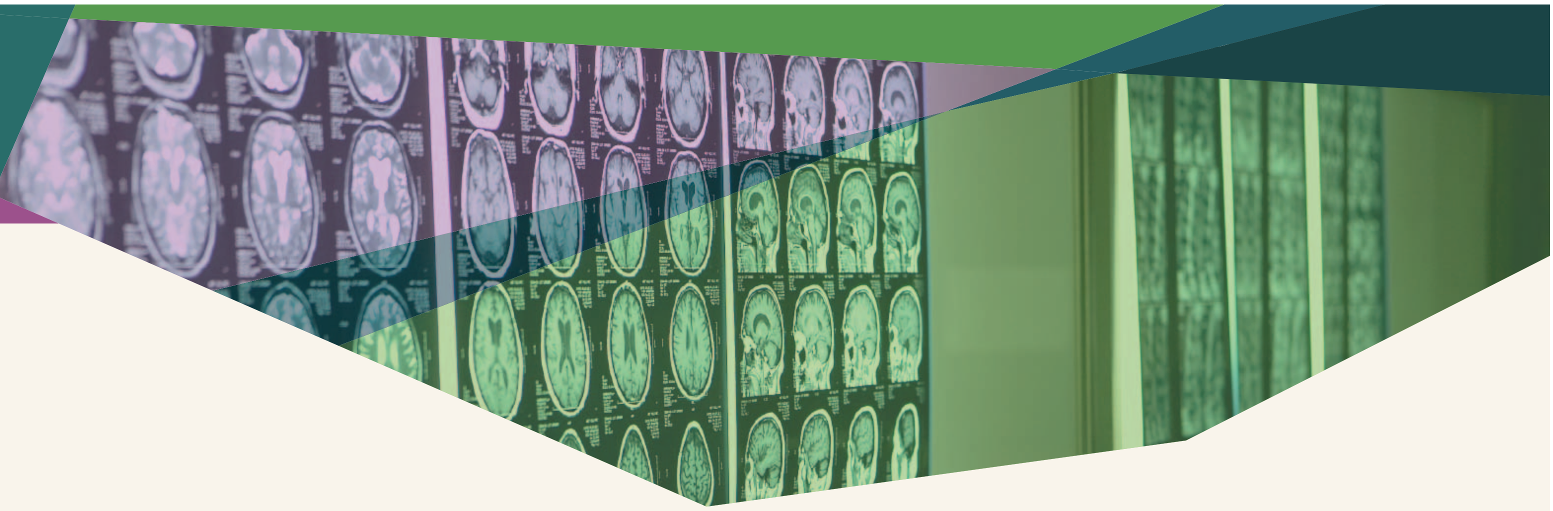
While the brain's well-known folded structure was always admired as nature's masterpiece of squeezing as many neurons as possible in a constrained space, a second anatomical feat of this structure was discovered only recently.

Turns out that the distance a neural signal has to travel is absolutely necessary to truly understand the brain s network: only when taking into account the unique time-delays for neuron-to-neuron signal transmission stemming from the brain's anatomy, one can successfully emulate the brain's measurable spatial-temporal patterns.

Without those innocuous time-delays (ranging from few to hundreds of milliseconds, depending on distance and direction), our brain would simply cease to work correctly.



Space-Time Structure of the brain: if signal transmission in the brain were instantaneous, all brain connectivity would collapse on a single plane (to the left), describing structural links between brain regions. As such is not the case, brain connectivity actually needs to unfold its space-time structure (to the right) over the signal transmission time delay Delta t to adequately describe communication.



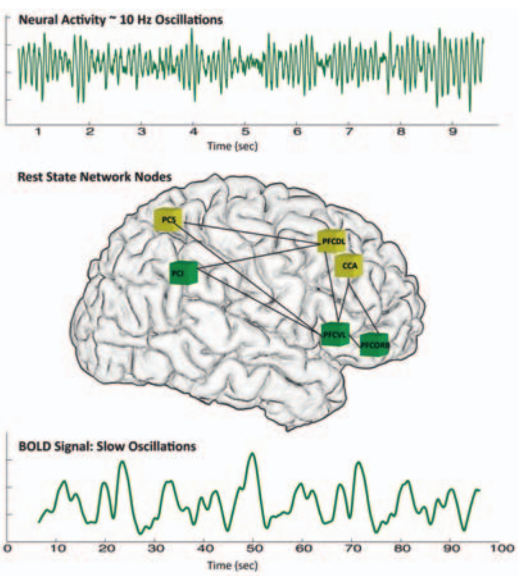
RESTING IS THE NEW ACTIVE

Historically, the human brain was understood to behave like a classic feed-forward information processing system: you exhibit it to an external stimulus (sensory input) or let it steer a task (motoric action) and its measurable signaling patterns will reflect this behaviour — somehow.

What's missing from this picture is a reasonable explanation of the undoubtedly ongoing brain activity when it's doing just... nothing. Is it only noise, irrelevant for functional processes or rather something else?

The fascinating results from a large number of experimental investigations in the last decade point to "something else": recent theo-retical analysis has indeed confirmed the major role of the so-called "resting state networks" within the brain. Their complex oscillations on different time-scales even provide the utter foundation of functional processes within the brain.

Metaphorically speaking, the resting state of the brain can be pictured as a nimble, always vigilant tennis player, waiting on his baseline for the new service of his opponent (which would be an outside stimulus or a task being performed). Thanks to his constant motion, mindfully envisioning possible routes, he can react more readily to events from various directions.



Multiscale simulation results from the resting state (see Deco, Jirsa, McIntosh 2011)

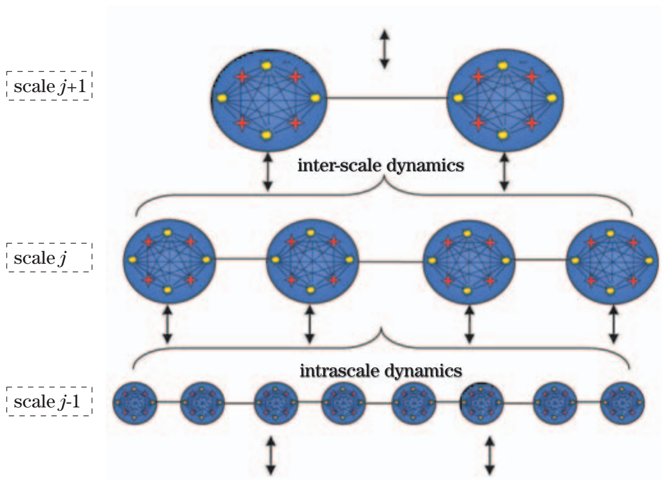
THE AUTONOMY OF SCALES

Traditional understanding of the brain divides it into different regions and lobes of varying size (from tiny to huge), each being responsible for some different cognitive abilities. Additionally, we know that the brain's signaling patterns show oscillations on different time-scales such as 10 Hz is involved in the resting brain, 4 Hz in memory and 40 Hz in the cognitive brain.

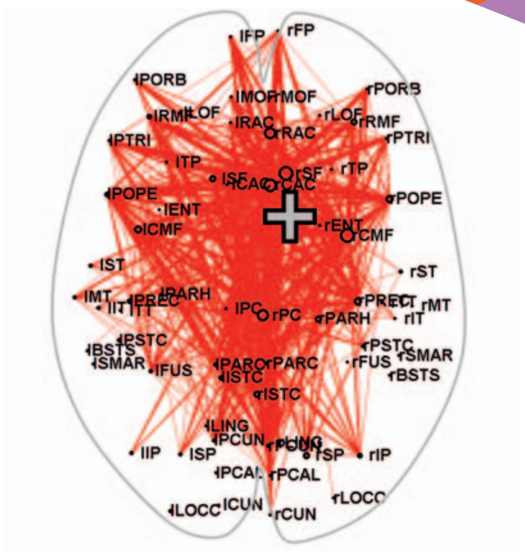
Unifying the observed behaviour and organization of the brain on multiple spatio-temporal scales, several approaches have been studied by perusing analogies from known physical phenomena (e.g. fluids or magnetization). However, none of them could explain, let alone model the brain's behaviour in a sufficiently solid way.

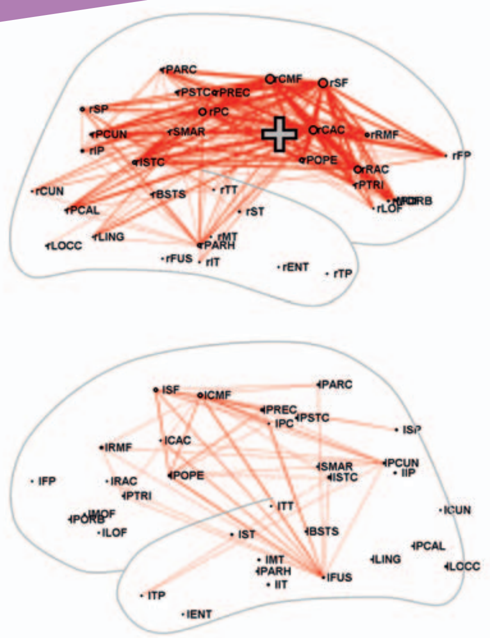
The Virtual Brain is well underway to invoke a clever blend between classic unifying multiscale frameworks and pyramid-style approaches seen in other informatics-oriented projects:

- Moving upwards through the scales, The Virtual Brain uses dimension reduction techniques to keep the principal influence of smaller scales on larger ones while leveling out their inherent complexity.
- Moving downwards through the scales, more detailed modeling parameters can be used, e.g. to test specific hypotheses.
- No particular scale is dominating the model. Instead, multiple scales operate through mutual interdependence which has also beneficial effects on the computational load of the model.



Multi-scale Framework: incorporating intra- and inter-scale principles of organization over a hierarchical tier of dynamics.





A single lesion (at the cross) results in a functional reorganization of the brain network. Interactions across the brain that were significantly changed (increased or decreased) are shown in a dorsal view of the brain (topmost plot) as well as within the left and right hemispheres (see Alstott et al 2009; Jirsa et al 2010).

EPILEPSY: SEIZING NETWORK BREAKDOWNS

Though a still mysterious hardship for people affected, epilepsy presents unique insights and learning experiences about the human brain's bearing with grave network disturbances, respectively seizures. Healing epilepsy is still a puzzle, where some pharmaceuticals only mitigate the effects. Surgical interventions are typically limited to focal epilepsy and largely fail to predict the behavioral after-effects of a resection or atrophy.

The project's sites in Marseille and Toronto are helping here by providing their exquisite expertise and extensive archive of epilepsy studies (longitudinal as well as cross-sectional). These cover state-of-the-art neuro-imaging data (scalp and intracranial) and extensive behavioral characterization.

The Virtual Brain uses the available epilepsy data to further two scientific topics:

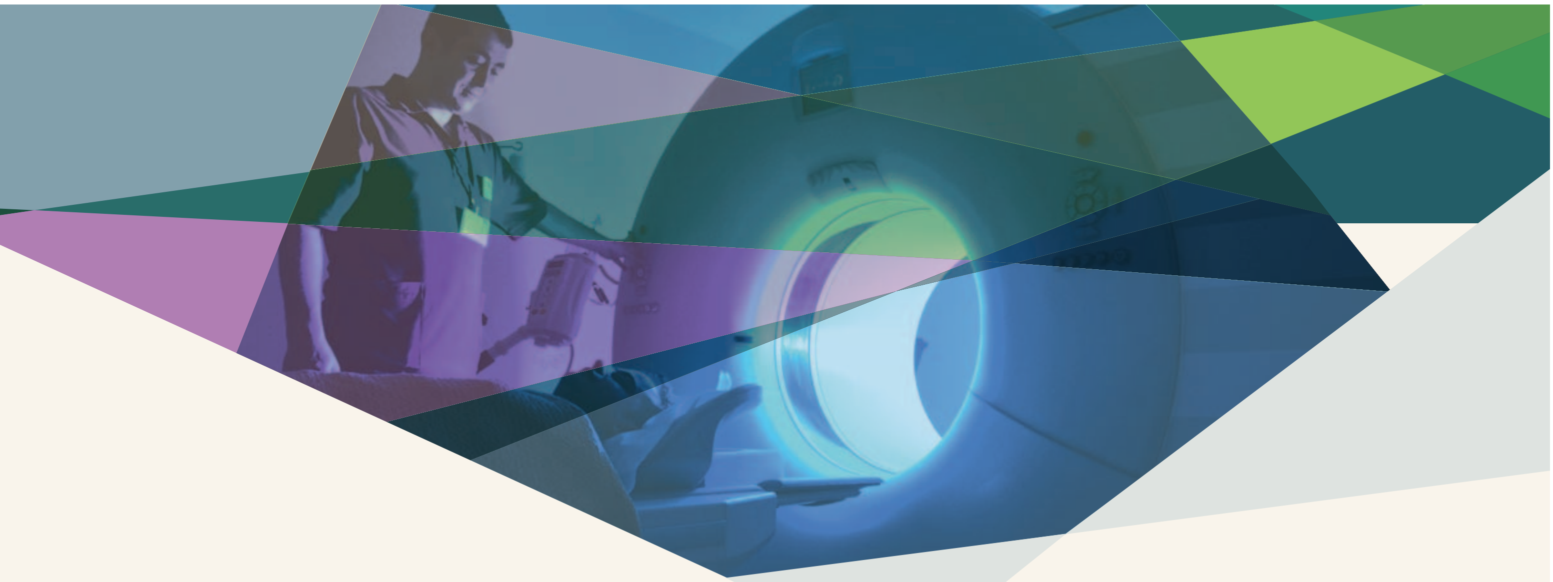
- Better understanding of the brain's fundamental mechanisms of structure/function relationships and effectively refine the simulation.
- Aggregation of pre-/post-surgery differences to ultimately predict the behavioral effects of any incision in a given brain region.

STROKE: THE PATH TO RECOVERY

Strokes still rank as the third-highest cause of death in the western world. Even when survived, strokes are largely responsible for mild to severe behavioral deficits, often resulting in years of treatment, which in itself isn t understood very well.

The Virtual Brain will assess a vast array of longitudinal and cross-sectional data of several hundred stroke patients from the project's sites in Berlin, London, Toronto and Irvine. These provide profound insight into the effects of clearly located lesions on the overall functionality and health of the human's brain.

Evaluating the ramifications of a stroke or a lesion gained by external injury is the prime example of deciphering how a really complex networks reacts to the isolated failure of some nodes — and the route to its recovery when analyzing post-treatment data.



PUTTING COMPUTERS ON A DIET

Obviously, simulating a human brain even halfway realistically requires a remarkable amount of computing power. The Virtual Brain won't be immune to the well-known teraflop disease but will have a remarkable edge in scalability — meaning up AND down.

Basically, the goal is to dramatically lower the barriers to access its computing power while also developing and providing less demanding incarnations for local, secluded usage.

The completely open-source architecture of The Virtual Brain is based on Python and Java — in line with lots of sister-projects in the neuroscience community.

The main system will be accessible through a simple web browser, making it very easy to upload imaging data, running 3D-animated simulations in WebGL and getting results back. By channeling communication through the browser, many scientists and doctors in laboratories and clinics can participate without having to host and run their own supercomputers.

While time-consuming model explorations must still run on several high-performance clusters available to the project team, simpler versions of The Virtual Brain can be very well executed on run-of-the-mill laptops in laboratories around the world. Though these versions won't offer the same level of detail, they will still provide useful ideas and hypotheses with ease and solitude.

WebGL Java python™

THE VISION

A BRAIN-HEALTH DECISION SYSTEM

Driven by the continuing collection and normalization of clinical data within The Virtual Brain, the simulation will get ever more refined. The combination with the important feedback-loop of virtual therapy proposals and their subsequent experimental validation leads towards a compelling vision:

Patients suffering from a brain-related disease/injury will be thoroughly scanned, collecting individual EEG, MEG and BOLD data. Complemented with a detailed demographic, genetic and physiological anamnesis, the doctor uploads this data to The Virtual Brain.

Evaluating the bespoken simulation, the doctor will be able to judge the patient's brain responses to different therapy approaches – all safely within a virtual framework.

SEASONED EXPERTS IN NEUROSCIENCE

Over the past five years, this consortium of 15 distinguished neuro-scientists joined their efforts to solve humankind's biggest mystery: understanding the human brain functions and dysfunctions — and create a way to simulate and predict its behaviour.

Spanning three continents and 10 sites, the team members combine extensive knowledge and experience from computational, cognitive and clinical neuroscience. Now, as solid and tested theoretical frameworks emerge through peer-reviewed research, this team makes its move towards a realistic and openly accessible virtual brain.

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