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A Global Challenge in Need of Innovation

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LIFE SCIENCES & BIOLOGY

MEDICAL & HEALTH SCIENCES

Stroke is the third leading cause of both death and disability worldwide, but unfortunately, current diagnostic tools are unsatisfactory. Dr Roustem Miftahof and Dr Alexander Hermann at Advanced Biosimulation Technologies LLC, USA, are overcoming the limitations of existing diagnostic tools with the development of the Neuro-Glia-Vascular Unit Engine. This transformative tool for clinicians and biomedical researchers provides patient-specific health insights with the potential to improve care not only in stroke but across a range of neurological disorders.

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Stroke: Incidence, Impact, and Care

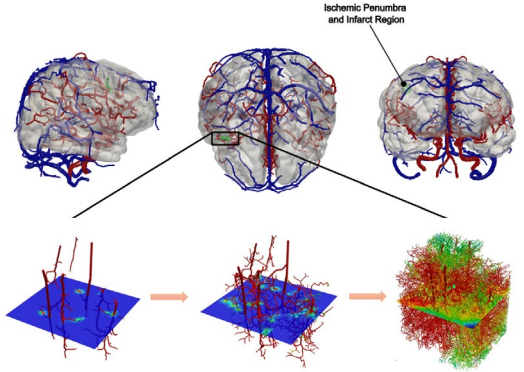
Stroke is the third leading cause of both death and disability worldwide. Globally, over 100 million people live with its debilitating sequelae, including direct physical effects such as paralysis, speech impairments, and difficulty swallowing, and physical and indirect effects such as mental fatigue, anxiety, and depression. While patient care is underpinned by the use of diagnostic tools that inform medical decision-making, patient-centred diagnosis is best practised through shared decision-making; an iterative dialogue between doctor and patient, which respects a patient's needs, values, preferences, and circumstances.

Limitations of Conventional Neuroimaging in Stroke: The Need for Dynamic, Patient-Specific Insights

Conventional medical imaging techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), CT perfusion, hybrid ultrasound computed tomography (US/CT), and positron emission tomography (PET/CT and PET/MRI), provide static high-resolution visualisation of brain anatomy and detect structural changes caused by strokes, however, they don't answer questions of the tissue viability, recoverability, and how the brain is actually functioning in real time. Although these modalities offer some physiological and potentially prognostication information, this information is often too coarse and inadequate for a specific stroke patient.

To address these limitations, scientists and computer engineers, led by Dr Roustem Miftahof and Dr Alexander Hermann at Advanced Biosimulation Technologies (ABS-Technologies), have developed a groundbreaking solution: the Neuro-Glia-Vascular Unit Engine (NG-VU Engine) computational platform. Based on the contemporary physiological concept of the neuro-glia-vascular unit, it replicates in *silico* the fundamental structural and functional elements of various regions of the human brain. By integrating a comprehensive map of neuronal connections (the connectome) and individual physiological information, the NGVU-Engine creates a digital analogue of the brain.

This engine delivers patient-specific health insights rather than typical generalised AI-generated assessments, enabling precise, individualised healthcare solutions and offering real-time, dynamic insights into brain tissue viability, functionality, and cognition across macro-, meso-, and microscale levels. Linked to available Internet of Things devices, the platform is capable to simulate physiological processes that are often inaccessible by other diagnostic tools. These include volumetric cerebral blood flow, oxygen and glucose consumption, and brain cell metabolism. Seamlessly integrating into existing hospital workflows, the platform can function as both a clinical decision-support tool for doctors and an invaluable information source for patients.



Established at birth, the large intracerebral vascular network grows postnatally, through the process of capillary angiogenesis. The "NGVU-E" capillary angiogenesis algorithm accurately extends the vascular network from 1.0 mm to 2-5 micrometer scale. The image above is adapted from: Ii S, Kitade H, Ishida S, Imai Y, Watanabe Y, Wada S (2020). Multiscale modeling of human cerebrovasculature: A hybrid approach using image-based geometry and a mathematical algorithm. PLoS Comput Biol 16(6): e1007943; https://doiorg/10.1371/journal.pcbi.1007943

The NGVU-E introduces a new approach to stroke management, evolving from the traditional 'time-brain' model to a more advanced 'time-tissue-brain' patient-specific perspective. This engine can predict strokes before they occur, enabling the implementation of prophylactic interventions. In cases of acute ischemic stroke, it accurately maps damaged brain areas (the infarcted zone) and at-salvageable zones (the penumbra). By analysing the effect of the stroke-affected area on viable brain regions using connectome data, the NG-VUE helps predict recovery potential and guides rehabilitation efforts, giving survivors the best chance for optimal functional recovery.

This precision helps doctors choose treatment strategies with laser precision. The platform offers the potential of lower radiation exposure for patients with stroke and shortens the time needed for diagnostic investigations by eliminating the need for scientifically imprecise studies, thus reducing healthcare costs.

Clinical Validation and Future Directions

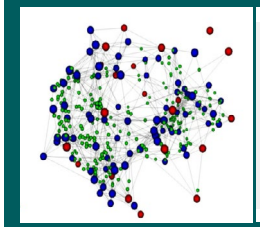
Following the successful completion of a retrospective cohort study on validating the NG VU Engine's accuracy in identifying salvageable brain tissue in patients with stroke, Dr Volker Hesselmann, Head of Interventional Neuroradiology at Asklepios Clinic North, Hamburg, Germany, explained, 'The future we've been dreaming of is now within reach. With its ability to simulate the brain's dynamic processes and integrate real-time data, the NG-VU Engine represents a transformative leap forward in stroke care and personalised medicine.' The platform will be imminently tested in real-time emergency settings. ABS Technologies is about to start another retrospective cohort study in collaboration with a prestigious US-based academic medical centre. This marks a paradigm shift in how doctors perceive and manage strokes.

Transforming Neurodegenerative Brain Disorder Management

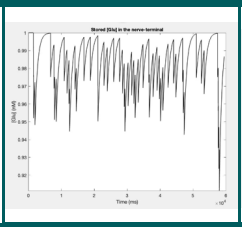
Beyond stroke care, the NG-VUE holds immense potential in addressing critical challenges associated with neurodegenerative brain disorders, including Alzheimer's, Parkinson's, and Huntington's diseases, as well as small vessel and frontotemporal dementia. These conditions present notable societal and economic challenges due to their increasing prevalence, complex permutations, and paucity of effective treatments. Patients with neurodegenerative disorders often experience progressive cognitive and motor disabilities, resulting in substantial dependence on caregivers, leading to profound emotional, physical, and financial strain on families and society.

The NGVU-E addresses these challenges by enabling accurate diagnoses of neurodegenerative disorders. It guides the selection of tailored treatment strategies while predicting disease trajectories for each patient. By offering clinicians advanced tools to forecast disease outcomes, the platform provides a quantitative, objective surrogate of cognitive function based on brain activity itself rather than relying on patient task performance and subjective external testing. Additionally, the NG VUE serves as a virtual environment for designing and testing pharmaceuticals, allowing researchers to evaluate their efficacy and safety in highly specific simulations. This allows more efficient ligand assessments and has the potential to shorten preclinical evaluations and especially tailor trials. All of these, especially the latter, will allow faster, more efficient, less expensive trials that will be more likely to reach successful endpoints.

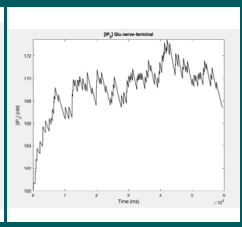
With its ability to simulate and analyse patient-specific brain dynamics, the NGVU-E stands as a transformative tool for clinicians and biomedical researchers. By tackling the diagnostic, treatment, and prognostic challenges of brain pathologies, it plays a role in significantly improving patient outcomes and reducing the burden on families and healthcare systems worldwide.



Neuronal network dynamics

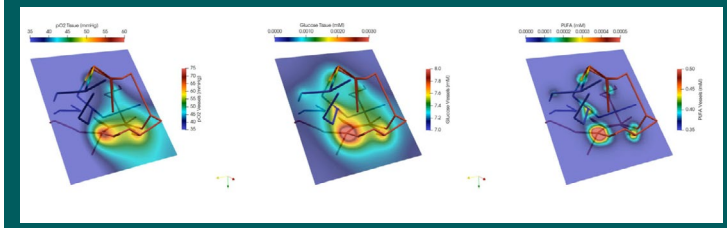


Glutamate release



IP3 production

⋀ The "NGVU-E" platform adds the 4th dimension (time) by providing insights to the dynamics of internal physiological processes underlining the vast repertoire of biological phenomena.

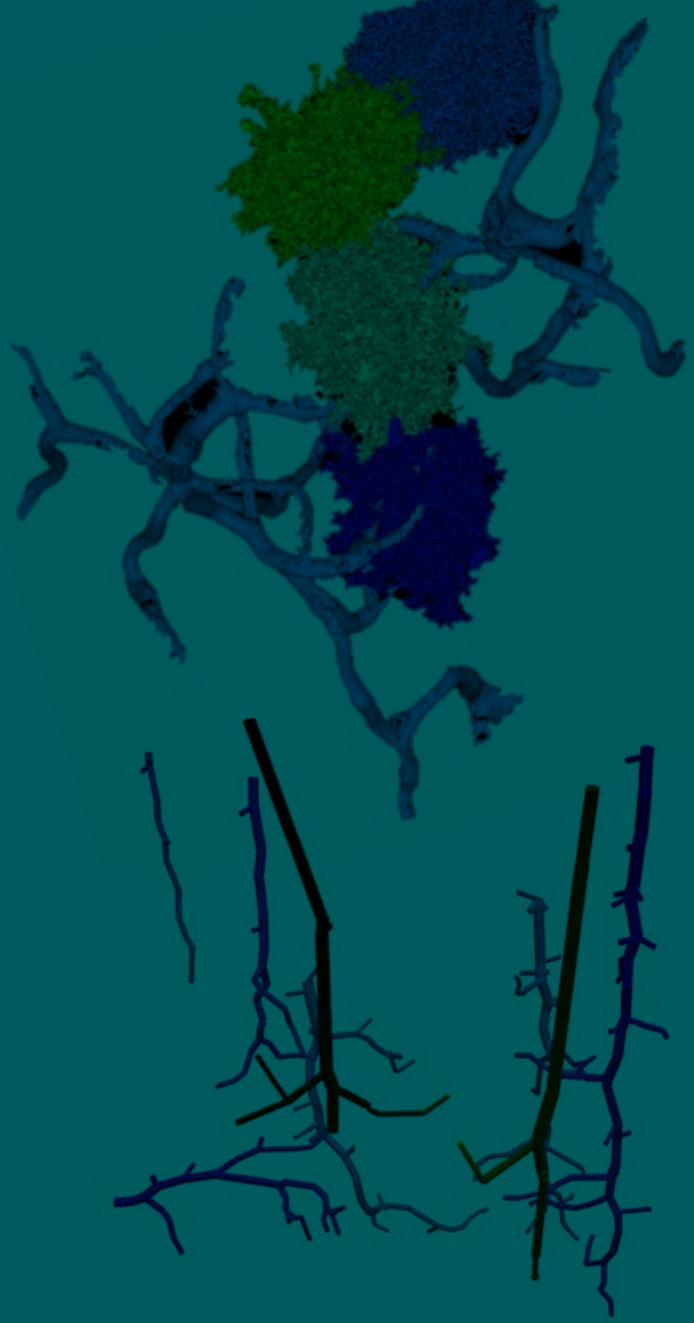


Oxygen distribution

Glucose distribution

Fatty acid distribution

⋀ Real-time information about cell metabolism and bioenergetics, oxygen, glucose and fatty acids delivery are essential for accurate assessment of the viability of brain tissue. The "NGVU-E" allows doctors to follow real-time changes of blood and nutrient supply, brain cellular activity during and after intervention/treatment.



∧ The NGVU-E accounts for variable cell morphology and physiology of the brain. Neuronal, glial and vascular networks are morpho-functionally interconnected to create an accurate "replica" of a region of interest of the brain.

MEET THE RESEARCHERS

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Dr Alexander Hermann holds a PhD in engineering and continuum mechanics. He specialises in computer simulations, heat and mass transfer modelling, and numerical investigations into human body-implant interactions. Dr Hermann also holds an MBA degree from the Northern Institute of Technology Management, Hamburg, Germany. He has coordinated and led various training sessions and workshops focused on Innovation and Design Thinking, fostering the development of innovative thought processes for both graduate and undergraduate students.

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Since 2006, Dr Volker Hesselmann has worked in the field of radiology and neuroradiology, focusing on interventional neuroradiology, at the University Hospital of Cologne, Münster. He currently works at the Asklepios Clinic North as Chief Physician for Diagnostic and Interventional Neuroradiology. This includes the interventional treatment of strokes, aneurysms, and arteriovenous malformations.

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Dr Roustem Miftahof, an emeritus Professor, Doctor of Medicine, Applied Mathematics and Technical Sciences. Internationally acclaimed as a leading scientist in the field of systems computational biology and medicine, he has authored eight books, 16 book chapters, and over 150 scientific publications. His research expertise lies in pathophysiology of psychosomatic disorders, mathematical modelling of the brain and drug discovery.

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