Enabling targeted drug delivery through the blood brain barrier

Controlling the oscillations of microbubbles to safely and reversibly open the blood-brain-barrier is a problem. There little state of the art of the modelling. Koopman operators have been applied to single free bubbles. Here we propose to exploit non-spherical oscillations.

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Microbubbles
Drug Delivery
Control Theory

Project Idea

I am an interdisciplinary applied mathematician, having worked worked with clinicians, engineers and measurement scientist. I received my Ph.D. in 2009 under the guidance of Prof. Gert van der Heijden at the Centre for Nonlinear Dynamics at University College London, motivated by the static post-buckling configuration of an charged elastic rod in a magnetic field. After my Ph.D. I took a post doctoral position at the department of Mechanical Engineering, also at UCL, as part of the ultrasound research group. The research moved from Hamiltonian dynamical systems to collective behaviour of driven nonlinear oscillators, investigating the oscillations of bubbles which can form in tissue when exposed to high-intensity therapeutic ultrasound.

This lead to an another post-doctoral position at the Institute of Cancer Research, where I designed a treatment planning platform for transcostal high-intensity focused ultrasound. This involved optimization of linear partial differential equations for acoustics on large domains, with constrained on where the acoustic field should be focused, while minimizing damage to surrounding structures. I then obtained a permanent position at the National Physical Laboratory, which is the government laboratory in the United Kingdom. My main responsibility was to lead the standardisation efforts for therapeutic ultrasound. A significant proportion of my work related to validating measurement-based simulations, i.e. simulations on domains computed from imaging data, with initial conditions taken measurement data. I am an active member the IEC technical committee on ultrasound, working to bring the knowledge to a standard.

At Fraunhofer MEVIS I have worked on a number of projects, expanding expertise into other areas of diagnostic ultrasound, image-guided therapy as well as systems biology. I have recently been awarded a Fraunhofer DISCOVER grant to investigate applications of computational topology in medical imaging.

Computational Topology in Medical Imaging

Classical medical image analysis is based upon geometric measures, such as lengths, angles, shapes etc. This is somewhat limited as such measures do not fully capture the complexity of information across lengths scales (as these are measured at single spatial scale), or global properties of data. Radiomics seeks to extend classical image analysis by looking at local variations in pixel-to-pixel intensity, giving a measure of texture. Such local measures seek to quantify intuitive concepts such as smoothness or roughness and have been applied to image segmentation. However, the are highly dependent on the imaging modality and are not reproducible.

Computational topology, and specifically a tool called persistent homology, has recently emerged as powerful tool which can provide insight which is distinct from pixel-based approaches by describing measures of connectedness between objects in an image . It is referred to characterising the shape of data. It has also been significant as embedding in highly connected networks.

I plan to apply techniques from computational topology to two fields: ultrasound thermometry and characterisation of aspects of liver function, via structure. The first application is to use specular information to correlate persistence diagrams with relative changes in temperature.

The second application has a number of aspects. The main aim is to quantitatively model changes in perfusion after resection, via persistence diagrams. Another topic

will be to develop tools which measure cell alignment, which characterise regeneration and also, from microscopy data, characterise the fenestrations along the liver endothelial cells which influence metabolic rates.

Continued [1] here.

Bibliography

[1] Hariharan Ravishankar, Rohan Patil, Vikram Melapudi, Harsh Suthar, Stephan Anzengruber, Parminder Bhatia, Kass-Hout Taha, and Pavan Annangi, "Sonosamtrack – segment and track anything on ultrasound images," arXiv preprint arXiv:2310.16872(2023)

Contribution

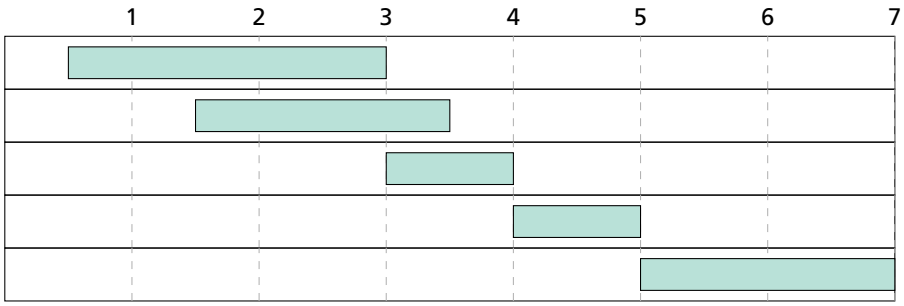
How does the Boost Fund contribute to your project goals?
Describe the "Boost" to your career: Let us know how the funding, career development program and fellowship community make a difference in your career (e.g. for your independence, your development as a researcher, for networking, collaborations, data collection, etc.).
What potential would remain untapped without this funding? You are welcome to be specific, personal, and authentic.

Time Scales

WP1: Model Duration Deliverable
Content
WP2: Coated Microbubbles Duration Deliverable
Content
WP3: Shape Duration Deliverable
Content

Tasks

1 First task
2 Second task
3 Another one
4 Another one
5 Yet another one



Budget Plan

Maximum total funding is € 120000 for a funding period of up to 24 months. Please list your funding requirement by calendar year.

Applying institution:	Fraunhofer Institute for Digital Medicine MEVIS
Name of applicant:	David Sinden
Funding period (max. 24 months, project start between 1 May and 1 Oct 2026)**:**	12

Funding for	**2026**	**2027**	**2028**	**Sum in EUR**
a) Staff (please specify status)				
David Sinden				0
				0
				0
				0
Total *Staff*	0	0	0	0
b) Material costs (please specify each item or group of items)				
				0
				0
				0
				0
				0
				0
				0
				0
				0
Total *Material costs*	0	0	0	0
c) Other costs (please specify each item)				
GPU computing				0
Cloud resources				0
Consumables				0
				0
				0
Total *Other costs*	0	0	0	0

Total Costs	**0**	**0**	**0**	**0**

max. 120000 €