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Research Statement

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 [2, 4]. It is referred to characterising the shape of data. It has also been significant as embedding in highly connected networks [6].

I plan to apply techniques from computational topology to two fields: ultrasound thermometry and characterisation of aspects of liver function, via structure [5]. The first application is to use specular information [3] 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 [1]. 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.

[1] Kei Takahashi, Ko Abe, Shimpei I Kubota, Noriaki Fukatsu, Yasuyuki Morishita, Yasuhiro Yoshimatsu, Satoshi Hirakawa, Yoshiaki Kubota, Tetsuro Watabe, Shogo Ehata, *et al.*, "An analysis modality for vascular structures combining tissue-clearing technology and topological data analysis," Nat. Commun. 13, 5239 (2022)

[2] Yashbir Singh, Colleen M Farrelly, Quincy A Hathaway, Tim Leiner, Jaidip Jagtap, Gunnar E Carlsson, and Bradley J Erickson, "Topological data analysis in medical imaging: current state of the art," Insights Imaging 14, 1–10 (2023)

[3] Emma J Harris, Naomi R Miller, Jeffrey C Bamber, J Richard N Symonds-Tayler, and Philip M Evans, "Speckle tracking in a phantom and feature-based tracking in liver in the presence of respiratory motion using 4D ultrasound," Phys. Med. Biol. 55, 3363 (2010)

[4] Pek Y Lum, Gurjeet Singh, Alan Lehman, Tigran Ishkanov, Mikael Vejdemo-Johansson, Muthu Alagappan, John Carlsson, and Gunnar Carlsson, "Extracting insights from the shape of complex data using topology," Sci. Rep. 3, 1–8 (2013)

[5] Jason W Rocks, Andrea J Liu, and Eleni Katifori, "Revealing structure-function relationships in functional flow networks via persistent homology," Phys. Rev. Res. 2, 033234 (2020)

[6] James R Clough, Nicholas Byrne, Ilkay Oksuz, Veronika A Zimmer, Julia A Schnabel, and Andrew P King, "A topological loss function for deep-learning based image segmentation using persistent homology," IEEE Trans. Pattern Anal. Mach. Intell. 44, 8766–8778 (2020)

Ultrasound & Thermal Therapies

The Right Dose In The Right Place

While focusing a therapeutic ultrasound device to a desired location has been studies as an inverse problem, the subsequent biological effects due to the ultrasound have only been investigated experimentally.

- A foundational tool would be an open-source model for histotripsy [1]. This would be a time-domain finite-volume solver which would solve for the acoustic field with spatially and temporally-varying material properties, including significantly, phase-changes due to both boiling and acoustic cavitation. The nucleation of bubbles would be modelled via a threshold for the peak-negative pressure. The frequency-dependent powerlaw for the absorption of the acoustic wave will be modelled as an integral, solved via convolutional quadrature [7]. The presence of bubbles would present a number of computational challenges, the main being that the bubble dynamics would need to be computed to determine the scatterer co-efficient. The bubble dynamics occur on a finer time scale than the wave equation. Furthermore, dense bubble clouds may require that the interaction between bubbles be taken into account. Preliminary numerical and analytical work has investigated homogenization strategies to reduce the computational cost [3]. The model would be written in a language which supports automatic differentiation, thus enabling optimization of settings in order to ensure only targeted tissue is treated in a computationally efficient manner.
- A measure of dose would be due to the mechanical damage induced by both the acoustic wave and the bubble activity.
- The second measure of biological effect would be to model the expression of heat-shock proteins, via a systems biology approach [6], and couple this to the measures of thermal dose.

- Following from this, a longer term goal would then be correlate the dependence of radio-sensitivity (via the linear-quadratic model) with the extended thermal dose, rather than temperature [5] as a more biologically relevant measure.

Quantitative Ultrasound

Typically image reconstruction and segmenting objects within the image are performed separately. However, in ultrasound, the most basic image formation approach neglects almost all variations in material properties, so produces images with significant artefacts.

Recently a joint segmentation and reconstruction approach has been proposed for image processing [2]. This applies a alternating iterative scheme to a variational problem. These will be ideally suited to ultrasound, and would be implemented by coupling the Computed Ultrasound Tomography in Echo mode (CUTE) method [4] to the Chan-Vese or Mumford-Shah equation via minimizing the Ginzberg-Landau energy in both steps of the scheme. Such an approach would have immediate impact in ultrasound imaging, thermometry and dosimetry. There is some literature on directly segmenting images from ultrasound data, but all approached have used deep-learning methods [8]. The drawback is that these methods typically required training on labelled data, and producing this can be a laborious process. Thus the methods are trained on synthetic data, and do not generalise well. The proposed approach would overcome this short-coming while still retaining the ability to include anatomical information via initial guesses for segmentation curves. To maximize impact, validation would have be performed on phantoms with known geometry. An open question is the whether the system can converge sufficiently quickly to reconstruct images in close to real time.

[1] Ki Joo Pahk, Pierre Gélat, David Sinden, Dipok Kumar Dhar, and Nader Saffari, "Numerical and experimental study of mechanisms involved in boiling histotripsy," Ultrasound Med. Biol. 43, 2848–2861 (2017)

[2] Jeremy M Budd, Yves van Gennip, Jonas Latz, Simone Parisotto, and Carola-Bibiane Schönlieb, "Joint reconstruction-segmentation on graphs," SIAM J. Imaging. Sci. 16, 911–947 (2023)

[3] D Sinden, E Stride, and N Saffari, "Approximations for acoustically excited bubble cluster dynamics," J. Phys.: Conf. Ser. 353, 012008 (2012)

[4] Patrick Stähli, Maju Kuriakose, Martin Frenz, and Michael Jaeger, "Improved forward model for quantitative pulse-echo speed-of-sound imaging," Ultrasonics 108, 106168 (2020)

[5] H Petra Kok, Johannes Crezee, Nicolaas AP Franken, Lukas JA Stalpers, Gerrit W Barendsen, and Arjan Bel, "Quantifying the combined effect of radiation therapy and hyperthermia in terms of equivalent dose distributions," Int. J. Radiat. Oncol. Biol. Phys. 88, 739–745 (2014)

[6] Grzegorz Dudziuk, Weronika Wronowska, Anna Gambin, Zuzanna Szymańska, and Mikołaj Rybiński, "Biologically sound formal model of HSP70 heat induction," J. Theor. Biol. 478, 74–101 (2019)

[7] Lehel Banjai and Maryna Kachanovska, "Fast convolution quadrature for the wave equation in three dimensions," J. Comp. Phys. 279, 103–126 (2014)

[8] Arun Asokan Nair, Kendra N Washington, Trac D Tran, Austin Reiter, and Muyinatu A Lediju Bell, "Deep learning to obtain simultaneous image and segmentation outputs from a single input of raw ultrasound channel data," IEEE Trans. Ultrason. Ferroelectr. Freq. Control 67, 2493–2509 (2020)