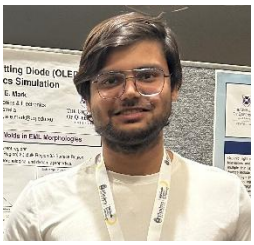
QUBIC SYMPOSIUM 2025
POSTER ABSTRACT BOOKLET

Representing Halogen σ-Hole Effects within Classical Force Fields for Drug Design



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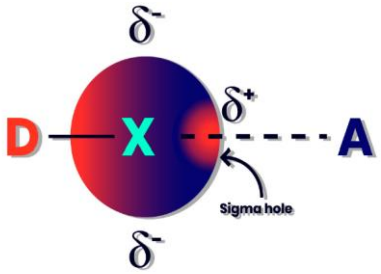

In the pharmaceutical world, halogen atoms play a crucial role, as halogen bonding interactions significantly affect drug–target recognition, potency, binding affinity and pharmacokinetic properties. Approximately 20% of approved drugs contain halogens. They are also important in crystal engineering, where halogens play a role in molecular packing. This interaction is characterized by the anisotropic distribution of electrostatic potential around the halogen atom, resulting in a positive region known as the σ-hole along the bond axis. The presence of σ-hole is not limited to halogen but also observed in elements of oxygen and nitrogen family[1,2].
Classical force fields are a fundamental tool for modelling molecular interactions using Newton's equations of motion. They are used in various fields, including drug discovery and molecular dynamics simulations, to gain insights into complex systems and interactions, such as halogen bonding and their underlying cause (σ -hole).

Molecular mechanics studies encounter significant challenges when attempting to incorporate and accurately model these types of non-covalent interactions. Conventional force fields do not account for the anisotropic nature of charge density around the atom. Charge density is typically represented by a single parameter called atomic partial charge[4], determined through fitting from an appropriate level of quantum mechanics (QM) and density functional theory (DFT). However, in the case of anisotropic charge density, these representations are not useful for predicting some physical properties or interactions like the halogen bond. Extra parameters are required to represent different types of regions. In these models, the σ-hole is represented by an extra point charge[3].
I will present a model to represent the anisotropic charge density of atoms, allowing us to observe and understand these types of intricate molecular interactions. This model will shed light on the nuanced behaviours exhibited by atoms in various molecular contexts, providing valuable insights into their causes.

1. *J. Mol. Model* 2007, 13, 1033-1038.
2. *ChemPhysChem* 2013, 14, 278-294.
3, *J. Comput. Chem.* 2011, 32, 2564-2574.
4. *J. Phys. Chem.* 1993, 97, 10269–10280.

Revealing the forces of our silent sentinels: platelets, nature's superglue

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Background

Platelets are small, anucleate suspension 'cells', functioning within the high-shear environment of circulating blood as silent sentinels, that rapidly and locally activate at the site of blood vessel injury to initiate blood clot formation. This is a vital process that prevents excessive bleeding and when dysregulated, the aberrant formation of blood clots can block vessels resulting in thrombotic disorders such as stroke, the second leading cause of death (11.6%) globally in 2021 contributing significantly to morbidity and mortality. Conversely, failure of our blood clotting systems after injury, can lead to uncontrolled bleeding and death within 5 minutes.

Platelets initially adhere, activate, and aggregate rapidly extending many cell protrusions (Pseudopodia) as part of the forming clot, transitioning blood from liquid to solid in a localised manner. The final stage of platelet aggregation is vital to establish a stable and mechanically strong blood clot contributing to 80% of the final clot strength, enabling it to withstand arterial blood flow like a 'super glue'.

Results and Future Evaluations

The current understanding is that platelets quintessential adhesive binding is mediated by the transmembrane integrin receptor αIIbβ3 that transitions to a low basal state to high affinity state in response to local factors in the platelet's microenvironment. This then enables their adhesion to binding motifs encoded with extracellular matrix proteins either from the damaged tissue/vessel or the concurrently forming blood clot matrix.

We will present a reductionist clot model system we have developed to interrogate the biophysical mediators of essential platelet functional roles in forming a stable and strong blood clot. With a focus on the central role of the soluble blood proteins, fibrinogen and fibronectin in regulating platelet-mediated aggregation, as individual monomers but also in their ultimate insoluble state that provides a specific steric orientation as a fibrin-fibronectin fibrillar matrix.

With the vision to employ a new quantum-limited microscopy technique developed by Bowen group, LIFE microscopy will be employed to detect unlabelled measurements of platelet morphology with much higher contrast than other phase-sensitive microscopy while simultaneously capturing the local viscoelastic properties of matrices to capture local cellular resolution insights. In particular, the technique will enable real-time imaging of viscoelastic changes as platelets engage with clot components, revealing how local mechanical properties evolve with the dynamic and rapid morphological changes, as well as functional changes of adhesion and activation. These measurements will provide new insight into the spatial and temporal coordination of platelet-driven clot formation and the role of fibronectin/fibrin architecture and steric arrangement in modulating clot stiffness and stability.

Electrostatically assembled nanodiamond films for single-use applications

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Nitrogen vacancy diamond related sensing techniques as investigative tools in fields such as biology, medicine, and chemistry are becoming increasingly more established in research. Single crystal diamonds for example have been utilized as viable high-resolution voltage and magnetic sensors, which has made them particularly interesting in the field of biology where processes tend to happen at the micro or even nanoscale[1,2]. Nevertheless, bulk diamonds are pricey, hard to clean, and can become cross contaminated after repeated use. Recent research has shown that nanodiamonds can be uniformly dispersed using electrostatic self-assembly, as a possible alternative for single crystal nitrogen vacancy sensing[3]. Here we further investigate electrostatically assembled nanodiamond films of three different sizes for distribution and sensing sensitivity.

The negatively charged carboxylated nanodiamond films are electrostatically assembled onto negatively charged glass substrates using poly(allylamine hydrochloride) (PAH) as a positively charged linker, see figure 1. The different nanodiamond sizes (50 nm, 70 nm, and 100 nm) will be compared for uniformity, brightness, and contrast, using SEM, AFM, ODMR, Rabi, and T1 measurements. Samples will additionally be tested in dry and wet conditions. We aim to further test their response to paramagnetic noise by exposing them to dotarem as proof of concept and sensitivity testing, see figure 1.

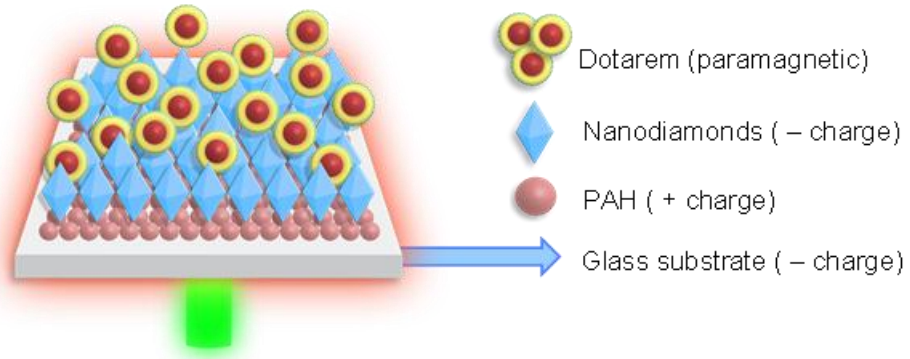

Figure 1. Schematic of the electrostatically assembled nanodiamond film on a glass slide, PAH shown in red is used as a positively charged linked for the nanodiamond film. Nanodiamonds are shown in blue can be used for sensing e.g. dotarem shown in green.

References:

[1]R. Schirhagl, K. Chang, M. Loretz, and C.L. Degen, "Nitrogen-vacancy centers in diamond: nanoscale sensors for physics and biology," Annu Rev Phys Chem 65, 83–105 (2014). https://doi.org/10.1146/annurev-physchem-040513-103659
[2]E.S. Grant, L.T. Hall, L.C.L. Hollenberg, G. McColl, and D.A. Simpson, "Nonmonotonic Superparamagnetic Behavior of the Ferritin Iron Core Revealed via Quantum Spin Relaxometry," ACS Nano 17(1), 372–381 (2023). https://doi.org/10.1021/acsnano.2c08698
[3]K. Chea, E.S. Grant, K.J. Rietwyk, H. Abe, T. Ohshima, D.A. Broadway, J.-P. Tetienne, G. Bryant, and P. Reineck, "Self-assembled fluorescent nanodiamond layers for quantum imaging," (2025). https://doi.org/10.48550/arXiv.2508.03028

Vibronic contributions to hyperfine-mediated spin kinetics

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Magnetosensing, the detection of magnetic fields, plays a crucial role in fields like navigation, security, and most relevantly, biology and medicine. The interactions of biological processes with magnetic fields can have significant impacts, and can be understood through many different theoretical models. The most well accepted is that of the radical pair mechanism, whereby an interaction due to the electron magnetic moment coupling to the nuclear magnetic moment (the hyperfine interaction) results in rapid spin-flipping. This interaction is incredibly sensitive to magnetic fields, but also to atomic perturbations. Understanding the coherent spin-transitions that occur in these systems through either experimental observations or theoretical modelling is vital in describing the biomagnetoptical mechanism, or more importantly to harness it. Existing theoretical models like the Franck-Condon approximation, which consider the nuclei as frozen, neglect the role of molecular vibrations; however, our results show that their complete exclusion will yield grossly underestimated kinetic pathways. In the zero-field, we show that when applied to the WT-AsLOV2 radical pair, this scaling is several orders of magnitude, shifting the state lifetimes from the microsecond timescale to the nanosecond timescale. Our preliminary application of this same theory to an ADP:Mg radical pair within an external field shows significant magnetic response as a function of the field strength, with triplet populations of the radical pair rapidly approaching zero as the field strength increases past 1 mT. This work addresses the hyperfine interaction taking into account high order vibronic contributions to the correlated electronic-spin state matrix element, without and within an external field to probe the effectiveness of the theory to describe a magnetic field response. his approach, which more readily incorporates realistic phenomena, represents an obvious yet novel step forward in the field, as vibronic contributions to the hyperfine interaction are explored in detail.

Enzyme-Inspired Computational Catalyst Design

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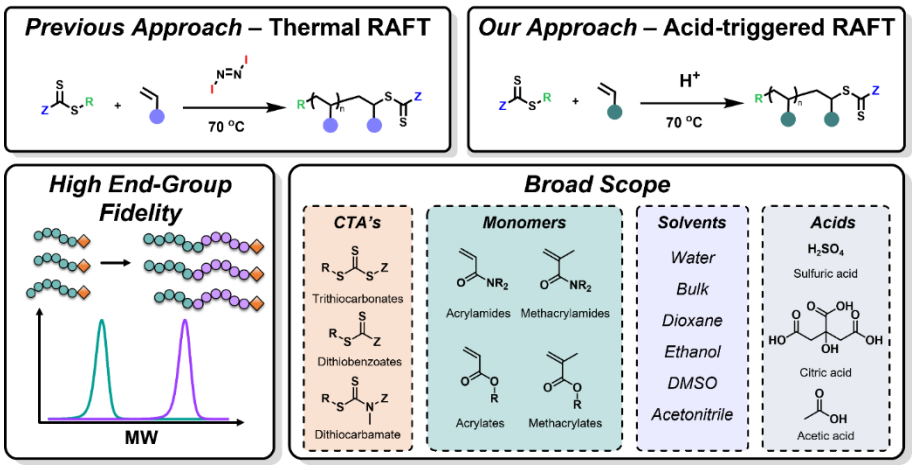
Most molecular species are polar or at least polarizable, meaning that strategically aligned electric fields could be employed to catalyze their reactions. In 2016, the Coote group and collaborators provided the first experimental demonstration of this by using Scanning Tunnelling Microscopy (STM) to orient reactants in an electric field and catalyze prototypical Diels Alder reactions.[1] Since this proof-of-principle, we have worked towards refining electrostatic catalysis and designing scalable solutions. In enzymes, charged residues serve to create large internal fields that bind substrates in a controlled manner that optimizes catalysis.[2, 3] Translating this to small-molecule-catalysis, we can envision that charged functional groups directly on the substrates could deliver localized oriented electric fields, meaning that electrostatic catalysis could be modulated simply through pH changes. Here, we show computationally and experimentally that abundant acids can be employed to create charged functional groups on a wide range of vinyl monomers, stabilizing both their initiation and propagation transition structures in their radical polymerizations.[4] We demonstrate that this not only makes typically explosive traditional initiators redundant but also provides access to cleaner polymerization reactions by avoiding initiator-driven side-reactions. Using the different polarizabilities of excited states, we show that the scope of this acid catalysis expands to photo polymerization.[5]



(1) Aragonès, A. C.; Haworth, N. L.; Darwish, N.; Ciampi, S.; Mannix, E. J.; Wallace, G. G.; Diez-Perez, I.; Coote, M. L. *Nature* **2016**, *531* (7592), 88-91. DOI: 10.1038/nature16989.
(2) Fried, S. D.; Bagchi, S.; Boxer, S. G. *Science* **2014**, *346* (6216), 1510-1514. DOI: 10.1126/science.1259802.
(3) Warshel, A.; Sharma, P. K.; Kato, M.; Xiang, Y.; Liu, H.; Olsson, M. H. M. *Chem. Rev.* **2006**, *106* (8), 3210-3235. DOI: 10.1021/cr0503106.
(4) Antonopoulou, M.-N.; Jones, G. R.; Kroeger, A. A.; Pei, Z.; Coote, M. L.; Truong, N. P.; Anastasaki, A. *Nat. Synth.* **2024**, *3* (3), 347-356. DOI: 10.1038/s44160-023-00462-9.
(5) Antonopoulou, M.-N.; Truong, N. P.; Egger, T.; Kroeger, A. A.; Coote, M. L.; Anastasaki, A. *Angew. Chem. Int. Ed* **2025**, *64* (9), e202420733. DOI: 10.1002/anie.202420733.

Illuminating the structure of single photon emitters in layered 2D materials

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Rhombohedral boron nitride (rBN) is an emerging wide-bandgap van der Waals (vdW) material that combines strong second-order nonlinear optical properties with the structural flexibility of layered 2D systems. We show that rBN hosts optically-addressable spin defects and single-photon emitters (SPEs). Both are fabricated deterministically, using site-specific techniques, and are compared to their analogues in hexagonal boron nitride (hBN). First-principles calculations of defects in hBN and rBN are used to elucidate the debated atomic structure of the B-center SPE in BN. The results establish rBN as a monolithic vdW platform that uniquely combines second-order nonlinear optical properties, optically addressable spin defects, and high-quality SPEs, opening new possibilities for integrated quantum photonics and nanoscale quantum sensing.

NEUROscope: Quantum Limited Imaging of Living Neuron Networks

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Dementia and Alzheimer's Disease recently became Australia's leading cause of death where the number of Australians living with dementia is projected to exceed 1 million by 2065. Our understanding of these neurodegenerative diseases is limited in fundamental ways requiring new tools. Current methods to understand these neurological processes are limited. Multielectrode arrays don't have single cell resolution; patch clamps cannot measure small networks; calcium imaging is affected by phototoxicity. We are developing NEUROscope to target these limitations with quantum limited precision and high temporal and spatial resolution. Designed to resolve intracellular dynamics at up to 5kHz and image small networks of neurons and surrounding glial cells, all label-free. The NEUROscope builds on a previous microscope design by using a CMOS camera to record. We aim to apply iSCAT to capture cytoskeletal structural dynamics involved in neuron spike signal propagation. Capturing this fundamental behaviour with subcellular precision is key to advancing our understanding of how disease risk factors develop in neural networks.

Multifit Atomic Partial Charges for Parameterising MD simulations

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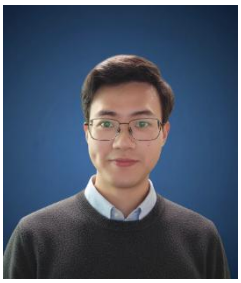
The accuracy and robustness of molecular dynamics calculations remain a significant limitation in their application across process, material and bio-pharmaceutical development. This is especially true in the case of structure-based drug design where protein-ligand binding free energy calculations have long been recognised as being key to lead optimisation but where the inability to uniformly achieve high accuracy impedes their widespread application in industry. Recent developments on a multi-molecular approach to the treatment of electrostatic parameters has shown potential to increase simulation accuracy past previous limits of error, hence making the technique more viable

Benchmarking multivariate statistical methods for integrating histological image and transcriptomic data



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Integrating histological images with transcriptomic data is a promising approach for linking tissue morphologies with molecular signatures. This strategy provides new opportunities to enhance our understanding of disease mechanisms, improve disease subtyping and inform precision therapies. However, the integration of imaging and omics data faces significant challenges, including the high dimensionality of the data, the lack of interpretability of the results and the variability of reproducibility across different approaches. Multivariate integration methods, such as Sparse Canonical Correlation Analysis (Sparse CCA), Joint Non-negative Matrix Factorisation (Joint NMF) and Angle-based Joint and Individual Variation Explained (AJIVE), enable dimensionality reduction while highlighting features associated with latent factors, thereby enhancing interpretability. These approaches have been successfully applied in imaging–genomics studies. However, systematic comparisons and assessments of their reproducibility remain limited.

Here, we constructed a benchmark pipeline using paired whole-slide images and gene expression data from TCGA breast cancer samples. We systematically compared Sparse CCA, Joint NMF and AJIVE to gain insights into how image and gene expression data can be jointly interpreted. We evaluated both the methodological characteristics and the outcomes produced by each approach.

The benchmark study revealed three key findings. First, multivariate integration methods enhance biological interpretation by linking morphological patterns to molecular signatures, e.g. nuclear morphological patterns and their associated genes were identified. Second, different approaches capture varied aspects of the data, highlighting distinct morphological and molecular patterns across samples. Third, the comparison revealed robust molecular signatures, with 1244 genes consistently identified across methods and enriched in RNA splicing and mitotic nuclear division. In addition, since each method had its own strengths, we provided practical guidelines for selecting the most appropriate approach based on the characteristics of individual datasets.

Diamond Voltage Imaging Microscopy for *in vitro* Neuroscience

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Voltage imaging encompasses the range of techniques which can spatially resolve variations in local electric potential. In neuronal electrophysiology, imaging electrical dynamics at sub-micron scales is key to unlocking new understanding of mechanisms underlying synaptic signaling and plasticity, neurological disease, and phenomena such as dendritic backpropagation and the compartmentalisation of the intracellular voltage. To date, existing voltage imaging techniques cannot achieve sub-micron resolutions with sufficient signal-to-noise and temporal stability to resolve these dynamics. Recently, we have demonstrated optical voltage imaging in solution using charge state switching of the diamond nitrogen-vacancy (NV) centre[1]. Dense ensembles of neutral NV centres formed proximal to a conductive hydrogenated diamond surface provide a means to optically sample local solvated charge accumulation on that surface. The high fluorescence contrast between the neutral (fluorescent) and positive (non-fluorescent) NV charge states allows for rapid, label-free, and quantitative voltage imaging at the optical diffraction limit. Here we show, for the first time, single-shot extracellular imaging of mammalian neuronal action potentials with sub-micron resolution using these diamond voltage imaging microscopes (DVIMs). These results open the door to studies of mesoscale neuronal network (hundreds to thousands of neurons) dynamics, with implications both for fundamental neuroscience and pathophysiology/neuro-pharmacology research.

[1] D. J. McCloskey, N. Dontschuk et al., *Nat. Photonics* **16**, 730-736 (2022). DOI: Author1, Author2, *J. Acronym.*, **2023,** *56*, 6515-6518. DOI: 10.1038/s41566-022-01064-1

An ensemble framework for NV-based surface noise spectroscopy

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The emergence of nitrogen vacancy (NV) sensing is motivated in part by great potential in field imaging and nanoscale NMR. These NV-based techniques excel in their sensitivity and spatial resolution, which are attributes directly improved by positioning sensors closer to the diamond surface. However, the amplification of surface noise signatures at shallow depth imposes damaging instability and strong decoherence on NV populations. Methods of surface characterization therefore become crucial in the pursuit of stable NVs very near-surface. Presented here is an extension of noise spectroscopy and nanoscale NMR methods to NV ensembles.

This work addresses the complications of applying ensemble data to the single NV framework for noise spectroscopy, which confound its direct implementation. We show that features appearing adverse in this approach are related to physical parameters of the NV population and can therefore be corrected. We also discuss how these features may be leveraged for novel information about the population, which may be corroborated with NMR measurements. Finally, we demonstrate the advantage of the ensemble framework for surface noise spectroscopy by contrasting its outcomes with analogous single NV studies in literature.

Magnetoencephalography for concussion diagnosis in sport

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Precision magnetometry for measuring brain activity signals provides a promising route to rapid concussion diagnosis for athletes. Traumatic brain injuries sustained in sport have long been a subject for concern. With increasing awareness around the long-term effects of repeated concussions, including chronic traumatic encephalopathy[1], the need for fast and reliable pitch-side diagnosis is clearer than ever. At present, the standard practice relies on athletes self-reporting and the assessment of behavioural symptoms, both of which are inherently subjective.

Magnetoencephalography (MEG) promises a more objective diagnosis method, involving direct measurement of an athlete's brain function. It is the study of the sub-picotesla magnetic fields generated when charged particles move around the brain, detected by placing precision magnetometers close to the scalp. Existing MEG studies have utilized SQUID magnetometers to report measurable changes to the brain activity detected in concussed individuals, as compared to healthy controls[2]. However, SQUIDs typically require bulky equipment such as extensive magnetic shielding and fridges for cryogenic operation, making them impractical for use pitch-side.

In this poster, I will outline our plans for developing a portable, room-temperature MEG device for concussion diagnosis at sporting events. We will incorporate commercially available, optically pumped magnetometers (OPMs) into a compact, helmet-like shielding. Meanwhile, we will optimize our own optomechanical magnetometers designed in-house[3] to enhance their sensitivities to brain signals[4].

1. M.L.M.D. Butler et al. 'Repeated head trauma causes neuron loss and inflammation in young athletes.' Nature (2025).DOI: 10.1038/s41586-025-09534-6.

2. I. Mavroudis et al. 'The Use of Magnetoencephalography in the Diagnosis and Monitoring of Mild Traumatic Brain Injuries and Post-Concussion Syndrome.' Brain Sciences 15 2 (2025). DOI: 10.3390/brainsci15020154.

3. F. Gotardo et al. 'Waveguide-integrated chip-scale optomechanical magnetometer.' Opt. Express 31, 37663-37672 (2023). DOI: 10.1364/OE.501960.

4. B. Carey et al. 'Ultrawide Bandwidth Optomechanical Magnetometery Using Flux Concentration' [In preparation] (2025)

Probing Molecular Conformations One Molecule at a time

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The shape and conformation of molecules are fundamental determinants of their reactivity and biological function. Yet, capturing these structural dynamics remains a major challenge: molecules are inherently flexible, and experimental techniques typically provide only time- and ensemble-averaged information. Methods such as X-ray crystallography or cryo-EM yield static snapshots, while NMR and FRET average over large molecular populations, masking rare or transient conformers. Computational simulations can explore countless possible conformations, but without experimental constraints it is difficult to identify which states are physically or biologically relevant. We propose a complementary approach—single-molecule detection using nitrogen-vacancy (NV) centers in diamond, based on NMR or DEER principles. NV centers are atomic-scale quantum sensors capable of detecting individual electron or nuclear spins. Advanced experiments have already demonstrated their ability to measure single spin labels in biomolecules. Building on these developments, we aim to utilize NV centers to study molecular conformational changes by monitoring interactions between two spin-label sites. Such sensitivity offers a path toward probing conformational dynamics at the level of individual molecules, potentially bridging the current gap between ensemble-averaged measurements and the true dynamic behavior of molecular systems.

Exploring the Selectivity of ClpS through Computational Thermodynamic and Kinetic Studies

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ClpS is a bacterial adaptor protein that exhibits the N-end rule pathway by recognizing peptides which have hydrophobic N-terminal residues and delivering them to the ClpAP protease. Structural studies have clarified many aspects of this process, however the molecular mechanisms governing residue selectivity and binding kinetics remain unresolved.

Here, we investigate the recognition of a model peptide by ClpS as well as the effects of protein mutations on peptide binding. Where the wild-type ClpS has Val72 and confers a slow peptide dissociation rate (k_{off}), the V72M mutation accelerates dissociation approximately eightfold, highlighting the sensitivity of peptide recognition to subtle changes in the binding pocket. Interestingly, when the same peptide is bound by an unrelated double mutant (L68M/Y100R), a bimodal distribution of k_{off} values is exhibited, suggesting the coexistence of two conformational states: one with fast dissociation and another with wild-type-like stability.[1] Using a combination of classical molecular dynamics, thermodynamic integration, and Gaussian-accelerated molecular dynamics, equilibrium and non-equilibrium processes are explored.

In addition to leucine, our analysis is extended to other hydrophobic residues to probe how side-chain chemistry influences recognition. Together, these results provide mechanistic insight into how ClpS distinguishes between potential N-terminal residues, revealing that single-point and combinatorial mutations can reshape both the thermodynamic and kinetic landscape of substrate binding. This work advances our understanding of adaptor-mediated substrate selection and may inform future efforts to engineer protein-degradation pathways.

[1] Mueller, Grimson, Paz, Fitch, Yu, Ribezzi-Crivellari, Griffiths, van Oijen, Spenkelink. *bioRχiv*, **2025**. DOI:10.1101/2025.08.28.672975

Dynamic, quantitative 3D live imaging for peptide uptake and biodelivery in macrophages.

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The efficient delivery of therapeutic drugs, vaccines, peptides, nucleic acids and nanoparticles into cells and tissues is of growing importance to medicine and the pharmaceutical industry. However, the methods for assessing the efficacy of fluid and particulate uptake in cells or defining their intracellular fates are currently inadequate. To examine peptide uptake in macrophages we use a fluorescently tagged, bioactive, plant cyclic peptide, SFTI-1 (de Veer et al, 2021). SFTI-1 is completely soluble and is taken up by macrophages as fluid-phase cargo in large, constitutive macropinosomes. For measuring and quantitating live imaging for peptide uptake, spinning disk confocal imaging is used to capture 3D stacks of images (5s per 80 Z-slices) through the full depth of cells. A high-content custom analysis script leveraging segmentation programs with deep-learning algorithm has been implemented and the peptide uptake can be defined, on a single-cell basis, to accurately measure delivery to cells under different conditions. The influence of inflammation on peptide uptake is shown here to demonstrate this capability.

After macropinocytosis, peptide cargo is trafficked through endocytic pathways within cells and routed for degradation in lysosomes or recycling to the cell surface for release from the cells. SFTI-1 is tracked through early and late endosomes using transfected fluorescent Rab GTPase as endosome markers. Live imaging reveals SFTI moving through maturing macropinosomes to early endosomes and thereafter its dispersal via tubules and vesicles to late endosomes, lysosomes and the cell surface. This tracking can define and quantify the fate of internalised peptide, and it can be used to investigate the influence of molecules within the cell trafficking machinery.

Additionally, lattice light sheet microscopy (LLSM) offers high-resolution and high-speed volume imaging of macropinocytosis including revealing the dynamics of membrane ruffles that close to initially form the macropinosomes for capture of fluorescent SFTI-1. LLSM generates terabyte-scale data sets that require high performance computing cluster and customised programming for data management and processing pipeline. Our imaging-based methods are providing therapeutic developers with tools for measuring cellular uptake. These methods can be further extended to generate new levels of information about cell uptake by addition of quantum imaging such as laser tweezers and diamond probes to the LLSM platform, allowing us to manipulate cell dynamics and measure cellular metrics that have never been investigated before.

Diamond nanopillar arrays for quantum sensing

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High resolution voltage imaging is essential to understanding neuronal network structure at the cellular and sub-cellular level. Diamond is an excellent candidate for interfacing with biological systems due to its biocompatibility, chemical inertness and optical properties. Optical voltage imaging with the charge-coupled fluorescence of nitrogen-vacancy centres in diamond has been shown previously, with sufficient sensitivity to record action potentials in neurons. Coupling to the intracellular space significantly enhances signal strength of neuronal communication, however this coupling is difficult to obtain on flat substrates. We present densely packed arrays of diamond nanopillars fabricated by reactive ion etching through a hydrogen silsesquioxane etch mask formed by electron beam lithography. The 1.3mm x 1.3mm arrays consist of 1-2μm tall parabolic nanopillars with sharp tips and 650nm-850nm base diameter, spaced at 2μm, 4μm, and 6μm pitches. Nanopillar geometry and packing density are designed to balance limits imposed by physical internalisation by neurons during cell culture and optical properties to enhance fluorescence collection. Fabricating these devices marks a step towards intracellular voltage imaging of neurons on diamond substrates.

Label-free quantum imaging with undetected photons in mid-infrared

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Current biomedical diagnostic methods like Enzyme-Linked Immunosorbent Assay and Fourier Transform Infrared (FTIR) are often slow, require reagents, and depend on bulky infrared systems. To address these challenges, we developed a mid-infrared (Mid-IR) quantum spectroscopy and imaging platform that uses visible light sources and detectors (Fig. 1.A), removing the need for traditional IR components while improving efficiency, portability, and noise performance [1,2]. The system generates entangled photon pairs through spontaneous parametric down conversion in nonlinear crystals for label-free detection of biomolecular absorption and refractive index. Cardiovascular biomarkers were first characterized using FTIR (Fig. 1.B), and their absorption data were used in modelling quantum interference visibility.

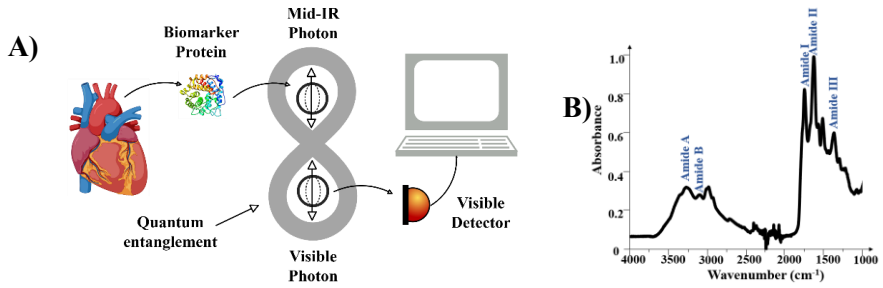

Figure 1: A) The general idea of the test, where MIR photons interact with biomarkers, while their counterparts in entangled photons in the Visible are detected. B) Biomarkers' signature in Mid-IR.

In spectroscopy, Silver Gallium Sulfide crystals were used to study how sample concentration, refractive index, and setup configuration affect quantum interference visibility. Modelling showed that higher concentrations reduced fringe visibility, while changes in refractive index shifted the fringe. Optimizing the setup improved the detection of these effects (Fig. 2.B). These results provide useful guidelines for designing sensitive quantum spectroscopy systems and emphasize the need for precise control of sample and system parameters. The quantum spectroscopy and imaging setup was then built in the laboratory. (Fig. 2.A).

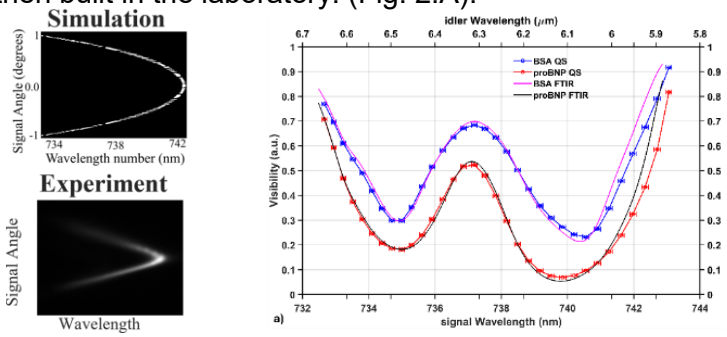

Figure 2: A) preliminary experiments data demonstrated successful detection of interference fringes. B) Modelling results showing the sensitivity of the method to molecular composition and temperature. Comparison between BSA and proBNP samples.

[1] A. S. Solntsev, G. K. Kitaeva, I. I. Naumova, A. N. Penin, Laser Phys. Lett., **2015**, 12, 095702. DOI: 10.1088/1612-2011/12/9/095702
[2] D. A. Kalashnikov, A. V. Paterova, S. P. Kulik, L. A. Krivitsky, Nat. Photon., **2016**, 10, 98–101. DOI: 10.1038/nphoton.2015.252

Ballistic Optical Tweezers for Measuring Fast Protein-Receptor Binding Dynamics

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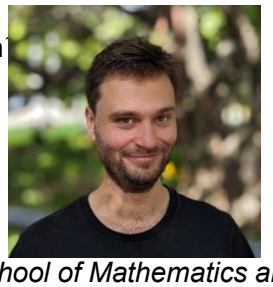
Despite significant advances in molecular biology and microscopy techniques, many questions remain regarding the interactions between a single cell and its environment. In particular, understanding protein-membrane binding is vital for optimizing the delivery of vaccines and medicines. By studying these transmembrane behaviours, we can improve drug delivery and increase the specificity of cell targeting. A powerful tool for probing these interactions is optical tweezers, which allow for the precise control and tracking of microparticles. I will present the use of state-of-the-art ultrafast Optical Tweezers to resolve the ballistic Brownian motion of functionalised microspheres and measure, with unprecedented speed and accuracy, the local viscosity changes during single protein-receptor binding.

Biomolecular Optomechanics for protein conformational control

Max Foreman[1], Jesse Slim[1], Warwick Bowen[1]



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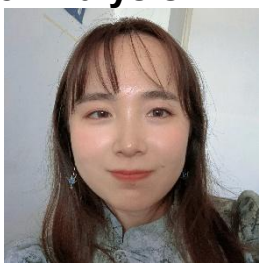
Proteins are the building blocks of life. There is accumulating evidence to suggest that collective vibrational modes in proteins are critical to not only enzyme catalysis, but many biological processes, ranging between energy transport, antibiotic resistance and protein folding. However, the mechanisms behind vibration-enabled biological function remain unclear and the tools for inquiry are limited---especially for unmodified proteins in physiologically relevant conditions.

We propose an optical tool to study and control long-range motion in label-free single biomolecules. It hinges on the interaction between Raman-active molecular vibrations and an optical nanocavity, which can be cast in the framework of cavity quantum optomechanics. By treating a molecule as a high-frequency mechanical oscillator, optomechanical control is thus made available to molecular biotechnology. Indeed, optical modulation of single-bond vibrations has already been demonstrated. This suggests that laser sideband cooling and heating techniques could amplify or suppress collective vibrational modes in proteins---although this remains to be demonstrated.

In this poster, I will report on our progress in modelling the interaction between a complex biomolecule and a laser-driven optical cavity. We model the anharmonicity intrinsic to molecular vibrations and simulate how one might control a protein conformational change using an optical cavity and appropriate laser drives. We report on the conditions to establish optical control over protein dynamics, and comment on the complexities of an experimental implementation. Achieving such precise control of the vibrational state of a biomolecule would provide an important tool to study how long-range collective vibrations drive enzyme dynamics and functionally important conformational changes in proteins.

Probing the Enzyme Dynamic Conformations of Ketosteroid Isomerase via and Computational Ensemble Analysis

Jiawa Wang,[a,b] Gökhan Tolun,[a,c] Haibo Yu[a,b]



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Enzyme catalysis is governed not only by static structure but by conformational dynamics. While traditional crystallography provides high-resolution snapshots, it transient yet functionally relevant motions are often overlooked. To capture these features, ensemble-based approaches are essential, particularly for enzymes like ketosteroid isomerase (KSI), whose catalytic efficiency is shaped by the distribution and interconversion of conformational states.

In this study, we employ molecular dynamics simulations of KSI under various conditions (temperature, environment, force field, and mutation) to investigate how these factors influence its conformational ensemble. We focus on the active-site residues that form a hydrogen-bond network for stabilising the intermediate state. Clustering and rotameric analyses were used to quantify residue flexibility and hydrogen-bonding patterns. Simulated ensembles were also benchmarked against experimental structures to assess shifts in residue-level dynamics across various conditions.

Our findings reveal that mutations may sensitise the active site to temperature, altering the flexibility within the hydrogen-bond network. This integrative comparative framework highlights how dynamics offers broader knowledge of enzymatic function through conformational ensemble analysis.

Evanescently-Coupled Gold Double Nanoholes: A Quantum Leap for Anti-Doping Tests

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Gold Double Nanoholes (DNHs) are now a staple of single-protein sensing. However, they suffer from low-throughput, require room-size devices to operate, and performance degrades from laser heating causing atom translocation.

Here, we present a novel DNH design that overcomes these issues without degrading sensitivity. We also present a new application: their use in anti-doping testing kits.

Our design represents a “quantum leap” for anti-doping testing that will ensure fairer competitions, safer athletes and greater trust in major sporting events.

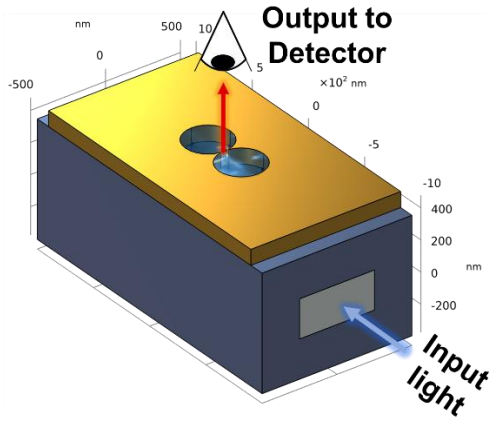

Figure 1: Our DNH design solution

Squeezing from a Chip

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Achieving high levels of squeezing from a mass-producible chip would enable seamless integration of quantum-enhanced sensitivity in optical biosensing and serve as a building block for scalable quantum computing architectures. Thin-film lithium niobate (TFLN) provides a promising platform with low loss waveguides and high nonlinearity; however, beyond loss, there are still many unknowns regarding noise sources that could limit the squeezing. Here, we develop and experimentally validate noise models and metrics to quantify phase and amplitude noise using TFLN test devices. We find that our TFLN test devices have excellent intrinsic phase stability and, within certain frequency bands, sufficiently low amplitude noise that record levels of squeezing could be feasible.

Quantum Spectroscopy with Undetected Photons for the Detection of Biomolecules

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Sensing and detection in the mid-infrared (MIR) range are crucial, as many molecules exhibit characteristic absorption bands in this frequency range[1]. However, traditional techniques like FTIR spectroscopy rely on costly lasers, complex and noisy detectors often requiring cryogenic cooling, all of which limit their applicability[2]. To address these limitations, we propose a quantum spectroscopy approach based on spontaneous parametric down-conversion (SPDC), where a single pump photon is converted into a pair of time–space correlated photons, one in the MIR (idler) and its partner in the near-infrared (NIR) or visible range (signal)[3]. Because of their strict energy–momentum correlations, detecting the signal photon provides full information about the idler's properties. This enables MIR spectral analysis without direct detection and measuring molecular absorption and refractive index using standard silicon-based devices.

Simulations using a 660 nm pump laser and an $AgGaS_2$ nonlinear crystal confirmed phase matching for signal photons between 732-743 nm and idler photons spanning 5.88-6.66 μm, covering the protein Amide I and II absorption bands. Quantum spectroscopy simulations were performed by incorporating experimental FTIR results of biomarker absorption (BSA and NT-proBNP molecules) to model the angular dispersion pattern of the signal photons. Variations in the visibility of the interference fringes formed by signal photons, indicate absorption within the sample, from which amplitude transmissivity is extracted. Higher visibility corresponds to lower absorption, while visibility minima reveal molecular absorption signatures. Both molecules exhibit distinct visibility dips aligned with their Amide I and II peaks (see Figure 1).

Strong agreement between the interference fringe visibility from the quantum spectroscopy approach and the amplitude transmissivity measured by classical FTIR confirms comparable accuracy in retrieving MIR spectral features of biomolecules without specialized MIR sources or detectors. Overall, this method offers a cost-effective, room-temperature alternative with a simplified the experimental configuration.

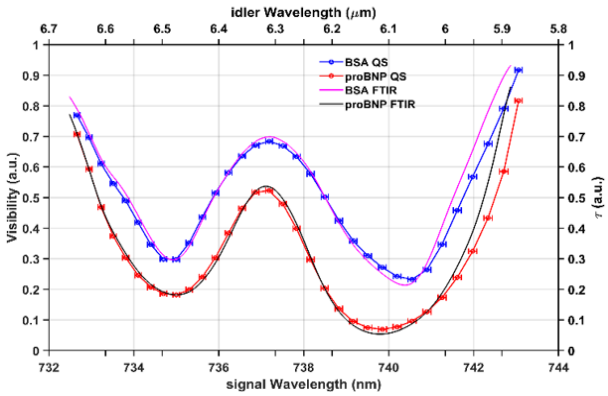

Fig. 1: Comparison between FTIR and Quantum spectroscopy results showing the sensitivity of the method to molecular composition through

[1] D. An, F. Sun, Y. Bian, J. Ni, Q. J. Wang, X. Yu, *Appl. Spectrosc. Rev.*, **2022**, 58, 834–868. DOI: 10.1080/05704928.2022.2156527

[2] J. Kong, S. Yu, *Acta Biochim. Biophys. Sin.*, **2007**, 39, 549–559. DOI: 10.1111/j.1745-7270.2007.00320.x

[3] A. V. Paterova, Z. S. D. Toa, H. Yang, L. A. Krivitsky, *ACS Photonics*, **2022**, 9, 2151–2159. DOI: 10.1021/acsphotonics.2c0046

Label free optical imaging of cell rheology.

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Conventional imaging systems mainly provide structural information. However, many essential cellular functions depend on the rheology of cells. Rheology requires dynamic information of the molecules and components inside the cell, so structural information alone cannot capture cell functionality. Here, I introduce the rheoSCAT microscope, a label-free, phase-sensitive microscope which can take measurements of intracellular dynamics at frequencies up to 50 kHz. To demonstrate the system's ability to detect motion, I measured A549 cancer cells and compared the results with those obtained from paraformaldehyde (PFA) fixed (motion-limited) cells. This setup opens new ways of studying cells and bacteria, that could help in the development of new drugs, proteins, and medical treatments.

Probing non-equilibrium systems with rotational optical tweezers

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Non-equilibrium dynamics are central to many microscopic systems, particularly in biological and energy-driven contexts, necessitating advanced tools for precises investigation. Rotational optical tweezers (ROTs) provide a powerful, non-invasive method to probe these systems by detecting rotational degrees of freedom of birefringent particles. They have been widely applied in microrheology and in studies of microscopic torques, exploiting the transfer of spin angular momentum and polarisation changes in the trapping light to directly measure torque and angular position.

Using vaterite microspheres, ROTs enable both active and passive rotational microrheometry, where probe motion is driven by optical torque or Brownian fluctuations. We have established that the rotational ballistic regime can be accessed with sufficient spatiotemporal resolution[1]. Here, we combine this capability with active-passive rheometry to extend the frequency range for sampling the complex shear modulus and extracting viscoelastic properties.

To further enhance angular sensitivity, we demonstrate how trapping sub-micron vaterite spheres modifies the balance between alignment and rotation torques. This can be exploited to improve the signal-to-noise ratio by tuning the properties of the circularly polarised measurement beam, highlighting the flexibility of ROT for optimising sensitivity toward the quantum limit.

Finally, we propose integrating ROTs with quantum sensors to access physical quantities in addition to viscoelasticity. Synthesising vaterite microspheres around fluorescent nitrogen-vacancy (NV) centre diamonds enables simultaneous rotational microrheology and nanoscale sensing of temperature or pH. These advances reveal exciting opportunities for probing non-equilibrium microsystems in distinctive detail.

[1] Watson, M. L., Stilgoe, A. B., Favre-Bulle, I. A., Rubinstein-Dunlop, H., *Optica*., **2025,** *12(2)*, 246-254. DOI: 10.1364/OPTICA.549215.

Dynamic Single-Particle Mapping of Receptor-Mediated Nanoparticle Trafficking and Recycling Pathways in Living Cells

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Understanding how individual nanoparticles behave inside living cells is critical for designing next-generation nanomedicines and virus-mimetic delivery systems. Here we establish a quantitative single-particle tracking (SPT) framework using upconversion nanoparticles (UCNPs) conjugated with fluorescent antibodies to visualise receptor-mediated endocytosis and recycling in spike-expressing cells. Dual-channel detection of UCNP luminescence (980 nm excitation) and antibody-Alexa 647 fluorescence verified single-particle integrity and enabled discrimination of intact conjugates from free or aggregated nanoparticles.

Continuous live-cell imaging under near-infrared illumination revealed a sequential transition from membrane exploration to clathrin-mediated uptake, followed by directed and confined endosomal transport. By classifying trajectories into directed, free, confined, and immobile motion states, we identified fast (<3 min) and slow (<30 min) recycling pathways consistent with Rab4- and Rab11-associated endosomal loops. Long-term dual-channel tracking showed partial dissociation of antibody ligands from UCNP carriers during late-endosomal processing despite non-cleavable linkers, indicating pH- or enzyme-dependent separation of cargo.

This study integrates physical motion analysis with biological trafficking mechanisms, providing an optical framework for probing the intracellular fate of receptor-targeted nanoconjugates at nanometre precision and minute-to-hour timescales. The approach informs rational design of antibody–drug conjugates, nano-vaccines, and spike-based therapeutic constructs, and demonstrates how upconverting microscopy overcomes photobleaching limits to enable long-term quantitative mapping of single-particle dynamics in living cells.

Moments-based quantum chemical calculations on a quantum computer

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Large-scale quantum computers have the potential to revolutionise quantum computational chemistry with clear applications to catalysis and drug design. However, the utility of pre-fault-tolerant and early fault-tolerant quantum computers is not so obvious. A key limitation is the use of variational ansatz circuits to represent the ground electronic state, leading to expensive minimisation loops and deep, error-prone circuits required to improve expressivity. One method to circumvent the need for such ansätze is to measure the Hamiltonian moments, $\langle H^p \rangle$, of a simpler ansatz and combine this additional information into a corrected ground-state energy estimate[1,2]. In addition to improving the accuracy of electronic structure calculations beyond what would normally be possible for the simpler ansatz[3,4], we have also seen that this method is highly robust against noise in the quantum hardware[5]. We additionally demonstrate, using IBM quantum hardware, that the Hamiltonian moments method can be adapted to obtain noise robust estimates of non-energetic properties of the electronic ground-state without needing to construct the state explicitly[6]. While current experiments have been limited in size and scope, preliminary work suggests that evaluating moments through a Hadamard-test circuit results in circuits dramatically shorter than those required to achieve the same accuracy through quantum phase estimation.

[1] LCL Hollenberg, NS Witte, *Phys. Rev. B*, **1996,** *54*, 16309. DOI:10.1103/PhysRevB.54.16309
[2] HJ Vallury, MA Jones, CD Hill, LCL Hollenberg, *Quantum*, **2020,** *4*, 373. DOI:10.22331/q-2020-12-15-373
[3] MA Jones, HJ Vallury, CD Hill, LCL Hollenberg, *Sci. Rep.*, **2022,** *12*, 8985. DOI:10.1038/s41598-022-12324-z
[4] MA Jones, HJ Vallury, LCL Hollenberg, *Phys. Rev. Appl.*, **2024,** *21*, 1240. DOI:10.1103/PhysRevApplied.21.064017
[5] HJ Vallury, MA Jones, GAL White, FM Creevey, CD Hill, LCL Hollenberg, *Quantum*, **2023,** *7*, 1109. DOI:10.22331/q-2023-09-11-1109
[6] MA Jones, HJ Vallury, MC Per, HM Quiney, LCL Hollenberg, *arXiv*, **2025,** DOI:10.48550/arXiv.2509.10758

Precision on-chip magnetometers for biomedicine

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Magnetometry enables non-invasive access to bioelectromagnetic signals such as those generated by the heart (magnetocardiography, MCG) and brain (magnetoencephalography, MEG). However, current systems rely on bulky, cryogenic sensors that limit accessibility and scalability. We present chip-scale optomechanical magnetometers that combine high sensitivity with low size, weight, and power requirements. By integrating optical readout and mechanical transduction on a silicon platform, these devices achieve compactness and robustness compatible with array-based and wearable applications. This technology opens a pathway to portable, high-resolution biomagnetic sensing, enabling next-generation tools for biomedical diagnostics and fundamental studies of electrophysiological activity.

Mechanistic Insights into Nanobody-Based Quenchbody Sensing via Structural Modelling and Molecular Simulations

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Nanobody-based quenchbodies are emerging tools for sensitive and specific detection of biomolecular targets.[1,2] Recent quenchbodies developed against the inflammatory cytokine interleukin-6 (IL6) exhibit variable fluorescence responses despite comparable antigen binding.[3] To investigate the molecular basis of this discrepancy, we combined data-driven structural predictions with physics-based molecular dynamics simulations. Using a small dataset of nanobody–lysozyme complexes, we found that HelixFold3 provides more accurate structural predictions than AlphaFold3. Built on this result, and in the absence of experimentally resolved structures for the IL6-binding quenchbodies, we used HelixFold3 to model their structures. Specifically, we sought to understand the differences between high- and low-performing quenchbodies that were obtained through *in vitro* directed evolution.[3] Our analyses revealed that poor responders exhibit solvent-exposed tryptophan residues, notably tryptophan 110 upon antigen binding, allowing fluorophore quenching and reduced fluorescence. In contrast, good responders adopt conformations in which these tryptophan residues are largely buried, resulting in a more pronounced fluorescence increase. These findings demonstrate that integrating HelixFold3 structural predictions with molecular dynamics simulations can elucidate mechanistic insights into quenchbody performance and guide the rational design of more effective fluorescent sensors.

References

[1] Dong, J.; Ueda, H. *Sensors*, **2021**, *21*, 1223.
[2] El Salamouni, N. S.; Cater, J. H.; Spenkelink, L. M.; Yu, H. *FEBS Open Bio*, **2025**, *15*, 236.
[3] Cater, J. H.; El Salamouni, N. S.; Mansour, G. H.; Hutchinson, S. et al. *Communications Biology*, **2025**, *8*, 1.

Quantum Magnetometry on a Chip for Next-Generation Brain Imaging

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The ability to map neural activity in real time is fundamental to understanding brain function and treating neurological disorders. However, existing magnetoencephalography (MEG) systems rely on cryogenic superconducting sensors, limiting scalability and clinical accessibility. We introduce a new paradigm in neural sensing based on integrated optomechanical magnetometers - miniature silicon chip devices that combine optical cavities with high Q mechanical resonators and magnetostrictive elements to detect neural magnetic fields at room temperature. This hybrid platform will leverage quantum-enhanced optical readout and advanced nanofabrication to achieve projected sensitivities in the femtotesla range. The compact form factor and scalability of our design will open the possibility of dense, wearable MEG arrays, enabling unprecedented access to dynamic brain activity with high spatial and temporal resolution.

Investigating the complex non-equilibrium behaviour of biological active matter using rotational optical tweezers and particle tracking

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Active matter describes systems that convert the energy in their surroundings at a single particle level to produce directed movements. The interactions between particles result in long-range dynamical and complex collective behaviours. These systems are far-from-equilibrium and can be observed at a wide range of length scales – from flocks of birds to swarms of bacteria and even mixtures of microtubules and motor proteins. At the microscale, it has been shown that dense swarms of bacteria can behave as an active bath where passive particles (i.e. those only driven by Brownian motion) can exhibit enhanced diffusion[1]. By tracking the dynamics of these passive particles, the non-equilibrium behaviour of active matter can be explored.

In this work, we use rotational optical tweezers to investigate how rotational dynamics of a birefringent probe particle (vaterite) are influenced by the non-equilibrium behaviour of an active bath of Escherichia coli bacteria. Rotational optical tweezers can confine the vaterite to an equilibrium orientation or generate a persistent optical torque to cause constant rotation. Rotating the vaterite in the trap introduces hydrodynamic effects, significantly changing the dynamics of individual bacteria in the active bath (Fig. 1). This change can be measured through a combination of deep-learning-based particle tracking and extracting information from the rotating vaterite. With rotational optical tweezers, we can investigate the complex dynamics of active matter and better understand how hydrodynamic effects influence the non-equilibrium behaviour of these systems with potential applications in biomedicine and engineering.

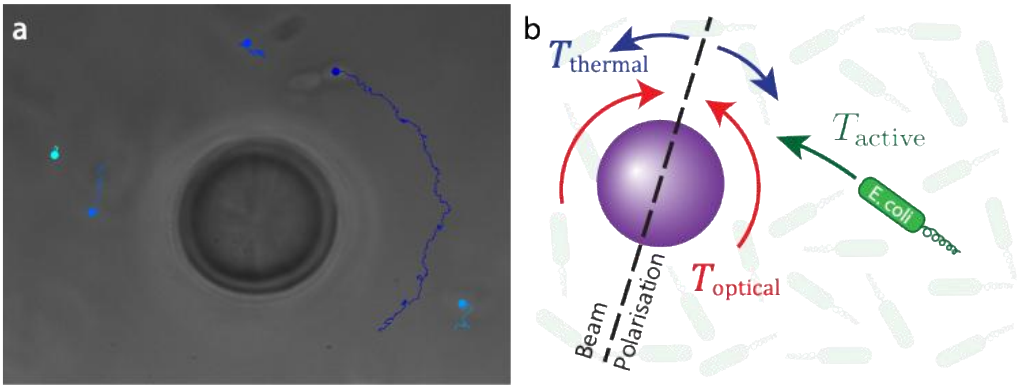

Fig. 1 [a] Experimental image of a vaterite particle (centre) immersed in an active bath of Escherichia coli (E. coli) bacteria. The colours represent different trajectories of the bacteria obtained using a deep-learning-based tracking algorithm. [b] Illustration of the torque contributions on a vaterite (purple sphere) that is optically trapped using rotational optical tweezers (ROTs) and immersed in an active bath of E. coli. The torques to consider include an optical torque (T_{optical}) due to the beam from the ROTs, a thermal torque due to the Brownian motion of the particle (T_{thermal}) as well as an 'active' torque (T_{active}) when the bacteria collide with the vaterite. The sum of the different torques result in the vaterite being in its aligned configuration along the beam's polarisation axis (black dashed line).

References

[1]A. Argun, A.-R. Moradi, E. Pinçe, G. B. Bagci, A. Imparato, and G. Volpe, "Non-Boltzmann stationary distributions and nonequilibrium relations in active baths," *Phys. Rev. E*, vol. 94, no. 6, p. 062150, Dec. 2016, doi: 10.1103/PhysRevE.94.062150.

Unveiling the Diradical Nature of Quinodimethanes: Insights into Their Role in Organic Chemistry

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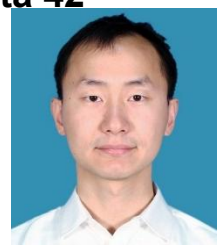
Quinodimethanes (QDMs) are diradicaloids characterized by unique electronic structures where the HOMO and LUMO are closely spaced.[1] This feature underpins their increasing popularity in electronic and spintronic devices as polycyclic aromatic hydrocarbons. In their single-molecule forms, these compounds exhibit cross-conjugation, which contributes to quantum interference in molecular electronics.[2] Moreover, their two simplest forms, *para*-quinodimethane (*p*-QDM) and *ortho*-quinodimethane (*o*-QDM), have been extensively utilized in organic synthesis for decades. Despite their versatility, the detailed electronic structures governing the chemical reactivities of QDM derivatives remain underexplored.

For instance, both *p*-QDM and *o*-QDM are known to be highly reactive species and can readily dimerize at the room temperature, but *p*-QDM favors an open-shell singlet transition state[3] while *o*-QDM prefers the typical [4+2] cycloaddition pathway.[4] Substituent effects on *p*-QDM can redirect its reactivity from dimerization to polymerization, and some derivatives are kinetically stable enough for isolation.[5] These behaviors underscore the importance of understanding the electronic nuances of QDMs.

Here, we integrate molecular orbital and valence bond theory to explore how these diradicaloids can be effectively analyzed computationally, providing deeper insights into their electronic structures. Additionally, high-level multireference CASPT2 methods were employed as benchmarks, enabling the identification of a reliable and accurate DFT approach for theoretical predictions. Supported by experimental validation, including TEMPO trapping, our findings propose a practical and feasible procedure for studying these unique systems with hidden diradical character.

Revisiting N-Terminal Chirality and Mutation-Induced Conformational Changes in Amyloid-beta 42

Qiang Zhu,[a] Haibo Yu[a]



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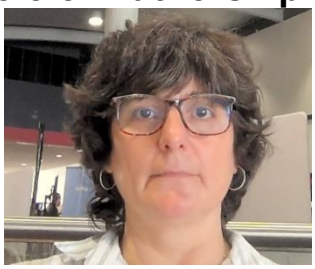
Amyloid beta (Aβ), one hallmark protein of Alzheimer's Diseases (AD), aggregates into plaques that are strongly linked to cognitive decline and neuronal death. Reducing its aggregation propensity may provide a potential strategy to slow the progression of AD. A variety of inhibitors, including small molecules, peptides, and antibodies, have been proposed. Among them, peptide-based treatments, particularly those involving sequence mutations and chirality modifications, show their promise in higher specificity and biocompatibility. In this study, we utilized temperature-replica exchange molecular dynamics simulations to comprehensively explore the conformational landscapes induced by mutations (A2T, A2V) and chirality inversion at the N-terminal of Aβ 42. Metrics based on the distribution of the radius of gyration (Rg) and the evolution of secondary structure indicate that sampling converged within approximately 0.8-1.2 μs per replica. By analyzing the interactions formed between pairwise residues and the secondary structure population, we concluded that the modulation at the N-terminal is not confined locally but also exerts effects on the C-terminal regions. We also broke down the contribution of secondary structures into individual residues. We disclosed that their contribution is highly dependent on its surrounding environments. These findings offer a deeper understanding on the effects of site-specific mutations and chirality and shed lights on the development of advanced therapeutic strategies for AD.

Making Collaboration work: The Role of Authorship

Rodriguez MA,[a]



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At QUBIC, collaboration is both an expectation and a challenge, a shared goal that unites diverse disciplines, but one that must be constantly negotiated in practice. Yet collaboration rarely unfolds as seamlessly as institutional narratives suggest. This poster examines how practices of authorship shape the conditions of collaboration, drawing on ethnographic work at QUBIC and comparative insights from interdisciplinary research environments.

Across teams, researchers often described conversations about authorship, who is named, when, and why, as rarely neutral. Different disciplinary traditions define contribution in distinct ways: some value experimental labour or data production, while others privilege conceptual or computational input. Formal frameworks such as CRediT and ICMJE aim to standardise these practices, yet in practice, decisions about authorship tend to follow local, contingent logics shaped by disciplinary cultures, interpersonal dynamics, and project-specific conditions. Formal guidelines often serve as reference points, but how they are taken up varies with local expectations, hierarchies, and collaborations.

These tensions are often managed quietly. Early-career researchers, in particular, described staying silent about credit to preserve trust and “keep collaboration smooth.” Such silences are not simply signs of passivity; they can also be read as strategies of belonging within a system that struggles to handle tension and tends to prefer apparent harmony. Yet they also make collaboration fragile: when authorship is left undefined, assumptions about contribution resurface at publication, sometimes weakening relationships that once seemed strong.

Rather than treating authorship as a technical or moral issue, this poster argues for seeing it as a collective practice—one that organises how collaboration happens, who participates, and who feels recognised. Making authorship an open, supported, and recurring conversation within QUBIC is not a threat to teamwork but a way to sustain it. By embedding these discussions in everyday research, collaboration can become not only productive but also equitable and durable.

Diamond based quantum sensing in tissues and organisms

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Free radical generation plays a key role in many biological processes including cell signaling, metabolism, immune responses and ageing. Free radical generation is also usually elevated if cells are under stress. This is for instance the case for many different diseases including cancer, infections or cardiovascular diseases. Recently, quantum sensing based on NV centers in diamond has been demonstrated as a versatile method to measure this radical generation at the nanoscale [1]. Here I will show you our latest work on the most complex samples we are currently measuring. I will show our first proof of principle data which proofs that we can detect free radical generation in tissue slices with this method[2]. More specifically, we investigated how liver tissue slices respond antioxidant treatments and exposure to toxic substances. In the second part of the work, I will show how the established methods have been applied in the first measurements in organisms [3]. There we investigated a Huntington disease model in c. elegans (a type of flat worm). We were able to measure free radical generation localized around poly-q aggregates which are involved in the disease progression. Further, we were able to quantify the stress responses in living worms from different cells of the body.

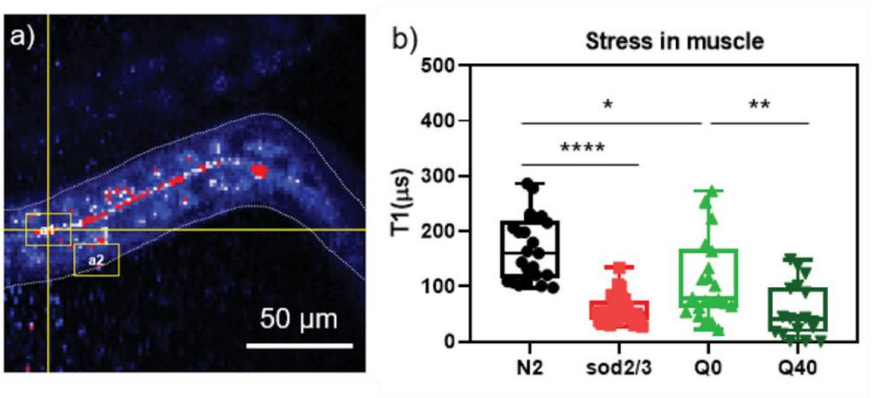

Figure 1. Measuring free radical generation in a Huntington disease model: (a) c elegans in our relaxometry equipment (b) A measurement of free radical generation in the muscle cells of healthy worms (N2), a mutant with impaired redox metabolism (sod2/3), a control which expresses fluorescent protein but no polQ (Q0) and the mutant which mimics the disease status (Q40)

1) Morita, A., Nusantara, A.C., Myzk, A., Martinez, F.P.P., Hamoh, T., Damle, V.G., van der Laan, K.J., Sigaeva, A., Vedelaar, T., Chang, M. and Chipaux, M., 2023. Detecting the metabolism of individual yeast mutant strain cells when aged, stressed or treated with antioxidants with diamond magnetometry. Nano Today, 48, p.101704. https://doi.org/10.1016/j.nantod.2022.101704
2) Zhang, Y., Sigaeva, A., Elías-Llumbet, A., Fan, S., Woudstra, W., de Boer, R., Escobar, E., Reyes-San-Martin, C., Kisabacak, R., Oosterhuis, D. and Gorter, A.R., 2024. Free radical detection in precision-cut mouse liver slices with diamond-based quantum sensing. Proceedings of the National Academy of Sciences, 121(43), p.e2317921121. https://doi.org/10.1073/pnas.23179211
3) Fan, S., Zhang, Y., Ainslie, A.P., Seinstra, R., Zhang, T., Nollen, E. and Schirhagl, R., 2025. In vivo nanodiamond quantum sensing of free radicals in caenorhabditis elegans models. Advanced Science, 12(14), p.2412300. https://doi.org/10.1002/advs.202412300

Multi-modal label-free biosensing with photonic crystal cavities

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Pavlina Naydenova, Jesse J. Slim,
Igor Marinkovic, Warwick P. Bowen

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Current single-protein analysis methods involve trade-offs between invasiveness and sensitivity. Labelled approaches can perturb the measurement, particularly of vibrations or conformation, while conventional Raman spectroscopy is insufficient for single-molecule signals. We are investigating whether tools from cavity optomechanics can be adapted for protein sensing applications.

Our approach combines photonic cavities with small mode volumes for optical trapping and fast sensitive measurements of individual proteins. We will discuss different experimental configurations and cavity designs optimized for various protein sensing modalities. We present preliminary results demonstrating trapping of larger (>100 kDa) proteins, mass metrology and enhanced Raman spectroscopy. Applications under exploration include fast tracking of conformational changes (in situ and under external stimuli), mass measurements of ferritin iron loading and protein discrimination.

Taking inspiration from quantum optomechanics, we are now investigating techniques to control protein dynamics. Using our photonic cavities we can enter the sideband-resolved optomechanical regime where our modelling suggests we can selectively cool/heat the protein's collective vibrations by pumping the (Anti-)Stokes shifted modes. In particular, we are interested in the low-THz range where there is accumulating evidence of underdamped vibrations, offering opportunities for efficient manipulation. We hope to investigate the functional importance of these underdamped vibrations, a topic of ongoing debate in the biological literature.

Entangled Photons and Upconversion Luminescence: Testing Quantum Enhancement in Rare-Earth Nanoparticles

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Entangled two-photon absorption (ETPA) has emerged as a promising quantum-optical process with potential to revolutionize spectroscopy, photochemistry, and imaging. Unlike classical two-photon absorption, which scales quadratically with light intensity, ETPA can scale linearly thus occuring at much lower photon flux thanks to quantum correlations between photon pairs.

Motivated by these prospects, we experimentally investigated whether entangled photon pairs can enhance upconversion luminescence in rare-earth doped nanoparticles—a model nonlinear system widely used in bioimaging and photonics. Photon pairs were generated via spontaneous parametric down-conversion and spectrally tuned to match the absorption bands of $NaYF_4$:Yb^{3+},Er^{3+} or Tb^{3+} (frequency degenerate excitation) or Nd^{3+} nanoparticles (non-degenerate excitation). The upconversion signal was recorded and compared against that obtained using continuous-wave diode laser excitation under equivalent photon flux conditions, polarisation and beam profile.

Our results show no considerable enhancement of upconversion luminescence induced by entangled photons relative to diode laser illumination. Within experimental uncertainty, the emission intensity scaling versus the excitation photon flux followed classical expectations, suggesting that this material system might not be affected by quantum-correlated excitation.

These findings provide a valuable experimental boundary for the applicability of entangled-photon nonlinear optics in solid-state media. While no enhancement was observed here, the study establishes a methodological framework for testing ETPA in other systems, including molecular or biological targets. Looking ahead, photochemistry enhanced via ETPA and/or quantum-enhanced bio-imaging at the Heisenberg limit have become compelling frontiers for our future explorations.

Macropinocytosis from amoeba to humans: novel strategies for monitoring environmental contaminants and cancer control

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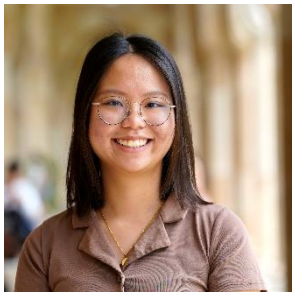

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The non-selective uptake of fluid by macropinocytosis, or cell gulping, has been sustained almost unchanged throughout evolution, serving to support cell nutrition and growth in organisms from amoeba to humans. In soil amoeba (slime molds), macropinocytosis ingests and concentrates a range of contaminants, including heavy metals, pesticides and pathogens, allowing these amoebae to be used for monitoring soil and water in vulnerable environments. Another ancient organism, red algae (*Gracilariopsis lemaneiformis*), also displays macropinocytic activity for nutrient scavenging and we will also be exploring the potential for environmental monitoring using these algae.

In human cancer cells, Ras mutations upregulate macropinocytosis resulting in increased nutrient uptake, promoting tumour growth and spread. Macropinocytosis in amoeba and humans relies on conserved and specialised regulators including actin polymerisation and Rab GTPases. My project aims to identify molecular regulators of macropinocytosis, that can be exploited for the upregulation of macropinocytosis in *Dictyostelium discoideum* to enhance environmental monitoring and for the downregulation of macropinocytosis in breast cancer cells to block metastatic cancer. Initial studies have focussed on the Rab5 family member Rab17 as a newly identified regulator of macropinocytosis in cancer cells. GFP-Rab17 is localised to macropinosomes and other endosomes, its overexpression increased macropinocytic activity and dramatically enhanced the size of aggressive breast cancer cell spheroids. Rab17 interacting proteins will be identified to reveal its mechanism for regulating macropinocytosis and proliferation in cancer cells. This and other members of the conserved Rab5 family will also be investigated as regulators of macropinocytosis in amoeba.

Key approaches for identifying and utilising Rab regulators of macropinocytosis are 3D live and fixed cell imaging and development of quantum microscopy will add exciting capabilities for measuring fluid and membrane changes for macropinosome size control.

CellDiffusio: a generative model to annotate single-cell and spatial RNA-seq using bulk references

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Annotating single-cell and spatial RNA-seq data can be greatly enhanced by leveraging bulk RNA-seq, which remains a cost-effective and well-established benchmark for characterising transcriptional activity in immune cell populations. However, a major technical hurdle lies in the contrasting properties of these data types: single-cell and spatial data are inherently sparse due to its cell-level sampling scheme, leading to much lower sequencing depth compared to bulk RNA-seq. We developed CellDiffusion, a generative machine learning (ML) tool that bridges this gap. CellDiffusion generates realistic virtual cells to augment the sparse singlecell and spatial data, improving signals and the representation of rare cell types. The augmented data are more comparable to bulk references, increasing the accuracy of cell type annotation using bulk references and automated ML classifiers. We benchmarked CellDiffusion on single-cell and spatial datasets from human peripheral blood samples, white adipose tissues, and breast tumours. Our method significantly outperforms state-of-the-art methods such as SingleR, Seurat, and scVI. In addition, CellDiffusion provides critical biological insights, including the identification of novel cell subtypes and their function during cell state transition; the discovery of new marker genes for tissue-resident immune cells, revealing their functional shifts in myeloid populations; and the accurate characterisation of cell subtypes in spatial transcriptomics to decipher tumour microenvironment.

Investigating the Role of ATP in Modulating TDP-43 Phase Separation

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Neurodegenerative diseases like amyotrophic lateral sclerosis (ALS) and dementia affect millions worldwide, leading to a tragic loss of life and quality of life. A key player in these diseases is a protein called Tar DNA binding Protein or TDP-43. Normally, TDP-43 helps in the functioning of nucleic acids and forms protective structures called biomolecular condensates during cellular stress, through a process known as liquid-liquid phase separation. However, under certain conditions, TDP-43 can misbehave and can form toxic aggregates that damage neurons, ultimately leading to neurodegeneration. Unfortunately, we still don't fully understand the molecular mechanisms that cause this process to go awry. This work aims to uncover the physiological factors that affect TDP-43's dynamic behavior and aggregation and if it can be prevented. Specifically, we investigate the role of ATP concentration on condensate formation. We aim to understand how low concentrations of ATP encourage LLPS and high concentrations of ATP reverse LLPS and shed light on which interactions are important for this process. Ultimately, by better understanding these transitions, we could help identify new ways to prevent or slow down the harmful aggregation of TDP-43, offering hope for future therapies against neurodegenerative diseases.

Quantum Kernel-Enhanced Dimensionality Reduction for Visualizing Single-Cell Developmental Data

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Single-cell time-development studies generate high-dimensional and noisy data, where preserving both local relationships and global developmental continuity is key to revealing cell trajectories. While methods like PHATE effectively capture such structures, their classical kernels often struggle to represent the complex nonlinear relationships present in biological manifolds.

We explore **quantum kernels** as a novel approach to manifold learning, focusing on their potential to enhance PHATE[1] embeddings for single-cell data. Unlike most prior work, which applies quantum kernels to supervised learning tasks, this study investigates their use in **unsupervised** settings. We evaluate both **fidelity** and **projected quantum kernels**[2] within a "Quantum PHATE" framework, comparing encoding strategies such as Chebyshev[3], amplitude, and angle encoding.

Our workflow first prototypes and optimizes quantum kernel circuits on **MNIST**[4] as a controlled benchmark, before transferring the best configurations to **single-cell data.** Embedding quality is assessed using metrics for structure preservation and pseudotime continuity.

Preliminary results show that **quantum kernels** can generate compact, hardware-efficient embeddings with competitive performance to classical baselines. Early findings also suggest that **Chebyshev encodings** better preserve large-scale developmental trajectories, motivating future experiments on quantum hardware and applications to broader multi-omics datasets.

References:

1. Moon, K. R., van Dijk, D., Wang, Z., et al. *Nat. Biotechnol.*, 2019, 37, 1482-1492. DOI: 10.1038/s41587-019-0336-3
2. Havlíček, V., Córcoles, A. D., Temme, K., et al. *Nature*, 2019, 567, 209-212. DOI: 10.1038/s41586-019-0980-2
3. Kreplin, D. A., & Roth, M. *Reduction of finite sampling noise in quantum neural networks*, 2023. arXiv:2306.01639. DOI: 10.48550/arXiv.2306.01639
4. LeCun, Y., Cortes, C., & Burges, C. J. *MNIST handwritten digit database*, 2010. URL: http://yann.lecun.com/exdb/mnist/
5. Huang, H. Y., Broughton, M., Mohseni, M., et al. *Nat. Commun.*, 2021, 12, 2631. DOI: 10.1038/s41467-021-22539-9