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PLASMA FOCUSED ION BEAM-SCANNING ELECTRON MICROSCOPY TO STUDY BONE CELLULAR AND SUB-CELLULAR NETWORK POROSITY

Tengteng Tang, (1); Asier Muñoz, (2); Aurélien GOURRIER (3); **Alessandra CARRIERO *** (4); Kathryn GRANDFIELD (1)

(1) McMaster University, Hamilton, Canada; (2) The City College of New York, New York, United States of America; (3) Universite Grenoble Aples, St Martin d'Heres, France; (4) The City College of New York, New York, United States of America

Bone is a major reservoir for mineral as it contains over 90% of the calcium of the human body. Calcium exchange between extracellular fluids and bone cells is an essential mechanism and disturbance of its homeostasis leads to severe pathologies. Osteocytes, the most abundant type of cells in bone form the lacuna-canalicular network (LCN) in bone, and are believed to play a role in calcium exchange through a process known as osteocytic osteolysis (OO)(1). However, the mechanisms underlying OO are poorly understood. Current research focuses on cellular and molecular signalling pathways associated with OO(2), yet there is limited information and direct evidence of mineral exchange and transport in the pericellular space around osteocytes. Here, we applied a new generation of sequential milling instrument, plasma focused ion beam-scanning electron microscopy (PFIB-SEM) to study the 3D mineral nanostructure and nanoporosity pathways in bone from healthy or diseased mice with osteogenesis imperfecta (OI). OI has been shown to alter the architecture of bone across the structural hierarchy, including changes at the tissue level in terms of mineralization(3) and the density and shape of osteocytes lacunae(4); and the molecular level pertaining to the substructure and chemical composition of collagen fibrils and mineral(5). Therefore, OI bone is a good candidate for testing the application of PFIB-SEM to study changes in mineralization and porosity in mice. Our PFIB-SEM results have revealed an extensive sub-canalicular, nanochannel network penetrating the mineralized matrix of OI mouse tibia with ~50 nm diameter. This previously unknown nanochannel network may provide an additional route for mineral ion transport and play a key role in mineral homeostasis. The architectural properties of the nanochannel network, such as volume fraction, surface area, and total accumulated length of the channels will be further quantified to enable us to characterize alterations in multiscale porosity networks and their role in mouse bone tissue mineralization that is fundamental to OO. REFERENCES: 1) Tsourdi et al. J. Musculoskelet. Neuronal Interact. 2018;18:292–303. 2)Robling et al. Annu. Rev. Physiol. 2020;82:485–506. 3) Roschger et al. Calcif. Tissue Int. 2008;82:263–70. 4) Carriero et al. Bone. 2014;61:116–24. 5) Kłosowski et al. ACS Biomater. Sci. Eng. 2017;3:2788–97.

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Principal Investigator: GRANDFIELD, Kathryn (Canada)

Co-Investigators: GOURRIER, Aurélien (France), CARRIERO, Alessandra (USA)

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UNIFIED FRAMEWORK FOR PERCEPTUAL DECISON MAKING

Davide Giana (1); Francesca Pulecchi, (1); Annachiara Guglietti, (1); **Mathew Diamond,** * (1)
(1) Sissa (International School for Advanced Studies), Trieste, Italy

Perceptual memories are the storage of our experience of the external world; such memories underlie our understanding of the world and thus guide our decisions. Research in this field is fast paced, but open questions remain. Behavioural and cognitive constructs tend to be custom built around a preferred task; principles that might generalize across tasks seem to be missing. Further, individual brain regions are usually assessed in relation to one aspect of memory, while a role in other memory tasks is not considered.

To address these questions, our HFSP project aims to build computational models comprised of interconnected functional units, each performing a specific task-independent operation; the interaction between units and the readout of the system is controlled in a top-down manner according to behavioural requirements. We aim to relate this model to neural activity in brain regions involved in perceptual decision making.

We trained each rat to perform two different tasks requiring the elaboration of whisker stimuli: (1) a reference memory categorization task, where a single stimulus has to be judged ("strong" or "weak") according to an implicit boundary, and (2) a working memory task, where a base stimulus must be stored in short-term memory for comparison to a successive stimulus.

We find that different aspects of history, such as recent stimuli and recent choice' outcomes, factor into the choice on the current trial; we produced a single model accounting for both tasks. We performed neural recordings during the execution of both tasks, showing how cortical activity can fill in the model's terms to produce behavioural output. Additionally, we perturbed neural activity by optogenetic stimulation, seeing a causal link between activity in frontal and parietal regions and distinct memory components.

Our results suggest that selected cortical regions are part of a multi-function network. Specific regions are predisposed by circuitry and connectivity to carry out specific operations, yet the network can be tuned to carry out different cognitive tasks. According to the task, the interactions among regions of the network are tuned, and the "readout" of one or the other region guides behaviour.

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Principal Investigator: DIAMOND, Mathew (Italy)
Co-Investigators: KEIM, Nathan (USA), BARAK, Omri (Israel)

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COMPUTATIONAL EXPLORATIONS OF COLLECTIVE DYNAMICS: BACTERIA AND ANTS

Kimberly BOWAL * (1); Lakshminarayanan Mahadevan, (1)
(1) Harvard University, Cambridge, United States of America

The natural world is full of multicomponent communities that dynamically self-organise to aid their collective function and survival. Investigating the design principles and emergent intelligence that define these behaviours provides a means of describing and understanding these complex living systems. In this work, we develop and apply an agent based model of self-propelled spherocylinders to explore two such collectives: a multispecies bacterial community and a crowded ant colony.

Bacteria play a significant role in human health, the environment, and industrial applications. In these environments bacteria are most often found in multispecies communities in which colonies containing different cell shapes interact closely. Recently, time-lapse microscopy has shown that these multispecies interactions can be cooperative or competitive (*eLife* **8**:e47365), presenting dynamic and complex behaviours hypothesised to be a consequence of the shape-dependent physical and chemical interactions. However, the role of shape polydispersity in individual and collective dynamics is poorly understood. We are employing a biophysical model of variable size sphere- and rod-shaped individuals to explore how shape polydispersity influences interspecies interactions and to develop a predictive understanding of multispecies spatiotemporal patterning.

Avoiding traffic jams in crowded environments is a significant challenge for collective systems, such migrating herds, cellular cargo transport, and pedestrian flows in an urban environment. Ants possess a remarkable ability to prevent jamming and maintain steady flows even at high densities - allowing efficient two-way traffic at 80% occupancy compared to human traffic limits of 40% (*eLife* **8**:e48945). This is believed to be a result of individual ants adjusting their behaviour in response to their local environment, although the exact mechanisms involved are not known. We are exploring potential mechanisms by applying our spherocylinder agent based model to investigate the role of responsive individual velocity adjustments on crowded traffic flows.

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Fellow: BOWAL, Kimberly
Host supervisor: MAHADEVAN, Lakshminarayanan

Preferred presentation method: Onsite paper poster presentation (A0 portrait format (0.70m x 1m)) and online poster presentation (a digital version of your poster + a short video to introduce your e-poster will be required)