Data-driven studies of biological systems at multiple scales of organization

Vikyath D. Rao – Research Statement – May 2017

In my doctoral research, I studied the social organization of a model organism, the honeybee, at multiple scales. To probe the relationship between individual bees and their properties at the societal level, I studied the network of interactions among bees using techniques from temporal network theory, and found that there are surprising similarities between human and bee societies. I also studied variation in foraging behaviour among nominally identical worker bees in a honeybee colony. In both these projects, I used tracking data collected by my experimental collaborators, as described in detail in the first two sections below. Separately, I also studied whether a honeybee's social group is related to its gut microbiome, namely the ecosystem of bacteria inhabiting its guts; this is described in the third section below. The relationship between an animal's behavioural phenotypes and the microbes it harbours has been gaining increasing scientific attention with the availability of data from modern sequencing technologies, and is of particular importance in the context of human health.

Underlying my research is the idea that biological systems are characterized by non-linearity and collective effects, and in order to gain conceptual insight, one has to study life at different scales—genes, cells, biofilms, organisms, societies, ecosystems, etc.—as well as the interactions among these disparate scales. The honeybee society, which displays complex traits like division of labour, is an ideal model system in which we can probe some of these interactions.

Interaction networks and power laws

If one could observe all the movements of individuals within a society, what can one deduce about how the society is organized? To begin to address this question in the context of a honeybee society, my collaborators devised an experiment to image individually barcoded bees moving inside a glass-walled observation hive at high spatiotemporal resolution (see Figure 1). From these images, they measured instances of trophallaxis, or liquid-food exchange, between bees. Trophallaxis is known to be not just a method of food-sharing in the colony, but also a means of communication among individuals.

We studied trophallaxis interactions using the framework of temporal networks, which allowed us to study both the topological and temporal features of the trophallaxis network, as well as the dynamics of processes—such as the spread of information or disease—that
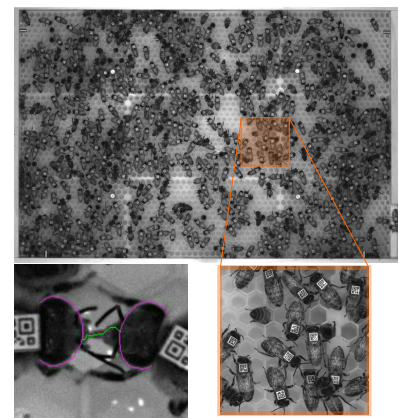

Figure 1: High-resolution tracking of a honeybee society. Clockwise from top: a single image showing the entire colony in an observation hive; zoomed-in cutout showing individual barcodes; two bees engaged in liquid-food transfer (trophallaxis).

might occur on the network. We found that the trophallaxis network shares some features with a wide range of human networks that arise in a social context, and that have been reported in the literature: these include electronic communication networks and face-to-face proximity networks. In particular, we found that like in human communication, trophallaxis interactions are bursty: that is, the time separating successive trophallaxis events follows a broad probability distribution that can be modelled as a power law.

In human networks, burstiness has been associated with a slow-down of spreading processes occurring on the network. We found that surprisingly, this does not hold in the trophallaxis network: that is, when we simulated spreading on the trophallaxis network using the susceptible-infected (SI) model, we found that the speed of spreading was faster on the trophallaxis network relative to reference networks that we constructed by randomizing temporal features of the empirical network in a carefully controlled manner.[1] In on-going work, I am using synthetic networks (i.e. artificial networks constructed *in silico* using a well-defined algorithm to incorporate specific topological and temporal features) to try to isolate those temporal features of a network that might generically be responsible for speeding up spreading.[2]

We also found that like human proximity networks, bee trophallaxis interactions have a power-law distribution $P(\Delta t) \sim [\Delta t]^{-\alpha}$ for the duration Δt of interaction (see Figure 2). Using a simple scaling argument, we predicted that the power-law exponent α should be related to the mechanism by which two individuals initiate an interaction. Qualitatively, α is determined by how abruptly an individual slows down as it approaches another individual to initiate an interaction; we tested this argument quantitatively using simulations of a model from the recent physics literature of heterogeneous random walkers interacting based on proximity.

Interindividual variation and behavioural plasticity

In a different tracking experiment, bees were equipped with RFID tags rather than the barcodes described above. In this setup, the entrance to the hive was equipped with two detectors that activated and read out a bee's tag as it passed by while making a foraging trip outdoors. The goal of this experiment was to study variation in foraging behaviour among individuals in the colony population: for example, are all bees equally hard working, as the popular idiom might have you believe, or are some bees in fact lazier than others?

To address this question, we measured the foraging activity of bees over the course of the experiment, and borrowed from economics the
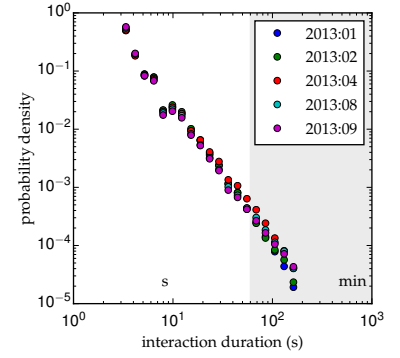

Figure 2: Power law distribution $P(\Delta t) \sim [\Delta t]^{-\alpha}$, measured using logarithmically-spaced bins in five different bee trophallaxis datasets. The exponent is estimated to be $\alpha \approx 2.25$.

[1] T. Gernat, V.D. Rao, M. Middendorf, H. Dankowicz, N. Goldenfeld, G.E. Robinson: Rapid spreading dynamics despite bursty interaction patterns in honeybee social networks. *(In review)*

[2] M. Li, V.D. Rao, T. Gernat, H. Dankowicz. Temporal-structure-preserving network transformations for characterizing the dynamics of spreading. *(To be submitted)*
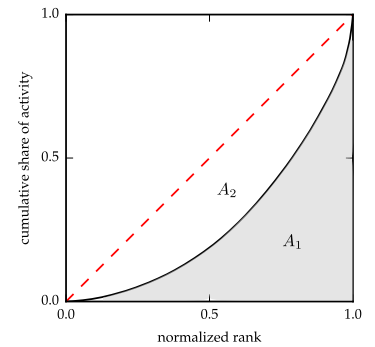

Figure 3: Lorenz curve for a bee society (black curve); the red line corresponds to a completely equitable distribution of activity. The Gini coefficient is computed from the areas as $A_2/(A_1 + A_2)$.

concepts of Lorenz curves and Gini coefficients to measure the degree of "inequality" in activity among the bees (see Figure 3). We found that the distribution of activity among worker bees is in fact highly skewed, with a Gini coefficient of 0.493 ± 0.032 (mean ± SD over five bee colonies).[3] (For comparison, the Gini coefficient for income inequality in the US is around 0.45.) We also found that this feature of the honeybee society is resilient to a demographic perturbation in which the active workers are removed from the society: in response to such a perturbation, previously quiescent worker bees increase their activity so that on the following day, there is again a skewed distribution of activity.

The honeybee gut microbiome and social organization

Modern sequencing technologies now allow us to study the microbial compositions of various environments such as the soil, the ocean, and the bodies of larger organisms, and thus to study how microbes interact and co-evolve with these environments. Each of us carries in our body ten times as many microbial cells as human cells, and we are now starting to uncover the implications of this for health and disease. In the context of honeybees, we asked the question: do honeybees of different social groups—which perform different tasks—have different gut microbiota? On the one hand, different tasks lead to varying exposure to ambient microbes in the environment; on the other hand, bees in a colony live in very close proximity to each other, constantly exchanging food amongst themselves.

Starting with sequences of the 16S rRNA gene extracted by my collaborator from the hindguts of honeybees, I reconstructed the microbial compositions in each sample using a combination of tools developed in our research group. We then performed clustering analyses and statistical tests to determine whether a bee's social group can be determined from its microbiome (see e.g. Figure 4). Our results indicate that while bees of all social groups share a core microbiome consisting of a fixed set of bacterial types (OTUs), the relative abundances of these types vary depending on the social group, and based on these differences, we can distinguish the reproductive members of the colony from worker bees.[4]

Ongoing work: social networks, behaviour, and the brain

I am presently studying the two-way relationship between behaviour and society. Specifically, my collaborators and I are probing how gene expression in a honeybee's brain is dependent on its social context, and reciprocally, how the set of genes expressed affects a bee's social network by modulating its behaviour.

[3] P. Tenczar, C.C. Lutz, V.D. Rao, N. Goldenfeld, G.E. Robinson (2014): Automated monitoring reveals extreme interindividual variation and plasticity in honeybee foraging activity levels. *Animal Behaviour*, 95, 41–48
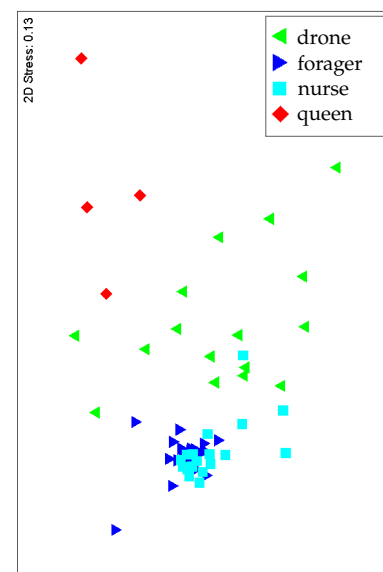

Figure 4: Non-metric multidimensional scaling (NMDS) plot for the microbiomes of 60 bees from 4 different castes, or social groups (indicated in the legend). We can see that worker bees—foragers and nurses—have similar microbiomes, while the reproductive castes—drones and queens—have distinct microbiomes.

[4] K.M. Kapheim*, V.D. Rao*, C.J. Yeoman, B.A. Wilson, B.A. White, N. Goldenfeld, G.E. Robinson (2015): Caste-specific differences in hindgut microbial communities of honey bees (Apis mellifera), *PLOS ONE*, 10(4), e0123911