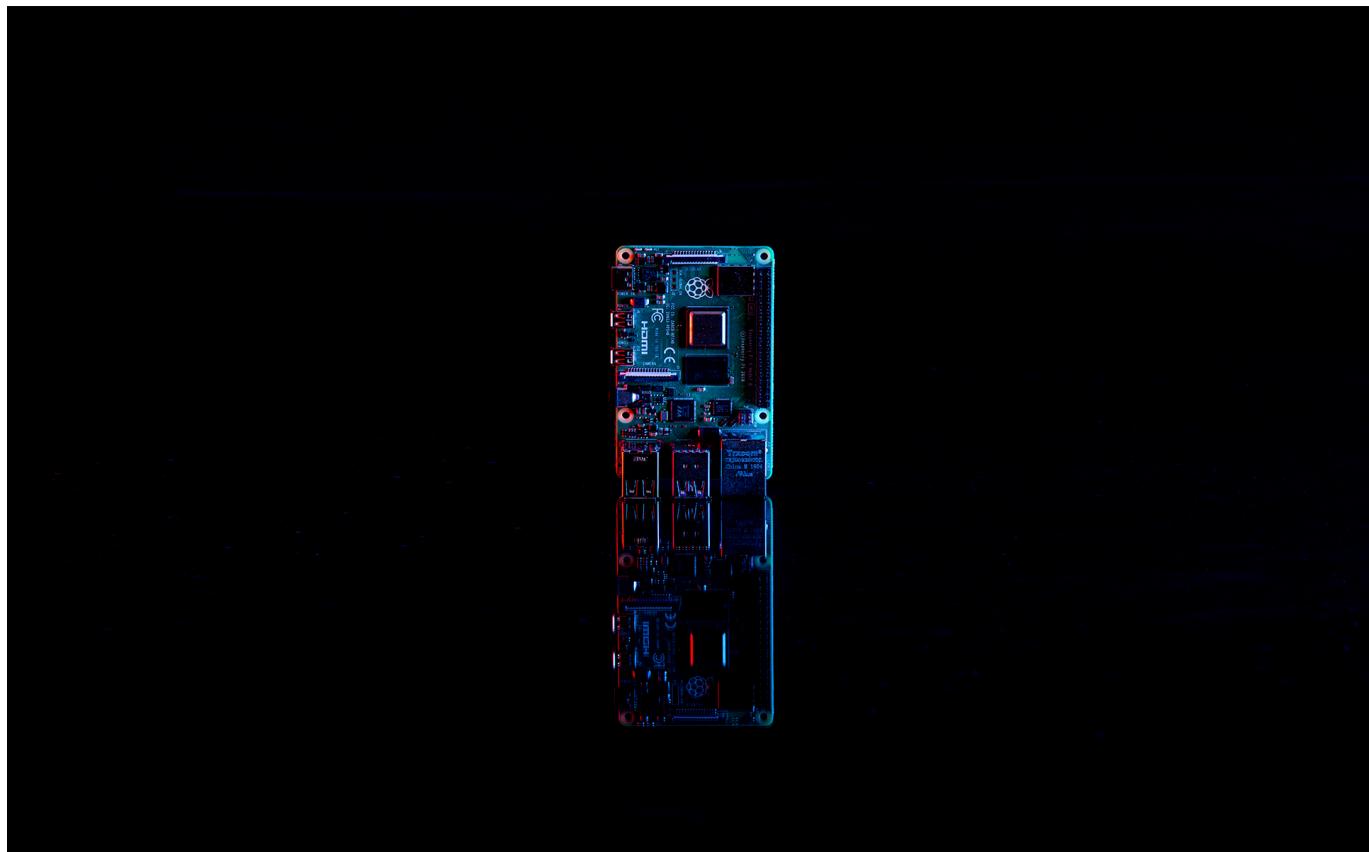


**Web Scraping science papers from site:
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SimBSI: An open-source Simulink library for developing closed-loop brain signal interfaces in animals and humans

<https://www.biorxiv.org/content/10.1101/769679v1>

Objective A promising application of BCI technology is in the development of personalized therapies that can target neural circuits linked to mental or physical disabilities. Typical BCIs, however, offer limited value due to simplistic designs and poor understanding of the conditions being treated. Building BCIs on more solid grounds may require the characterization of the brain dynamics supporting cognition and behavior at multiple scales, from single-cell and local field potential (LFP) recordings in animals to non-invasive electroencephalography (EEG) in humans. Despite recent efforts, a unifying software framework to support closed-loop studies in both animals and humans, is still lacking. The objective of this paper is to develop such a neurotechnology software framework.

Inexpensive, scalable camera system for tracking rats in large spaces

<https://www.biorxiv.org/content/10.1101/285460v2>

Most studies of neural correlates of spatial navigation are restricted to small arenas ($\approx 1 \text{ m}^2$) because of the limits imposed by the recording cables. New wireless recording systems have a larger recording range. However, these neuronal recording systems lack the ability to track animals in large area, constraining the size of the arena. We developed and benchmarked an open-source, scalable multi-camera tracking system based on low-cost hardware. This camera system was used in combination with a wireless recording system for characterizing neural correlates of space in environments of sizes up to 16.5 m^2 . This system improved accuracy in estimating spatial firing characteristics, theta phase precession, and head direction tuning of neurons compared to a popular commercial system, due to its better temporal accuracy. This improved temporal accuracy is crucial for accurately aligning videos from multiple cameras in large spaces and characterizing spatially modulated cells in a large environment.

Taking off the training wheels: Measuring auditory P3 during outdoor cycling using an active wet EEG system

<https://www.biorxiv.org/content/10.1101/157941v2>

Mobile EEG allows the investigation of brain activity in increasingly complex environments. In this

study, EEG equipment was adapted for use and transportation in a backpack while cycling. Participants performed an auditory oddball task while cycling outside and sitting in an isolated chamber inside the lab. Cycling increased EEG noise and marginally diminished alpha amplitude. However, this increased noise did not influence the ability to measure reliable event related potentials (ERP). The P3 was similar in topography, and morphology when outside on the bike, with a lower amplitude in the outside cycling condition. There was only a minor decrease in the statistical power to measure reliable ERP effects. Unexpectedly, when biking outside significantly decreased P2 and increased N1 amplitude were observed when evoked by both standards and targets compared with sitting in the lab. This may be due to attentional processes filtering the overlapping sounds between the tones used and similar environmental frequencies. This study established methods for mobile recording of ERP signals. Future directions include investigating auditory P2 filtering inside the laboratory.

A biomimetic five-module chimeric antigen receptor (5MCAR) designed to target and eliminate antigen-specific T cells

<https://www.biorxiv.org/content/10.1101/2020.01.24.916932v1>

T cells express clonotypic T cell receptors (TCRs) that recognize peptide antigens in the context of class I or II MHC molecules (pMHC_{I/II}). These receptor modules associate with three signaling modules (CD3 β γ , ζ , and η), and work in concert with a coreceptor module (either CD8 or CD4), to drive T cell activation in response to pMHC_{I/II}. Here we describe a first generation biomimetic 5-module chimeric antigen receptor (5MCAR). We show that: (i) chimeric receptor modules built with the ectodomains of pMHC_{II} assemble with CD3 signaling modules into complexes that redirect cytotoxic T lymphocyte (CTL) specificity and function in response to the clonotypic TCRs of pMHC_{II}-specific CD4+ T cells; and, (ii) surrogate coreceptor modules enhance the function of these complexes. Furthermore, we demonstrate that adoptively transferred 5MCAR-CTLs can mitigate type I diabetes by targeting autoimmune CD4+ T cells in NOD mice. This work provides a framework for the construction of biomimetic 5MCARs that can be used as tools to study the impact of particular antigen-specific T cells in immune responses, and may hold potential for ameliorating diseases mediated by pathogenic T cells.

Dynamic sound field audiology: static and dynamic spatial hearing tests in the full horizontal plane

<https://www.biorxiv.org/content/10.1101/849836v1>

Although spatial hearing is of great importance in everyday life, today's routine audiological test batteries and static test setups assess sound localization, discrimination and tracking abilities rudimentarily and thus provide only a limited interpretation of treatment outcomes regarding spatial hearing performance. To address this limitation, we designed a dynamic sound field test setup and evaluated the sound localization, discrimination and tracking performance of 12 normal-hearing subjects. During testing, participants provided feedback either through a touchpad or through eye tracking. In addition, the influence of head movement on sound-tracking performance was investigated. Our results show that tracking and discrimination performance was significantly better in the frontal azimuth than in the dorsal azimuth. Particularly good performance was observed in the backward direction across localization, discrimination and tracking tests. As expected, free head movement improved sound-tracking abilities. Furthermore, feedback via gaze detection led to larger tracking errors than feedback via the touchpad. We found statistically significant correlations between the static and dynamic tests, which favor the snapshot theory for auditory motion perception.

Facile assembly of an affordable miniature multicolor fluorescence microscope made of 3D-printed parts enables detection of single cells

<https://www.biorxiv.org/content/10.1101/592170v1>

Fluorescence microscopy is one of the workhorses of biomedical research and laboratory diagnosis; however, their cost, size, maintenance, and fragility has prevented their adoption in developing countries or low-resource settings. Although significant advances have decreased their size, cost and accessibility, their designs and assembly remain rather complex. Here, inspired on the simple mechanism from a nut and a bolt we report the construction of a portable fluorescence microscope that operates in bright field mode and in three fluorescence channels: UV, green, and red. It is assembled in under 10 min from only six 3D printed parts and basic electronic components that can be readily purchased in most locations or online for US \$85. Adapting a microcomputer and a touch LCD screen, the microscope can capture time-lapse images and videos. We characterized its resolution and illumination conditions and benchmarked its performance against a high-end fluorescence microscope by tracking a biological process in single cells. We also demonstrate its application to image cells inside a microfluidic device in bright-field and fluorescence mode. Our microscope fits in a CO₂ chamber and can be operated in time-lapse mode. Our portable

microscope is ideal in applications where space is at a premium, such as lab-on-a-chips or space missions, and can find applications in clinical research, diagnostics, telemedicine and in educational settings.

Molecular characterization of a novel cytorhabdovirus with a unique genomic organization infecting yerba mate (*Ilex paraguariensis*) in Argentina

<https://www.biorxiv.org/content/10.1101/2020.01.28.923201v1>

The genome of a novel rhabdovirus was detected in yerba mate (*Ilex paraguariensis* St. Hil.). The newly identified virus, tentatively named yerba mate virus A (YmVA), has a genome of 14,961 nucleotides. Notably, eight open reading frames were identified in the antigenomic orientation of the negative-sense, single-stranded viral RNA, including two novel accessory genes, in the order 3'-N-P-3-4-M-G-L-8-5'. Sequence identity of the encoded proteins as well as phylogenetic analysis suggest that YmVA is a new member of the genus Cytorhabdovirus, family Rhabdoviridae. YmVA unique genomic organization and phylogenetic relationships indicate that this virus likely represents a distinct evolutionary lineage within the cytorhabdoviruses.

Sonic Kayaks: Environmental monitoring and experimental music by citizens

<https://www.biorxiv.org/content/10.1101/167833v1>

The Sonic Kayak is a musical instrument with which to investigate nature, developed during open hacklab events. Kayaks rigged with underwater environmental sensors allow paddlers to hear real-time water temperature sonifications and underwater sounds, generating live music from the marine world. Sensor data is also logged every second with GPS, time and date, allowing fine scale mapping of water temperatures and underwater noise that was previously unattainable using standard research equipment. The system provides the paddler with an extra dimension of senses with which to explore the underwater climate, while enabling citizens to gather data for scientific research. The system can be used as a citizen-science data-collection device, research equipment for professional scientists, or a sound-art installation in its own right, and has been implemented in a public setting at the British Science Festival 2016, demonstrating the considerable advantages of adopting transdisciplinary approaches during project development. Here we present instructions for building the open-hardware and open-source software, tests of the sensors used, and preliminary data demonstrating applications for the Sonic Kayak in marine climate and noise-pollution research.

Autopilot: Automating behavioral experiments with lots of Raspberry Pis

<https://www.biorxiv.org/content/10.1101/807693v1>

Neuroscience needs behavior, and behavioral experiments require the coordination of large numbers of heterogeneous hardware components and data streams. Currently available tools strongly limit the complexity and reproducibility of experiments. Here we introduce Autopilot, a complete, open-source Python framework for behavioral neuroscience that distributes experiments over networked swarms of Raspberry Pis. Autopilot enables qualitatively greater experimental flexibility by allowing arbitrary numbers of hardware components to be combined in arbitrary experimental designs. Research is made reproducible by documenting all data and task design parameters in a human-readable and publishable format at the time of collection. Autopilot provides an order-of-magnitude performance improvement over existing tools while also being an order of magnitude less costly to implement. Autopilot's flexible, scalable architecture allows neuroscientists to design the next generation of experiments to investigate the behaving brain.

Raspberry Pi Powered Imaging for Plant Phenotyping

<https://www.biorxiv.org/content/10.1101/183822v1>

Premise of the study: Image-based phenomics is a powerful approach to capture and quantify plant diversity. However, commercial platforms that make consistent image acquisition easy are often cost-prohibitive. To make high-throughput phenotyping methods more accessible, low-cost microcomputers and cameras can be used to acquire plant image data.

Affordable Remote Monitoring of Plant Growth and Facilities using Raspberry Pi Computers

<https://www.biorxiv.org/content/10.1101/586776v1>

Premise of the study: Environmentally controlled facilities, such as growth chambers, are essential tools for experimental research. Automated remote monitoring of such facilities with low-cost hardware can greatly improve both the reproducibility and the accurate maintenance of their conditions.

Leveraging host metabolism for bisdemethoxycurcumin production in *Pseudomonas putida*

<https://www.biorxiv.org/content/10.1101/753889v2>

Pseudomonas putida is a saprophytic bacterium with robust metabolisms and strong solvent

tolerance making it an attractive host for metabolic engineering and bioremediation. Due to its diverse carbon metabolisms, its genome encodes an array of proteins and enzymes that can be readily applied to produce valuable products. In this work we sought to identify design principles and bottlenecks in the production of type III polyketide synthase (T3PKS)-derived compounds in *P. putida*. T3PKS products are widely used as nutraceuticals and medicines and often require aromatic starter units, such as coumaroyl-CoA, which is also an intermediate in the native coumarate catabolic pathway of *P. putida*. Using a randomly barcoded transposon mutant (RB-TnSeq) library, we assayed gene functions for a large portion of aromatic catabolism, confirmed known pathways, and proposed new annotations for two aromatic transporters. The 1,3,6,8-tetrahydroxynaphthalene synthase of *Streptomyces coelicolor* (RppA), a microbial T3PKS, was then used to rapidly assay growth conditions for increased T3PKS product accumulation. The feruloyl/coumaroyl CoA synthetase (Fcs) of *P. putida* was used to supply coumaroyl-CoA for the curcuminoid synthase (CUS) of *Oryza sativa*, a plant T3PKS. We identified that accumulation of coumaroyl-CoA in this pathway results in extended growth lag times in *P. putida*. Deletion of the second step in coumarate catabolism, the enoyl-CoA hydratase-lyase (Ech), resulted in increased production of the type III polyketide bisdemethoxycurcumin.

Low-cost, sub-micron resolution, wide-field computational microscopy using opensource hardware

<https://www.biorxiv.org/content/10.1101/460055v1>

The revolution in low-cost consumer photography and computation provides fertile opportunity for a disruptive reduction in the cost of biomedical imaging. Conventional approaches to low-cost microscopy are fundamentally restricted, however, to modest field of view (FOV) and/or resolution. We report a low-cost microscopy technique, implemented with a Raspberry Pi single-board computer and color camera combined with Fourier ptychography (FP), to computationally construct 25-megapixel images with sub-micron resolution. New image-construction techniques were developed to enable the use of the low-cost Bayer color sensor, to compensate for the highly aberrated re-used camera lens and to compensate for misalignments associated with the 3D-printed microscope structure. This high ratio of performance to cost is of particular interest to high-throughput microscopy applications, ranging from drug discovery and digital pathology to health screening in low-income countries. 3D models and assembly instructions of our microscope are made available for open source use.

Engineered illumination devices for optogenetic control of cellular signaling dynamics

<https://www.biorxiv.org/content/10.1101/675892v1>

Spatially and temporally varying patterns of morphogen signals during development drive cell fate specification at the proper location and time. However, current *in vitro* methods typically do not allow for precise, dynamic, spatiotemporal control of morphogen signaling and are thus insufficient to readily study how morphogen dynamics impact cell behavior. Here we show that optogenetic Wnt/β-catenin pathway activation can be controlled at user-defined intensities, temporal sequences, and spatial patterns using novel engineered illumination devices for optogenetic photostimulation and light activation at variable amplitudes (LAVA). The optical design of LAVA devices was optimized for uniform illumination of multi-well cell culture plates to enable high-throughput, spatiotemporal optogenetic activation of signaling pathways and protein-protein interactions. Using the LAVA devices, variation in light intensity induced a dose-dependent response in optoWnt activation and downstream Brachyury expression in human embryonic stem cells (hESCs). Furthermore, time-varying and spatially localized patterns of light revealed tissue patterning that models embryonic presentation of Wnt signals *in vitro*. The engineered LAVA devices thus provide a low-cost, user-friendly method for high-throughput and spatiotemporal optogenetic control of cell signaling for applications in developmental and cell biology.

A ride in the park: Cycling in different outdoor environments modulates the auditory evoked potentials

<https://www.biorxiv.org/content/10.1101/455394v2>

In this study, we investigated the effect of environmental sounds on ERPs during an auditory task, by having participants perform the same dual task in two different outdoor environments. Participants performed an auditory oddball task while cycling outside both in a quiet park and near a noisy roadway. While biking near the roadway, an increased N1 amplitude was observed when evoked by both standard and target tones. This may be due to attentional processes of enhancing sound processing in the noisier environment. No behavioural differences were found. Future directions include investigating auditory ERPs in more realistic studies outside of laboratory.

Stalk Lodging: A Portable Device for Phenotyping Stalk Bending Strength of Maize and Sorghum

<https://www.biorxiv.org/content/10.1101/567578v1>

Background Stalk lodging (breakage of plant stems prior to harvest) is a major problem for both farmers and plant breeders. A limiting factor in addressing this problem is the lack of a reliable method for phenotyping stalk strength. Previous methods of phenotyping stalk strength induce failure patterns different from those observed in natural lodging events. This paper describes a new device for field-based phenotyping of stalk strength called "DARLING" (Device for Assessing Resistance to Lodging IN Grains). The DARLING apparatus consists of a vertical arm which is connected to a horizontal footplate by a hinge. The operator places the device next to a stalk, aligns the stalk with a force sensor, steps on the footplate, and then pushes the vertical arm forward until the stalk breaks. Force and rotation are continuously recorded during the test and these quantities are used to calculate two quantities: stalk flexural stiffness and stalk bending strength.

Ethoscopes: an open platform for high-throughput ethomics

<https://www.biorxiv.org/content/10.1101/113647v5>

We present ethoscopes, machines for high-throughput analysis of behaviour in *Drosophila* and other animals. Ethoscopes provide a software and hardware solution that is reproducible and easily scalable; they perform, in real-time, tracking and profiling of behaviour using a supervised machine learning algorithm; they can deliver behaviourally-triggered stimuli to flies in a feedback-loop mode; and they are highly customisable and open source. Ethoscopes can be built easily using 3D printing technology and rely on Raspberry Pi microcomputers and Arduino boards to provide affordable and flexible hardware. All software and construction specifications are available at <http://lab.gilest.ro/ethoscope>.

Spinâž an improved miniaturized spinning bioreactor for the generation of human cerebral organoids from pluripotent stem cells

<https://www.biorxiv.org/content/10.1101/687095v1>

Three-dimensional (3D) brain organoids derived from human pluripotent stem cells (hPSCs), including human embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs), have become a powerful system to study early development events and to model human disease. Cerebral organoids are generally produced in static culture or in a culture vessel with active mixing, and the two most widely used systems for mixing are a large spinning flask and a miniaturized multi-well spinning bioreactor (also known as Spin Omega (Spin[®])). The Spin[®] provides a system that is amenable to drug testing, has increased throughput and reproducibility, and utilizes less

culture media. However, technical limitations of this system include poor stability of select components and an elevated risk of contamination due to the inability to sterilize the device preassembled. Here, we report a new design of the miniaturized bioreactor system, which we term Spinâž that overcomes these concerns to permit long-term experiments.

Tagger: BeCalm API for rapid named entity recognition

<https://www.biorxiv.org/content/10.1101/115022v1>

Most BioCreative tasks to date have focused on assessing the quality of text-mining annotations in terms of precision of recall. Interoperability, speed, and stability are, however, other important factors to consider for practical applications of text mining. The new BioCreative/BeCalm TIPS task focuses purely on these. To participate in this task, I implemented a BeCalm API within the real-time tagging server also used by the Reflect and EXTRACT tools. In addition to retrieval of patent abstracts, PubMed abstracts, and Pub-Med Central open-access articles as required in the TIPS task, the BeCalm API implementation facilitates retrieval of documents from other sources specified as custom request parameters. As in earlier tests, the tagger proved to be both highly efficient and stable, being able to consistently process requests of 5000 abstracts in less than half a minute including retrieval of the document text.

Increasing the Mobility of EEG Data Collection Using a Latte Panda Computer

<https://www.biorxiv.org/content/10.1101/263376v1>

Background Electroencephalography (EEG) experiments often require several computers to ensure accurate stimulus presentation and data collection. However, this requirement can make it more difficult to perform such experiments in mobile settings within, or outside, the laboratory

An Open-Source Plate Reader

<https://www.biorxiv.org/content/10.1101/413781v1>

Microplate readers are foundational instruments in experimental biology and bioengineering that enable multiplexed spectrophotometric measurements. To enhance their accessibility, we here report the design, construction, validation, and benchmarking of an open-source microplate reader. The system features full-spectrum absorbance and fluorescence emission detection, *in situ* optogenetic stimulation, and stand-alone touch screen programming of automated assay protocols.

The total system costs <\$3500, a fraction of the cost of commercial plate readers, and can detect the fluorescence of common dyes down to \sim 10 nanomolar concentration. Functional capabilities were demonstrated in context of synthetic biology, optogenetics, and photosensory biology: by steady-state measurements of ligand-induced reporter gene expression in a model of bacterial quorum sensing, and by flavin photocycling kinetic measurements of a LOV (light-oxygen-voltage) domain photoreceptor used for optogenetic transcriptional activation. Fully detailed guides for assembling the device and automating it using the custom Python-based API (Application Program Interface) are provided. This work contributes a key technology to the growing community-wide infrastructure of open-source biology-focused hardware, whose creation is facilitated by rapid prototyping capabilities and low-cost electronics, optoelectronics, and microcomputers.

Shake-it-off: A simple ultrasonic cryo-EM specimen preparation device

<https://www.biorxiv.org/content/10.1101/632125v1>

Although microscopes and image analysis software for electron cryomicroscopy (cryo-EM) have improved dramatically in recent years, specimen preparation methods have lagged behind. Most strategies still rely on blotting microscope grids with paper to produce a thin film of solution suitable for vitrification. This approach loses more than 99.9% of the applied sample and requires several seconds, leading to problematic air-water interface interactions for macromolecules in the resulting thin film of solution and complicating time-resolved studies. Recently developed self-wicking EM grids allow use of small volumes of sample, with nanowires on the grid bars removing excess solution to produce a thin film within tens of milliseconds from sample application to freezing. Here we present a simple cryo-EM specimen preparation device that uses components from an ultrasonic humidifier to transfer protein solution onto a self-wicking EM grid. The device is controlled by a Raspberry Pi single board computer and all components are either widely available or can be manufactured by online services, allowing the device to be constructed in laboratories that specialize in cryo-EM, rather than instrument design. The simple open-source design permits straightforward customization of the instrument for specialized experiments.

GPI-anchored SKU5/SKS are maternally required for integument development in Arabidopsis

<https://www.biorxiv.org/content/10.1101/813733v2>

Glycosylphosphatidylinositol-anchored proteins (GPI-APs) play crucial roles in various processes in eukaryotes. In Arabidopsis, SKS1, SKS2, SKS3 and SKU5 from SKU5/SKS gene family could

encode GPI-anchored proteins, and they were recently reported to regulate cell polar expansion and cell wall synthesis redundantly in roots. Here, we report that, they are also redundantly crucial for seed production and seed morphogenesis in Arabidopsis through regulating maternal integument development. Their loss-of-functions resulted in disrupted development of integuments that failed to protect embryo sacs from exposure to external space due to physical restriction, and lead to female gametophytic abortion. Interestingly, those less defective ovules could be fertilized and develop into seeds normally, however, their seed morphogenesis was largely affected.

Lightweight bioinformatics: evaluating the utility of Single Board Computer (SBC) clusters for portable, scalable Real-Time Bioinformatics in fieldwork environments via benchmarking

<https://www.biorxiv.org/content/10.1101/337212v1>

The versatility of the current DNA sequencing platforms and the development of portable, nanopore sequencers means that it has never been easier to collect genetic data for unknown sample ID. In fact, the distinction between fieldwork and the laboratory is becoming blurred since genome-scale data can now be collected in challenging conditions in a matter of hours. However, the full scientific and societal benefits of these new methods can only be realised with equally rapid and portable analyses. At present, field-based analyses of genomic data, despite advances in computing technology, remain problematic; laptop computers are relatively expensive and limited in scalability, while cloud- and cluster-based analyses depend, for the time being, on sufficiently reliable high-bandwidth data uplinks to transmit primary data for analysis.

A Programmable Optical Stimulator for the Drosophila Eye

<https://www.biorxiv.org/content/10.1101/147389v1>

A programmable optical stimulator for Drosophila eyes is presented. The target application of the stimulator is to induce retinal degeneration in fly photoreceptor cells by exposing them to light in a controlled manner. The goal of this work is to obtain a reproducible system for studying age-related changes in susceptibility to environmental ocular stress. The stimulator uses light emitting diodes and an embedded computer to control illuminance, color (blue or red) and duration in two independent chambers. Further, the stimulator is equipped with per-chamber light and temperature sensors and a fan to monitor light intensity and to control temperature. An ON/OFF temperature control implemented on the embedded computer keeps the temperature from reaching levels that will induce the heat shock stress response in the flies. A custom enclosure was fabricated to house

the electronic components of the stimulator. The enclosure provides a light-impermeable environment that allows air flow and lets users easily load and unload fly vials. Characterization results show that the fabricated stimulator can produce light at illuminances ranging from 0 to 16000 lux and power density levels from 0 to 7.2 mW/cm² for blue light. For red light the maximum illuminance is 8000 lux which corresponds to a power density of 3.54 mW/cm². The fans and the ON/OFF temperature control are able to keep the temperature inside the chambers below 28.17°C. Experiments with white-eye male flies were performed to assess the ability of the fabricated simulator to induce blue light-dependent retinal degeneration. Retinal degeneration is observed in flies exposed to 8 hours of blue light at 7949 lux. Flies in a control experiment with no light exposure show no retinal degeneration. Flies exposed to red light for the similar duration and light intensity (8 hours and 7994 lux) do not show retinal degeneration either. Hence, the fabricated stimulator can be used to create environmental ocular stress using blue light.

DNA transistors switched by the Hofmeister effect

<https://www.biorxiv.org/content/10.1101/784561v1>

We are nearing the end of a remarkable period that began in the 1960s in which semiconductor manufacturers succeeded in shrinking die and feature sizes logarithmically, thus growing transistor counts exponentially with time. As we reach the theoretical physical limits of classical MOSFET semiconductors, DNA is a highly attractive candidate for future miniaturization of microprocessors. Here we show a foundational electronic device - a transistor - can be constructed from DNA. The nanodevice is comprised of two strands, one of which can be selectively switched between a G-quadruplex and duplex or single-stranded conformations. This switching ability arises from our discovery that perchlorate, a chaotropic Hofmeister ion, selectively destabilizes duplex over G-quadruplex DNA. By varying perchlorate concentration, we show that the device can be operated as a switch or signal amplifier. State switching can be achieved in three ways: thermally, by dilution, or by concentration. In each case, when operated in the presence of the cofactor hemin, the device catalyzes electron transfer in only the G-quadruplex state.

The High-throughput WAFFL System for Treating and Monitoring Individual *Drosophila melanogaster* Adults

<https://www.biorxiv.org/content/10.1101/428037v2>

Non-mammalian model organisms have been essential for our understanding of the mechanisms

and control of development, disease, and physiology, but are underutilized in pharmacological phenotypic screening assays due to low throughput compared to cell-based systems. To increase the utility of using *Drosophila melanogaster* in screening, we have designed the whole animal feeding flat (WAFFL), a novel, flexible, and complete system for feeding, monitoring, and assaying flies in a high throughput format. Our system was conceived keeping in mind the use of off-the-shelf, commercial, 96-well consumables and equipment in order to be amenable to experimental needs. Here we provide an overview of the design and 3-D printing manufacture specifications.

A Low-Cost, Open Source, Self-Contained Bacterial EVolutionary biorEactor (EVE)

<https://www.biorxiv.org/content/10.1101/729434v2>

Recently, a concerted effort has been made to study the evolution of drug resistance in organisms at increasingly smaller time scales and in a high-throughput manner. One effective approach is through the use of customized bioreactors – devices that can continuously culture bacteria and monitor this growth in real time. These devices can be technically challenging and expensive to implement for scientists, let alone students or teachers who seek an innovative and intuitive way of studying evolution. We seek to provide a flexible and open source automated continuous culture device framework for the academic setting to study biological concepts such as population dynamics and evolution; a framework that is capable of replicating the functionality of many prominent and expensive bioreactors in the market today. Within the educational environment, our goal is to foster interaction and interest between the engineering and biological fields by allowing teachers and students to build their own systems and design experiments on the proposed open framework. We present a continuous culture device designed for bacterial culture that is easily and inexpensively constructed, lends itself to evolution experiments, and can be used both in the academic and educational environments.

Mesoscale cortical calcium imaging reveals widespread synchronized infraslow activity during social touch in mice

<https://www.biorxiv.org/content/10.1101/430306v1>

We employ cortical mesoscale GCaMP6s imaging of intracellular calcium levels to establish how brain activity is correlated when two mice engage in a staged social touch-like interaction. Using a rail system, two head-fixed mice begin at a distance where social touch is not possible (160 mm), after 90s they are brought so that macrovibrissae contact each other (6-12 mm snout to snout) for

an additional 135s. During the period before, during, and after contact cortical mesoscale GCAMP6 signals were recorded from both mice simultaneously. When the mice were together we observed bouts of mutual whisking resulting in cross-mouse correlated barrel cortex activity. While correlations between whisker cortices were expected given mutual whisking, we also found significant synchronized brain-wide calcium signals at a frequency band of 0.01-0.1Hz when the mice were together. We present dual mouse brain imaging as new paradigm to assess social interactions in a more constrained manner. The effects of social interaction extend outside of regions associated with mutual touch and have global synchronizing effects on cortical activity.

Social foraging extends associative odor-food memory expression in an automated learning assay for Drosophila

<https://www.biorxiv.org/content/10.1101/636399v3>

Animals socially interact during foraging and share information about the quality and location of food sources. The mechanisms of social information transfer during foraging have been mostly studied at the behavioral level, and its underlying neural mechanisms are largely unknown. The fruit fly *Drosophila melanogaster* has become a model for studying the neural bases of social information transfer, as fruit flies show a rich repertoire of social behaviors and provide a well-developed genetic toolbox to monitor and manipulate neuronal activity. Social information transfer has already been characterized for fruit fliesâ€™ egg laying, mate choice, foraging and aversive associative learning, however the role of social information transfer on associative odor-food learning during foraging are unknown. Here we present an automated learning and memory assay for walking flies that allows studying the effect of group size on social interactions and on the formation and expression of associative odor-food memories. We found that both inter-fly attraction and the duration of odor-food memory expression increase with group size. We discuss possible behavioral and neural mechanisms of this social effect on odor-food memory expression. This study opens up opportunities to investigate how social interactions are relayed in the neural circuitry of learning and memory expression.

The ecological cocktail party: Measuring brain activity during an auditory oddball task with background noise

<https://www.biorxiv.org/content/10.1101/371435v3>

Most experiments using EEG recordings take place in highly isolated and restricted environments,

limiting their applicability to real-life scenarios. New technologies for mobile EEG are changing this by allowing EEG recording to take place outside of the laboratory. However, before results from experiments performed outside the laboratory can be fully understood, the effects of ecological stimuli on brain activity during cognitive tasks must be examined. In this experiment, participants performed an auditory oddball task while also listening to concurrent background noises of silence, white noise and outdoor ecological sounds, as well as a condition in which the tones themselves were at a low volume. We found a significantly increased N1 and decreased P2 when participants performed the task with outdoor sounds and white noise in the background, with the largest differences in the outdoor sound condition. This modulation in the N1 and P2 replicates what we have previously found outside while people ride bicycles (Scanlon et al., 2017b). No behavioural differences were found in response to the target tones. We interpret these modulations in early ERPs as indicative of sensory filtering of background sounds, and that ecologically valid sounds require more filtering than synthetic sounds. Our results reveal that much of what we understand about the brain will need to be updated as we step outside the lab.

Custom built scanner and simple image processing pipeline enables low-cost, high-throughput phenotyping of maize ears

<https://www.biorxiv.org/content/10.1101/780650v2>

High-throughput phenotyping systems are becoming increasingly powerful, dramatically changing our ability to document, measure, and detect phenomena. Unfortunately, taking advantage of these trends can be difficult for scientists with few resources, particularly when studying nonstandard biological systems. Here, we describe a powerful, cost-effective combination of a custom-built imaging platform and open-source image processing pipeline. Our maize ear scanner was built with off-the-shelf parts for <\$80. When combined with a cellphone or digital camera, videos of rotating maize ears were captured and digitally flattened into projections covering the entire surface of the ear. Segregating GFP and anthocyanin seed markers were clearly distinguishable in ear projections, allowing manual annotation using ImageJ. Using this method, statistically powerful transmission data can be collected for hundreds of maize ears, accelerating the phenotyping process.

Schistocephalus parasite infection alters sticklebacks' movement ability and thereby shapes social interactions

<https://www.biorxiv.org/content/10.1101/849737v1>

Parasitism is ubiquitous in the animal kingdom. Although many fundamental aspects of host-parasite relationships have been unravelled, few studies have systematically investigated how parasites affect organismal movement. Here we combine behavioural experiments of *Schistocephalus solidus* infected sticklebacks with individual-based simulations to understand how parasitism affects individual movement ability and how this in turn influences social interaction patterns. Detailed movement tracking revealed that infected fish swam slower, accelerated slower, turned more slowly, and tended to be more predictable in their movements than did non-infected fish. Importantly, the strength of these effects increased with increasing parasite load (% of body weight), with the behaviour of more heavily infected fish being more impaired. When grouped, pairs of infected fish moved more slowly, were less cohesive, less aligned, and less coordinated than healthy pairs. Mixed pairs exhibited intermediate behaviours and were primarily led by the non-infected fish. These social patterns emerged naturally in model simulations of self-organised groups composed of individuals with different speeds and turning tendency, consistent with changes in mobility and manoeuvrability due to infection. Together, our results demonstrate how infection with a complex life cycle parasite affects the movement ability of individuals and how this in turn shapes social interactions, providing important mechanistic insights into the effects of parasites on host movement dynamics.

DeepInsight: a general framework for interpreting wide-band neural activity

<https://www.biorxiv.org/content/10.1101/871848v1>

Rapid progress in technologies such as calcium imaging and electrophysiology has seen a dramatic increase in the size and extent of neural recordings, yet their interpretation still depends on time-intensive manual operations. Decoding provides a means to infer the information content of such recordings but typically requires highly processed data and prior knowledge of variables. Here, we developed DeepInsight - a deep-learning-framework able to decode sensory and behavioural variables directly from wide-band neural data. The network requires little user input and generalizes across stimuli, behaviours, brain regions, and recording techniques. Critically, once trained, it can be analysed to determine elements of the neural code that are informative about a given variable. We validated this approach using data from rodent auditory cortex and hippocampus, identifying a novel representation of head direction encoded by CA1 interneurons. Thus, we present a robust, user-friendly tool for characterising and decoding neural recordings in an automated way. Code is available at <https://github.com/CYHSM/DeepInsight>.

MazeMaster: an open-source Python-based software package for controlling virtual reality experiments

<https://www.biorxiv.org/content/10.1101/2020.01.27.921148v1>

In the last 15 years, virtual realities have revolutionized behavior experiments in particular for rodents. In combination with treadmills, running wheels, or air-floating balls, the implementation of a virtual reality (VR) provides not only the opportunity to simultaneously explore behavior and neuronal activity in head-fixed animals under nearly natural conditions, but also allows full control over the visual sensory input presented to the animal. Furthermore, VRs can be combined with other sensory modalities such as auditory, tactile or olfactory stimuli. Despite the power of using VRs in animal experiments, available software packages are very limited, expensive and lack the required flexibility to design appropriate behavior and neurophysiology experiments. For this reason, we have developed the versatile, adaptable and easy to use VR environment MazeMaster, an open-source, Python-based software package for controlling virtual reality setups and behavior experiments. The software package includes a graphical user interface (GUI) and can be integrated into standard electrophysiology and imaging setups even by non-programmers. Ready-made behavioral experiments such as multisensory discrimination in T-mazes are already implemented including full control for reward supply and bias correction. For more individual setup designs, the modularity of MazeMaster allows more programming-affine users to extend the software with potentially missing features. With MazeMaster, we offer a free and easy-to-use VR controller that will facilitate the implementation of VR setups in scientific laboratories. In addition, MazeMaster allows the design and control of common head-fixed rodent behavior paradigms with extensive acquisition of meta-data required for reproducible VR experiments. The MazeMaster VR package, therefore, offers a collaboration tool for reproducible research within and across neuroscience laboratories according to the FAIR principles.

A generalizable experimental framework for automated cell growth and laboratory evolution

<https://www.biorxiv.org/content/10.1101/280867v1>

In the post-genomics era, exploration of phenotypic adaptation is limited by our ability to experimentally control selection conditions, including multi-variable and dynamic pressure regimes. While automated cell culture systems offer real-time monitoring and fine control over liquid cultures, they are difficult to scale to high-throughput, or require cumbersome redesign to meet diverse experimental requirements. Here we describe eVOLVER, a multipurpose, scalable DIY framework

that can be easily configured to conduct a wide variety of growth fitness experiments at scale and cost. We demonstrate eVOLVERâ€™s versatility by configuring it for diverse growth and selection experiments that would be otherwise challenging for other systems. We conduct high-throughput evolution of yeast across different population density niches. We perform growth selection on a yeast knockout library under temporally varying temperature regimes. Finally, inspired by large-scale integration in electronics and microfluidics, we develop novel millifluidic multiplexing modules that enable complex fluidic routines including multiplexed media routing, cleaning, vial-to-vial transfers, and automated yeast mating. We propose eVOLVER to be a versatile design framework in which to study, characterize, and evolve biological systems.

Mouse Academy: high-throughput automated training and trial-by-trial behavioral analysis during learning

<https://www.biorxiv.org/content/10.1101/467878v2>

Progress in understanding how individual animals learn will require high-throughput standardized methods for behavioral training but also advances in the analysis of the resulting behavioral data. In the course of training with multiple trials, an animal may change its behavior abruptly, and capturing such events calls for a trial-by-trial analysis of the animalâ€™s strategy. To address this challenge, we developed an integrated platform for automated animal training and analysis of behavioral data. A low-cost and space-efficient apparatus serves to train entire cohorts of mice on a decision-making task under identical conditions. A generalized linear model (GLM) analyzes each animalâ€™s performance at single-trial resolution. This model infers the momentary decision-making strategy and can predict the animalâ€™s choice on each trial with an accuracy of ~80%. We also assess the animalâ€™s detailed trajectories and body poses within the apparatus. Unsupervised analysis of these features revealed unusual trajectories that represent hesitation in the response. This integrated hardware/software platform promises to accelerate the understanding of animal learning.

Robotic microscopy for everyone: the OpenFlexure Microscope

<https://www.biorxiv.org/content/10.1101/861856v1>

Optical microscopes are an essential tool for both the detection of disease in clinics, and for scientific analysis. However, in much of the world access to high-performance microscopy is limited by both the upfront cost and maintenance cost of the equipment. Here we present an open-source, 3D-printed, and fully-automated laboratory microscope, with motorised sample positioning and focus

control. The microscope is highly customisable, with a number of options readily available including trans- and epi-illumination, polarisation contrast imaging, and epi-florescence imaging. The OpenFlexure Microscope has been designed to enable low-volume manufacturing and maintenance by local personnel, vastly increasing accessibility. We have produced over 100 microscopes in Tanzania and Kenya for educational, scientific, and clinical applications, demonstrating that local manufacturing can be a viable alternative to international supply chains that can often be costly, slow, and unreliable.

PlasmoTron: an open-source platform for automated culture of malaria parasites

<https://www.biorxiv.org/content/10.1101/241596v2>

We have created a system which allows an inexpensive opensource liquid-handling robot to automate most aspects of bloodstage malaria parasite culture. Parasites are cultured in multiwell microplates, with their details recorded in a database. Information in the database is used to generate commands for the robot to feed, monitor and passage parasite cultures. We show that the system is capable of raising cultures after transfection and then maintaining them at desired parasitaemias, facilitating significant scale up of both routine culture and experimental genetic modification. The PlasmoTron software is available at plasmotron.org.

Optogenetic control of *Neisseria meningitidis* Cas9 genome editing using an engineered, light-switchable anti-CRISPR protein

<https://www.biorxiv.org/content/10.1101/858589v1>

Optogenetic control of CRISPR-Cas9 systems has significantly improved our ability to perform genome perturbations in living cells with high precision in time and space. As new Cas orthologues with advantageous properties are rapidly being discovered and engineered, the need for straightforward strategies to control their activity via exogenous stimuli persists. The Cas9 from *Neisseria meningitidis* (Nme) is a particularly small and target-specific Cas9 orthologue, and thus of high interest for in vivo genome editing applications.

Integrated Cognitive Assessment: Speed and Accuracy of Visual Processing as a Reliable Proxy to Cognitive Performance

<https://www.biorxiv.org/content/10.1101/335463v1>

Various mental disorders are accompanied by some degree of cognitive impairment. Particularly in neurodegenerative disorders, cognitive impairment is the phenotypical hallmark of the disease. Effective, accurate and timely cognitive assessment is key to early diagnosis of this family of mental disorders. Current standard-of-care techniques for cognitive assessment are primarily paper-based, and need to be administered by a healthcare professional; they are additionally language and education-dependent and typically suffer from a learning bias. These tests are thus not ideal for large-scale pro-active cognitive screening and disease progression monitoring. We developed the Integrated Cognitive Assessment (ICA), a 5-minute computerized cognitive assessment tool based on a rapid visual categorization task, in which a series of carefully selected natural images of varied difficulty are presented to participants. Overall 448 participants, across a wide age-range with different levels of education took the ICA test. We compared participants' ICA test results with a variety of standard pen-and-paper tests that are routinely used to assess cognitive performance. ICA had excellent test-retest reliability, and was significantly correlated with all the reference cognitive tests used here, demonstrating ICA's ability as one unified test that can assess various cognitive domains.

Visual looming and receding networks in awake marmosets investigated with fMRI

<https://www.biorxiv.org/content/10.1101/749309v1>

An object that is looming toward a subject or receding away contains important information for determining if this object is dangerous, beneficial or harmless to them. This information (motion, direction, identity, time-to-collision, size, velocity) is analyzed by the brain in order to execute the appropriate behavioral responses depending on the context: fleeing, freezing, grasping, eating, exploring. In the current study, we performed ultra-high-field functional MRI (fMRI) in awake marmosets to explore the patterns of brain activation elicited by visual stimuli looming toward or receding away from the monkey. We found that looming and receding visual stimuli both activate a large cortical network in frontal, parietal, temporal and occipital cortex in areas involved in the analysis of motion, shape, identity and features of the objects. Looming stimuli strongly activated a network composed of the pulvinar, superior colliculus, prefrontal cortex and temporal cortical areas. This may underlie the existence of an alert network that processes the visual stimuli looming toward their peripersonal space by extracting the crucial information brought by the stimulus and evaluating its potential consequences to the observer. We hypothesize that this network is involved in the planning of protective behaviors (e.g. fleeing or freezing) and in emotional reaction (e.g. anxiety,

fear). These findings support the view that this network is preserved through evolution and that the marmoset is a viable model to study visual and multisensory processes by using fMRI to guide further invasive recordings and/or pharmacological manipulations.

Rapid identification of an *Arabidopsis* NLR gene conferring susceptibility to *Sclerotinia sclerotiorum* using time-resolved automated phenotyping

<https://www.biorxiv.org/content/10.1101/488171v1>

The broad host range necrotrophic fungus *Sclerotinia sclerotiorum* is a devastating pathogen of many oil and vegetable crops. Plant genes conferring complete resistance against *S. sclerotiorum* have not been reported. Instead, plant populations challenged by *S. sclerotiorum* exhibit a continuum of partial resistance designated as quantitative disease resistance (QDR). Because of their complex interplay and their small phenotypic effect, the functional characterization of QDR genes remains limited. How broad host range necrotrophic fungi manipulate plant programmed cell death is for instance largely unknown. Here, we designed a time-resolved automated disease phenotyping pipeline and assessed the kinetics of disease symptoms caused by seven *S. sclerotiorum* isolates on six *A. thaliana* natural accessions with unprecedented resolution. We hypothesized that large effect polymorphisms common to the most resistant *A. thaliana* accessions, but absent from the most susceptible ones, would point towards disease susceptibility genes. This identified highly divergent alleles of the nucleotide-binding site leucine-rich repeat gene LAZ5 in the resistant accessions Rubenzhnoe and Lip-0. Two LAZ5-deficient mutant lines in the Col-0 genetic background showed enhanced QDR to *S. sclerotiorum*, whereas plants mutated in the closely related CSA1 gene responded like the wild type. These findings illustrate the value of time-resolved image-based phenotyping for unravelling the genetic bases of complex traits such as QDR. Our results suggest that *S. sclerotiorum* manipulates plant sphingolipid pathways guarded by LAZ5 to trigger programmed cell death and cause disease.

Genomic investigation of the strawberry pathogen *Phytophthora fragariae* indicates pathogenicity is associated with transcriptional variation in three key races

<https://www.biorxiv.org/content/10.1101/860619v2>

The oomycete *Phytophthora fragariae* is a highly destructive pathogen of cultivated strawberry (*Fragaria* — ananassa), causing the root rotting disease, “red core”™. The host-pathogen interaction has a well described gene-for-gene resistance relationship, but to date neither candidate

avirulence nor resistance genes have been identified. We sequenced a set of American, Canadian and UK isolates of known race type, along with three representatives of the closely related pathogen of the raspberry (*Rubus idaeus*), *Phytophthora rubi*, and found a clear population structure, with a high degree of nucleotide divergence seen between some race types and abundant private variation associated with race types 4 and 5. In contrast, between isolates defined as UK races 1, 2 & 3 (UK1-2-3) there was no evidence of gene loss or gain; or the presence of insertions/deletions (INDELs) or Single Nucleotide Polymorphisms (SNPs) within or in proximity to putative pathogenicity genes could be found associated with race variation. Transcriptomic analysis of representative UK1-2-3 isolates revealed abundant expression variation in key effector family genes associated with pathogen race; however, further long read sequencing did not reveal any long range polymorphisms to be associated with avirulence to race UK2 or UK3 resistance, suggesting either control in trans or other stable forms of epigenetic modification modulating gene expression. This work reveals the combined power of population resequencing to uncover race structure in pathosystems and in planta transcriptomic analysis to identify candidate avirulence genes. This work has implications for the identification of putative avirulence genes in the absence of associated expression data and points towards the need for detailed molecular characterisation of mechanisms of effector regulation and silencing in oomycete plant pathogens.

Olfactory object recognition based on fine-scale stimulus timing in *Drosophila*

<https://www.biorxiv.org/content/10.1101/418632v2>

Odorants of behaviorally relevant objects (e.g., food sources) intermingle with those from other sources. Therefore, to sniff out whether an odor source is good or bad — without actually visiting it — animals first need to segregate the odorants from different sources. To do so, animals could use temporal cues, since odorants from one source exhibit correlated fluctuations, while odorants from different sources are less correlated. However, it remains unclear whether animals can rely solely on temporal cues for odor source segregation. Here we show that 1) flies can use a few milliseconds differences in odorant arrival to segregate a target odorant from a binary mixture, 2) segregation does not improve when the target odorant arrives first, and 3) segregation works for odorants with innate, as well as learned valences. These properties of odor segregation parallel those of concurrent sound segregation and figure-ground segregation by onset asynchrony in humans.

Stereo In-Line Holographic Digital Microscope

<https://www.biorxiv.org/content/10.1101/790535v1>

Biologists use optical microscopes to study plankton in the lab, but their size, complexity and cost makes widespread deployment of microscopes in lakes and oceans challenging. Monitoring the morphology, behavior and distribution of plankton in situ is essential as they are excellent indicators of marine environment health and provide a majority of Earth's oxygen and carbon sequestration. Direct in-line holographic microscopy (DIHM) eliminates many of these obstacles, but image reconstruction is computationally intensive and produces monochromatic images. By using one laser and one white LED, it is possible to obtain the 3D location of plankton by triangulation, limiting holographic reconstruction to only the voxels occupied by the plankton, reducing computation by several orders of magnitude. The color information from the white LED assists in the classification of plankton, as phytoplankton contains green-colored chlorophyll. The reconstructed plankton images are rendered in a 3D interactive environment, viewable from a browser, providing the user the experience of observing plankton from inside a drop of water.

Cost Effective Acoustic Monitoring of Biodiversity and Bird Populations in Kenya

<https://www.biorxiv.org/content/10.1101/072546v1>

With the increasing need to effectively monitor a growing number of ecosystems of interest due to risks posed to these ecosystems by human activity and climate change, novel approaches to biodiversity monitoring are needed. In this work we demonstrate the application of low cost acoustic recorders based on the Raspberry Pi microprocessor to biodiversity monitoring. The recorders are capable of capturing audio recordings from which we can compute acoustic indices of biodiversity and identify bird species of interest. We compare the acoustic indices of biodiversity and results of point counts aimed at determining bird species presence and find that the acoustic complexity index has a significant positive correlation to point count results. In addition, we show that the presence of the Hartlaub's Turaco, a ubiquitous species in montane forests in Kenya with a distinct call, can be automatically determined using recordings obtained using our setup. Montane species are of interest for long-term automatic monitoring since they are particularly vulnerable to the effects of climate change. Our system is able to deal with the large amounts of data generated by the acoustic recorders. The automatic screening of approximately five hours of recordings for presence of the Hartlaub's Turaco call is achieved in approximately three minutes representing a large time saving that makes use of audio recordings for species identification feasible.

A conveyor feeder for animal experiments

<https://www.biorxiv.org/content/10.1101/801993v1>

Several different types of open source feeders have been used in animal experiments in cognitive biology, neuroscience, psychology and related fields. These feeders use either dry pellets, which have hard surface and simple shape, or liquid food types such as sucrose solution. These food types can be rather easily manipulated due to its physical attributes. Although it is beneficial in terms of controllability, animal subjects often lose motivation to interact with operant conditioning devices offering such food items. Using natural food items such as fruits, insects, worms and pieces of meat will be helpful to keep the subject's motivation high, however, those food items are not very well suited for currently available open source feeders due to its physical attributes, including its complex shape, sticky and delicate texture. We made a feeder to deliver such natural food items to animal subjects for operant conditioning, using relatively cheap and easily obtainable parts. For a validation, we built a full operant conditioning device for wolves and dogs, containing two of these feeders, a pressure-sensitive monitor and a speaker.

In vivo CRISPRa decreases seizures and rescues cognitive deficits in a rodent model of epilepsy

<https://www.biorxiv.org/content/10.1101/431015v3>

Epilepsy is a major health burden, calling for new mechanistic and therapeutic insights. CRISPR-mediated gene editing shows promise to cure genetic pathologies, although hitherto it has mostly been applied ex-vivo. Its translational potential for treating non-genetic pathologies is still unexplored. Furthermore, neurological diseases represent an important challenge for the application of CRISPR, because of the need in many cases to manipulate gene function of neurons in situ. A variant of CRISPR, CRISPRa, offers the possibility to modulate the expression of endogenous genes by directly targeting their promoters. We asked if this strategy can effectively treat acquired focal epilepsy, focusing on ion channels because their manipulation is known to be effective in changing network hyperactivity and hypersynchronisation. We applied a doxycycline-inducible CRISPRa technology to increase the expression of the potassium channel gene Kcna1 (encoding Kv1.1) in mouse hippocampal excitatory neurons. CRISPRa-mediated Kv1.1 upregulation led to a substantial decrease in neuronal excitability. Continuous video-EEG telemetry showed that AAV9-mediated delivery of CRISPRa, upon doxycycline administration, decreased spontaneous generalized tonic-clonic seizures in a model of temporal lobe epilepsy, and rescued cognitive

impairment and transcriptomic alterations associated with chronic epilepsy. The focal treatment minimizes concerns about off-target effects in other organs and brain areas. This study provides the proof of principle for a translational CRISPR-based approach to treat neurological diseases characterized by abnormal circuit excitability.

Visual recognition of the female body axis drives spatial elements of male courtship in *Drosophila melanogaster*

<https://www.biorxiv.org/content/10.1101/576322v1>

Like other mating behaviors, the courtship ritual exhibited by male *Drosophila* towards a virgin female is comprised of spatiotemporal sequences of innate behavioral elements. Yet, the specific stimuli and neural circuits that determine when and where males release individual courtship elements are not well understood. Here, we investigated the role of visual object recognition in the release of specific behavioral elements during bouts of male courtship. By using a computer vision and machine learning based approach for high-resolution analyses of the male courtship ritual, we show that the release of distinct behavioral elements occur at stereotyped locations around the female and depends on the ability of males to recognize visual landmarks present on the female. Specifically, we show that independent of female motion, males utilize unique populations of visual projection neurons to recognize the eyes of a target female, which is essential for the release of courtship behaviors at their appropriate spatial locations. Together, these results provide a mechanistic explanation for how relatively simple visual cues could play a role in driving both spatially- and temporally-complex social interactions.

A framework for predicting soft-fruit yields and phenology using embedded, networked microsensors, coupled weather models and machine-learning techniques

<https://www.biorxiv.org/content/10.1101/565010v1>

Predicting harvest timing is a key challenge to sustainably develop soft fruit farming and reduce food waste. Soft fruits are perishable, high-value and seasonal, and sales prices are typically time-sensitive. In addition, fruit harvesting is labour-intensive and increasingly expensive making accurate phenological predictions valuable for growers. A novel approach for predicting soft fruit phenology and yields was developed and tested, using strawberries as the model crop. Seedlings were planted in polytunnels, and environmental and yield data were collected throughout the growing season. Over 1.2 million datapoints were collected by networked microsensors which

measured spatial and temporal variability in air temperature, relative humidity (RH), soil moisture and photosynthetically active radiation (PAR). Fleeces were added to a subset of the plants to generate additional within-polytunnel variation. Cumulative fruit yields followed logistic growth curves and the coefficients of these curves were dependent on micro-climatic growing conditions. After 10,000 iterations, machine learning revealed that RH was the optimal factor informing the coefficients of these curves, perhaps because it is an integrative metric of air temperature and water status. Trigonometric models transformed weather forecasts, which showed a relatively low agreement with polytunnel air temperature ($R^2 = 0.6$) and RH ($R^2 = 0.5$) measurements, into more accurate polytunnel-specific predictions for temperature and RH (both $R^2 = 0.8$). We present a framework for using machine-learning techniques to calculate curve coefficients and parametrise coupled weather models which can predict fruit yields and timing to a greater degree of accuracy than previously possible. Dataloggers measuring environmental and yield data could infer model parameters using iterative training for novel fruit varieties or crop types growing in different locations without a-priori phenological information. At this stage in the development of artificial intelligence and networked microsensors, this is a step forward in generating bespoke phenological prediction models to inform and support growers.

CropQuant: An automated and scalable field phenotyping platform for crop monitoring and trait measurements to facilitate breeding and digital agriculture

<https://www.biorxiv.org/content/10.1101/161547v2>

Automated phenotyping technologies are capable of providing continuous and precise measurements of traits that are key to today's crop research, breeding and agronomic practices. In addition to monitoring developmental changes, high-frequency and high-precision phenotypic analysis can enable both accurate delineation of the genotype-to-phenotype pathway and the identification of genetic variation influencing environmental adaptation and yield potential. Here, we present an automated and scalable field phenotyping platform called CropQuant, designed for easy and cost-effective deployment in different environments. To manage infield experiments and crop-climate data collection, we have also developed a web-based control system called CropMonitor to provide a unified graphical user interface (GUI) to enable realtime interactions between users and their experiments. Furthermore, we established a high-throughput trait analysis pipeline for phenotypic analyses so that lightweight machine-learning modelling can be executed on CropQuant workstations to study the dynamic interactions between genotypes (G), phenotypes (P),

and environmental factors (E). We have used these technologies since 2015 and reported results generated in 2015 and 2016 field experiments, including developmental profiles of five wheat genotypes, performance-related traits analyses, and new biological insights emerged from the application of the CropQuant platform.

Real brains in virtual worlds: Validating a novel oddball paradigm in virtual reality

<https://www.biorxiv.org/content/10.1101/749192v2>

Electroencephalography (EEG) research is typically conducted in controlled laboratory settings. This limits the generalizability to real-world situations. Virtual reality (VR) sits as a transitional tool that provides tight experimental control with more realistic stimuli. To test the validity of using VR for event-related potential (ERP) research, we used a well-established paradigm, the oddball task. Standard stimuli were presented 80% of the time and target stimuli which were responded to, 20% of the time. For our first study, we compared traditional to VR stimulus presentation using standard visual and auditory oddball tasks. We found that ERPs collected using VR head mounted displays and typical monitors were comparable on measures of latency, amplitude, and spectral composition. In a second study, we implemented a novel depth-based oddball task. We demonstrated that typical oddball ERPs elicited by the presentation of near and far stimuli. Interestingly, we observed significant differences in early ERPs components between near and far stimuli, even after controlling for the effects of the oddball task. Current results suggest that VR can serve as a valid means of stimulus presentation in novel or otherwise inaccessible environments for EEG experimentation. We demonstrated the capability of the depth-based oddball to reliably elicit P3 responses. We also found an interaction between the depth at which objects are presented and early ERP responses. Further research is warranted to better explain this influence of depth on the ERP components.

Low-Cost Touchscreen Driven Programmable Dual Syringe Pump for Life Science Applications

<https://www.biorxiv.org/content/10.1101/288290v1>

Syringe pumps are powerful tools able to automate routine laboratory practices that otherwise consume large amounts of manual labor time. Commercially available syringe pumps are expensive, difficult to customize, and often preset for a narrow range of operations. Here, we show how to build a programmable dual syringe pump (PDSP) that overcomes these limitations. The PDSP is driven by a Raspberry Pi paired with a stepper motor controller to allow maximal customization via Python

scripting. The entire setup can be controlled by a touchscreen for use without a keyboard or mouse. Furthermore, the PDSP is structured around 3D printed parts, enabling users to change any component for their specific application. We demonstrate one application of the PDSP by using it to generate whole cell lysates using a cell homogenizer in an automated fashion.

An Open-Hardware sample mounting solution for inverted light-sheet microscopes with large detection objective lenses

<https://www.biorxiv.org/content/10.1101/636977v3>

Implementations of light-sheet microscopes are often incompatible with standard methods of sample mounting. Light-sheet microscopy uses orthogonal illumination and detection to create a thin sheet of light which does not illuminate the sample outside of the depth of field of the detection axis. Typically, this configuration involves a pair of orthogonal objectives which constrains the positioning of a length of coverslips or microscope slides in range of the detection objective. We present an open-hardware (1, 2) sample mounting system for light-sheet microscopes using large detection objectives.

Fluctuating light experiments and semi-automated plant phenotyping enabled by self-built growth racks and simple upgrades to the IMAGING-PAM

<https://www.biorxiv.org/content/10.1101/795476v2>

Background Over the last years, several plant science labs have started to employ fluctuating growth light conditions to simulate natural light regimes more closely. Many plant mutants reveal quantifiable effects under fluctuating light despite being indistinguishable from wild-type plants under standard constant light. Moreover, many subtle plant phenotypes become intensified and thus can be studied in more detail. This observation has caused a paradigm shift within the photosynthesis research community and an increasing number of scientists are interested in using fluctuating light growth conditions. However, high installation costs for commercial controllable LED setups as well as costly phenotyping equipment can make it hard for small academic groups to compete in this emerging field.

Speed breeding in growth chambers and glasshouses for crop breeding and model plant research

<https://www.biorxiv.org/content/10.1101/369512v1>

To meet the challenge of feeding a growing population, breeders and scientists are continuously looking for ways to increase genetic gain in crop breeding. One way this can be achieved is through “speed breeding” (SB), which shortens the breeding cycle and accelerates research studies through rapid generation advancement. The SB method can be carried out in a number of ways, one of which involves extending the duration of a plant’s daily exposure to light (photoperiod) combined with early seed harvest in order to cycle quickly from seed to seed, thereby reducing the generation times for some long-day (LD) or day-neutral crops. Here we present glasshouse and growth chamber-based SB protocols with supporting data from experimentation with several crop species. These protocols describe the growing conditions, including soil media composition, lighting, temperature and spacing, which promote rapid growth of spring and winter bread wheat, durum wheat, barley, oat, various members of the Brassica family, chickpea, pea, grasspea, quinoa and the model grass *Brachypodium distachyon*. Points of flexibility within the protocols are highlighted, including how plant density can be increased to efficiently scale-up plant numbers for single seed descent (SSD) purposes. Conversely, instructions on how to perform SB on a small-scale by creating a benchtop SB growth cabinet that enables optimization of parameters at a low cost are provided. We also outline the procedure for harvesting and germinating premature wheat, barley and pea seed to reduce generation time. Finally, we provide troubleshooting suggestions to avoid potential pitfalls.

PARbars: cheap, easy to build ceptometers for continuous measurement of light interception in plant canopies

<https://www.biorxiv.org/content/10.1101/481218v1>

Short Abstract Detailed instructions on how to build, calibrate and collect research quality data from PARbar ceptometers are presented.

Single-cell RNA-seq of rheumatoid arthritis synovial tissue using low cost microfluidic instrumentation

<https://www.biorxiv.org/content/10.1101/140848v1>

Droplet-based single cell RNA-seq has emerged as a powerful technique for massively parallel cellular profiling. While these approaches offer the exciting promise to deconvolute cellular heterogeneity in diseased tissues, the lack of cost-effective, reliable, and user-friendly

instrumentation has hindered widespread adoption of droplet microfluidic techniques. To address this, we have developed a microfluidic control instrument that can be easily assembled from 3D printed parts and commercially available components costing approximately \$540. We adapted this instrument for massively parallel scRNA-seq and deployed it in a clinical environment to perform single cell transcriptome profiling of disaggregated synovial tissue from a rheumatoid arthritis patient. We sequenced 8,716 single cells from a synovectomy, revealing 16 transcriptomically distinct clusters. These encompass a comprehensive and unbiased characterization of the autoimmune infiltrate, including inflammatory T and NK subsets that contribute to disease biology. Additionally, we identified fibroblast subpopulations that are demarcated via THY1 (CD90) and CD55 expression. Further experiments confirm that these represent synovial fibroblasts residing within the synovial intimal lining and subintimal lining, respectively, each under the influence of differing microenvironments. We envision that this instrument will have broad utility in basic and clinical settings, enabling low-cost and routine application of microfluidic techniques, and in particular single-cell transcriptome profiling.

CHIME: CMOS-hosted in-vivo microelectrodes for massively scalable neuronal recordings

<https://www.biorxiv.org/content/10.1101/570069v3>

Mammalian brains consist of 10s of millions to 100s of billions of neurons operating at millisecond time scales, of which current recording techniques only capture a tiny fraction. Recording techniques capable of sampling neural activity at such temporal resolution have been difficult to scale: The most intensively studied mammalian neuronal networks, such as the neocortex, show layered architecture, where the optimal recording technology samples densely over large areas. However, the need for application-specific designs as well as the mismatch between the three-dimensional architecture of the brain and largely two-dimensional microfabrication techniques profoundly limits both neurophysiological research and neural prosthetics.

PiVR: an affordable and versatile closed-loop platform to study unrestrained sensorimotor behavior

<https://www.biorxiv.org/content/10.1101/2019.12.20.885442v1>

Tools enabling closed-loop experiments are crucial to delineate causal relationships between the activity of genetically-labeled neurons and specific behaviors. We developed the Raspberry Pi Virtual Reality system (PiVR) to conduct closed-loop optogenetic stimulation of neural functions in

unrestrained animals. PiVR is an experimental platform that operates at high-temporal resolution (>50 Hz) with low latencies (~10 ms), while being affordable (<\$500) and easy to build (<6 hours). This tool was designed to be accessible to a wide public, from highschool students to professional researchers studying systems neuroscience. We illustrate the functionality of PiVR by focusing on sensory navigation in response to gradients of chemicals (chemotaxis) and light (phototaxis). We show how Drosophila flies perform negative chemotaxis by modulating their locomotor speed to avoid locations associated with optogenetically-evoked bitter taste. In Drosophila larvae, we use innate positive chemotaxis to compare orientation behavior elicited by real- and virtual-odor gradients with static shapes as well as by turbulent virtual-odor plumes. Finally, we examine how positive phototaxis emerges in zebrafish larvae from the modulation of turning maneuvers during the ascent of virtual white-light gradients. Besides its application to study chemotaxis and phototaxis, PiVR is a versatile tool designed to bolster efforts to map and to functionally characterize neural circuits.

A real-time multiplexed microbial growth intervalometer for capturing high resolution growth curves

<https://www.biorxiv.org/content/10.1101/533356v1>

Batch cultures are a low maintenance and routine culturing method used in anaerobic microbiology. Automated tools that measure growth curves from anaerobic microorganisms grown in traditional laboratory glassware, such as Balch-type tubes, are not commercially available. Here we present a new MicrobiAI Growth Intervalometer (MAGI) that captures microbial growth curves through photoconductivity of the medium using a diffused light pattern of specified frequency, rather than photo-attenuation of collimated light used in traditional systems, and is configured with an offset photodetector/emitter to minimize direct impingement of light from the source to improve the resolution of the solution's density. MAGI is operated by software-driven automation and offers investigators a low noise/high gain instrument with capabilities for remote visualization and data acquisition. MAGI is a low maintenance, low cost, and robust platform primarily for anaerobic cultivation and growth monitoring. We demonstrate the utility of this device by first showing that growth rates and generation times in *Escherichia coli* K-12 are reproducible to previously published results. We then tested MAGI to measure growth curves of an environmental organism, *Intrasporangium calvum*, under various media compositions. Our results demonstrate that MAGI is a versatile platform to measure growth curves in media under various redox conditions (microaerobic

and anaerobic), complex mediums such as Luria-Bertani (LB) broth and minimal media, and for resolving diauxic growth curves when *I. calvum* is grown on a disaccharide. Lastly, we demonstrate that the device can resolve growth curves for $\hat{1}\frac{1}{4}M$ concentrations of resources that yield low biomass. This research advances the tools available to microbiologist aiming to monitor growth curves in a variety of disciplines, such as environmental microbiology, clinical microbiology, and food sciences.

Target Capture Sequencing Unravels Rubus Evolution

<https://www.biorxiv.org/content/10.1101/703926v1>

Background Rubus (Rosaceae) comprises more than 500 species with additional commercially cultivated raspberries and blackberries. The most recent (> 100 years old) global taxonomic treatment of the genus defined 12 subgenera; two subgenera were subsequently described and some species were rearranged. Intra- and interspecific ploidy levels and hybridization make phylogenetic estimation of Rubus challenging. Our objectives were to: estimate the phylogeny of 94 geographically diverse species and 3 cultivars using chloroplast DNA sequences and target capture of approximately 1,000 low copy nuclear genes; estimate divergence times between major Rubus clades; and examine the historical biogeography of species diversification.

The ESCRT-III Isoforms CHMP2A And CHMP2B Display Different Effects On Membranes Upon Polymerization

<https://www.biorxiv.org/content/10.1101/756403v1>

ESCRT-III proteins are involved in many membrane remodeling processes including multivesicular body biogenesis as first discovered in yeast. In humans, CHMP2 exists as two potential isoforms, CHMP2A and CHMP2B, but their physical characteristics have not been compared yet. Here, we use a combination of technics on biomimetic systems and purified proteins to study their affinity and effects on membranes. We establish that CHMP2B binding is enhanced in the presence of PI(4,5)P₂ lipids. In contrast, CHMP2A does not display lipid specificity and requires CHMP3 for binding significantly to membranes. On the micrometer scale and at moderate bulk concentrations, CHMP2B forms a reticular structure on membranes whereas CHMP2A (+CHMP3) binds homogeneously. Eventually, CHMP2A and CHMP2B unexpectedly induce different mechanical effects to membranes: CHMP2B strongly rigidifies them while CHMP2A (+CHMP3) has no significant effect. Altogether, we conclude that CHMP2B and CHMP2A cannot be considered as

isoforms and might thus contribute differently to membrane remodeling processes.

An inexpensive remotely-operated video recording system for continuous behavioral observations

<https://www.biorxiv.org/content/10.1101/596106v3>

Video recording technology is an important tool for studies of animal behavior because it reduces observer effects and produces a record of experiments, interactions among subjects, and contextual information, however it remains cost prohibitive for many researchers. Here we present an inexpensive method for building a remotely-operated video recording system to continuously monitor behavioral or other biological experiments. Our system employs Raspberry Pi computers and cameras, open-source software, and allows for wireless networking, live-streaming, and the capacity to simultaneously record from several cameras in an array. To validate this system, we continuously monitored home-cage behavior of California mice (*Peromyscus californicus*) in a laboratory setting. We captured video in both low- and bright-light environments to record behaviors of this nocturnal species, and then quantified mating interactions of California mouse pairs by analyzing the videos with an open-source event logging software. This video recording platform offers users the flexibility to modify the specifications for a range of tasks and the scalability to make research more efficient and reliable to a larger population of scientists.

Proximity sensors reveal social information transfer in maternity colonies of Common noctule bats

<https://www.biorxiv.org/content/10.1101/421974v2>

Bats are a highly gregarious taxon suggesting that social information should be readily available for making decision. Social information transfer in maternity colonies might be a particularly efficient mechanism for naïve pups to acquire information on resources from informed adults. However, such behaviour is difficult to study in the wild, in particular in elusive and small-bodied animals such as bats.

Real-time markerless video tracking of body parts in mice using deep neural networks

<https://www.biorxiv.org/content/10.1101/482349v1>

Markerless and accurate tracking of mouse movement is of interest to many biomedical,

pharmaceutical, and behavioral science applications. The additional capability of tracking body parts in real-time with minimal latency opens up the possibility of manipulating motor feedback, allowing detailed explorations of the neural basis for behavioral control. Here we describe a system capable of tracking specific movements in mice at a frame rate of 30.3 Hz. To achieve these results, we adapt DeepLabCut – a robust movement-tracking deep neural network framework – for real-time tracking of body movements in mice. We estimate paw movements of mice in real time and demonstrate the concept of movement-triggered optogenetic stimulation by flashing a USB-CGPIO controlled LED that is triggered when real time analysis of movement exceeds a pre-set threshold. The mean time delay between movement initiation and LED flash was 93.44 ms, a latency sufficient for applying behaviorally-triggered feedback. This manuscript presents the rationale and details of the algorithms employed and shows implementation of the system using behaving mice. This system lays the groundwork for a behavior-triggered –closed loop™ brain-machine interface with optogenetic stimulation of specific brain regions for feedback.

Using QC-Blind for quality control and contamination screening of bacteria DNA sequencing data without reference genome

<https://www.biorxiv.org/content/10.1101/438655v1>

Quality control in next generation sequencing has become increasingly important as the technique becomes widely used. Tools have been developed for filtering possible contaminants in the sequencing data of species with known reference genome. Unfortunately, reference genomes for all the species involved, including the contaminants, are required for these tools to work. This precludes many real-life samples that have no information about the complete genome of the target species, and are contaminated with unknown microbial species.

Development of honeybee waggle dance and its differences between recruits and scouts

<https://www.biorxiv.org/content/10.1101/179408v1>

The lifetime development of the waggle dance of 14 honeybees was automatically recorded just after the imaginal molt using high-definition camera modules connected with a Raspberry Pi computer and numbered radio-frequency identification tags fitted to the back of each bee. For most honeybees, waggle dance follow preceded the appearance of the first waggle dance from 1 week after the imaginal molt. The duration per trip increased just after waggle dance follow. Before the appearance of the first waggle dance, the honeybee repeatedly follows waggle dances that indicate

a limited number (2–6) of food source locations. We discriminated between two types of foragers with different roles, recruits and novice scouts, by comparing the vectors indicated by the bees' first waggle dance (sending vectors) with dances they had previously followed (received vectors). Of 14 tagged honeybees, 11 were categorized as recruits and 2 as novice scouts. For recruits (but not for novice scouts), the duration per trip increased significantly after waggle dances follow and substantially increased just before the appearance of the first waggle dance. Moreover, recruits increased the number of times they followed waggle dances indicating the same location, and their first waggle dance indicated this location. These results suggest that the differentiation of these two types of foragers is partly related to behavioral differences after waggle dance follows: whether trip is activated or not by follows a waggle dance.

Sustained Activation of PV+ Interneurons in Core Auditory Cortex Enables Robust Divisive Gain Control for Complex and Naturalistic Stimuli

<https://www.biorxiv.org/content/10.1101/832642v2>

Sensory cortices must flexibly adapt their operations to internal states and external requirements. Modulation of specific inhibitory interneurons may provide a network-level mechanism for adjustments on behaviourally relevant timescales. Understanding of the computational roles of such modulation has mostly been restricted to phasic optogenetic activation and short, transient stimuli. Here, we aimed to extend the understanding of modulation of cortical inhibition by using sustained, network-wide optogenetic activation of parvalbumin-positive interneurons in core auditory cortex to study modulation of responses to transient, sustained, and naturalistic stimuli. We found highly conserved spectral and temporal tuning, despite profoundly reduced overall network activity. This reduction was predominantly divisive, and consistent across simple, complex, and naturalistic stimuli. A recurrent network model with power-law input-output functions replicated our results. We conclude that modulation of parvalbumin-positive interneurons on timescales typical of more sustained neuromodulation may provide a means for robust divisive gain control conserving stimulus representations.

Robust, real-time and autonomous monitoring of ecosystems with an open, low-cost, networked device

<https://www.biorxiv.org/content/10.1101/236075v3>

Automated methods of monitoring ecosystems provide a cost-effective way to track changes in

natural system's dynamics across temporal and spatial scales. However, methods of recording and storing data captured from the field still require significant manual effort.

Neuromodulatory selection of motor neuron recruitment patterns in a visuomotor behavior increases speed

<https://www.biorxiv.org/content/10.1101/683649v2>

Animals generate locomotion at different speeds to suit their behavioral needs. Spinal circuits generate locomotion at these varying speeds by sequential activation of different spinal interneurons and motor neurons. Larval zebrafish can generate slow swims for prey capture and exploration by activation of secondary motor neurons and much faster and vigorous swims during escapes and struggles via the additional activation of primary motor neurons. Neuromodulators are known to alter motor output of spinal circuits yet their precise role in speed regulation is not understood well. Here, in the context of optomotor response (OMR), an innate, evoked locomotor behavior, we show that dopamine (DA) provides an additional layer to regulation of swim speed in larval zebrafish. Activation of D1-like receptors increases swim speed during OMR in free-swimming larvae. By analysing tail bend kinematics in head-restrained larvae, we show that the increase in speed is actuated by larger tail bends. Whole cell patch clamp recordings from motor neurons reveal that during OMR, typically only secondary motor neurons are active while primary motor neurons are quiescent. Activation of D1-like receptors increases motor drive from secondary motor neurons by decreasing spike threshold and latency. In addition, D1-like receptor activation enhances excitability and recruits quiescent primary motor neurons. Our findings provide an example of neuromodulatory reconfiguration of spinal motor neuron speed modules such that members are selectively recruited and motor drive is increased to effect changes in locomotor speed.

Cellular and molecular mechanisms of photoreceptor tuning for prey capture in larval zebrafish

<https://www.biorxiv.org/content/10.1101/744615v2>

In the eye, the function of same-type photoreceptors must be regionally adjusted to process a highly asymmetrical natural visual world. Here we show that UV-cones in the larval zebrafish area temporalis are specifically tuned for UV-bright prey capture in their upper frontal visual field, which uses the signal from a single cone at a time. For this, UV-detection efficiency is regionally boosted 42-fold. Next, *in vivo* 2-photon imaging, transcriptomics and computational modelling reveal that

these cones use an elevated baseline of synaptic calcium to facilitate the encoding of bright objects, which in turn results from expressional tuning of phototransduction genes. Finally, this signal is further accentuated at the level of glutamate release driving retinal networks. These regional differences tally with variations between peripheral and foveal cones in primates and hint at a common mechanistic origin. Together, our results highlight a rich mechanistic toolkit for the tuning of neurons.

Microsecond Interaural Time Difference Discrimination Restored by Cochlear Implants After Neonatal Deafness

<https://www.biorxiv.org/content/10.1101/498105v3>

Cochlear implants (CIs) can restore a high degree of functional hearing in deaf patients but enable only poor spatial hearing or hearing in noise. Early deaf CI users are essentially completely insensitive to interaural time differences (ITDs). A dearth of binaural experience during an early critical period is often blamed for this shortcoming. However, here we show that neonatally deafened rats provided with precisely synchronized CI stimulation in adulthood can be trained to localize ITDs with essentially normal behavioral thresholds near $50 \frac{1}{4}$ s. Furthermore, neonatally deaf rats show high physiological sensitivity to ITDs immediately after binaural implantation in adulthood. This suggests that the insensitivity to ITDs seen in human children who are born deaf is similarly unlikely to be caused by lack of early auditory experience, and more likely due to prolonged stimulation with CI processors which do not encode sub-millisecond temporal fine structure of sounds.

Low cost and open source multi-fluorescence imaging system for teaching and research in biology and bioengineering

<https://www.biorxiv.org/content/10.1101/194324v1>

The advent of easy-to-use open source microcontrollers, off-the-shelf electronics and customizable manufacturing technologies has facilitated the development of inexpensive scientific devices and laboratory equipment. In this study, we describe an imaging system that integrates low-cost and open-source hardware, software and genetic resources. The multi-fluorescence imaging system consists of readily available 470 nm LEDs, a Raspberry Pi camera and a set of filters made with low cost acrylics. This device allows imaging in scales ranging from single colonies to entire plates. We developed a set of genetic components (e.g. promoters, coding sequences, terminators) and vectors following the standard framework of Golden Gate, which allowed the fabrication of genetic

constructs in a combinatorial, low cost and robust manner. In order to provide simultaneous imaging of multiple wavelength signals, we screened a series of long stokes shift fluorescent proteins that could be combined with cyan/green fluorescent proteins. We found CyOFP1, mBeRFP and sfGFP to be the most compatible set for 3-channel fluorescent imaging. We developed open source Python code to operate the hardware to run time-lapse experiments with automated control of illumination and camera and a Python module to analyze data and extract meaningful biological information. To demonstrate the potential application of this integral system, we tested its performance on a diverse range of imaging assays often used in disciplines such as microbial ecology, microbiology and synthetic biology. We also assessed its potential for STEM teaching in a high school environment, using it to teach biology, hardware design, optics, and programming. Together, these results demonstrate the successful integration of open source hardware, software, genetic resources and customizable manufacturing to obtain a powerful, low cost and robust system for STEM education, scientific research and bioengineering. All the resources developed here are available under open source licenses.

Deletion of Stk11 and Fos in mouse BLA projection neurons alters intrinsic excitability and impairs formation of long-term aversive memory

<https://www.biorxiv.org/content/10.1101/787325v2>

Conditioned taste aversion (CTA) is a form of one-trial learning dependent on basolateral amygdala projection neurons (BLApn). Its underlying cellular and molecular mechanisms are poorly understood, however. We used RNAseq from BLApn to identify learning-related changes in Stk11, a kinase with well-studied roles in growth, metabolism and development, but not previously implicated in learning. Deletion of Stk11 restricted to BLApn completely blocks memory when occurring prior to training, but not following it, despite altering neither BLApn-dependent encoding of taste palatability in gustatory cortex, nor transcriptional activation of BLApn during training. Deletion of Stk11 in BLApn also increases their intrinsic excitability. Conversely, BLApn activated by CTA to express the immediate early gene Fos had reduced excitability. BLApn knockout of Fos also increased excitability and impaired learning. These data suggest that Stk11 and Fos expression play key roles in CTA long-term memory formation, perhaps by modulating the intrinsic excitability of BLApn.

Utilizing Social Media and Video Games to Control #DIY Microscopes

<https://www.biorxiv.org/content/10.1101/053470v1>

Open-source lab equipment is becoming more widespread with the popularization of fabrication tools such as 3d-printers, laser cutters, CNC machines, open source microcontrollers and open source software. Although many pieces of common laboratory equipment have been developed, software control of these items is sometimes lacking. Specifically, control software that can be easily implemented and enable user-input and control over multiple platforms (PC, smartphone, web, etc.). The aim of this proof-of-principle study was to develop and implement software for the control of a low-cost, 3d-printed microscope. Here, we present two approaches, which enable microscope control by exploiting the functionality of the social media platform Twitter or player actions inside of the videogame Minecraft. The microscope was constructed from a modified web-camera and implemented on a Raspberry Pi computer. Four aspects of microscope control were tested, including single image capture, focus control and time-lapse imaging. The Twitter-embodiment enabled users to send “tweets” directly to the microscope. Image data acquired by the microscope was then returned to the user through a Twitter reply and stored permanently on the photo-sharing platform Flickr, along with any relevant metadata. Local control of the microscope was also implemented by utilizing the video game Minecraft, in situations where Internet connectivity is not present or stable. A virtual laboratory was constructed inside the Minecraft world and player actions inside the laboratory were linked to specific microscope functions. Here, we present the methodology and results of these experiments and discuss possible limitations and future extensions of this work.

Male parental investment reflects the level of partner contributions and brood value in tree swallows

<https://www.biorxiv.org/content/10.1101/216119v1>

Biparental care presents an interesting case of cooperation and conflict between unrelated individuals. Several models have been proposed to explain how parents should respond to changes in each other’s parental care to maximize their own fitness, predicting no change, partial compensation, or matching effort as a response. Here, we present an experiment in tree swallows (*Tachycineta bicolor*) in which we increased the parental care of females by presenting them, but not their mates, with additional nestling begging calls using automated playbacks. We performed this experiment in two populations differing in future breeding opportunities and thus the intensity of conflict over current parental care. We found that in response to a temporary increase in female parental effort, males in the northern population with lower sexual conflict matched the increased

effort, whereas males in the southern population did not. We also found that increases in parental care during playbacks were driven by the females (i.e., females initiated the increased effort and their mates followed them) in the northern population but not the southern population. These results support the idea that with incomplete information about the brood value and need, cues or signals from the partner might become important in coordinating parental care.

An ultralight head-mounted camera system integrates detailed behavioral monitoring with multichannel electrophysiology in freely moving mice

<https://www.biorxiv.org/content/10.1101/294397v1>

Breakthroughs in understanding the neural basis of natural behavior require neural recording and intervention to be paired with high-fidelity multimodal behavioral monitoring. An extensive genetic toolkit for neural circuit dissection, and well-developed neural recording technology, make the mouse a powerful model organism for systems neuroscience. However, methods for high-bandwidth acquisition of behavioral signals in mice remain limited to fixed-position cameras and other off-animal devices, complicating the monitoring of animals freely engaged in natural behaviors. Here, we report the development of an ultralight head-mounted camera system combined with head-movement sensors to simultaneously monitor eye position, pupil dilation, whisking, and pinna movements along with head motion in unrestrained, freely behaving mice. The power of the combined technology is demonstrated by observations linking eye position to head orientation; whisking to non-tactile stimulation; and, in electrophysiological experiments, visual cortical activity to volitional head movements.

Heating quinoa shoots results in yield loss by inhibiting fruit production and delaying maturity

<https://www.biorxiv.org/content/10.1101/727545v1>

Increasing global temperatures and a growing world population create the need to develop crop varieties that yield more in warmer climates. There is growing interest in expanding quinoa cultivation, because of quinoa's ability to produce nutritious grain in poor soils, with little water and at high salinity. However, the main limitation to expanding quinoa cultivation is quinoa's susceptibility to temperatures above ~32°C. This study investigates the phenotypes, genes, and mechanisms that may affect quinoa seed yield at high temperatures. By using a differential heating system where only roots or only shoots were heated, quinoa yield losses were attributed to shoot

heating. Plants with heated shoots lost 60% to 85% yield as compared to control. Yield losses were due to lower fruit production, which lowered the number of seeds produced per plant. Further, plants with heated shoots had delayed maturity and more non-reproductive shoot biomass, while plants with both heated roots and heated shoots produced more yield from panicles that escaped heat than control. This suggests that quinoa uses a type of avoidance strategy to survive heat. Gene expression analysis identified transcription factors differentially expressed in plants with heated shoots and low yield that had been previously associated with flower development and flower opening. Interestingly, in plants with heated shoots, flowers stayed closed during the day while control flowers were open. Although a closed flower may protect floral structures, this could also cause yield losses by limiting pollen dispersal, which is necessary to produce fruit in quinoa's mostly female flowers.

Building customizable auto-luminescent luciferase-based reporters in plants

<https://www.biorxiv.org/content/10.1101/809533v1>

Bioluminescence is a powerful biological signal that scientists have repurposed to design reporters for gene expression in plants and animals. However, there are some downsides associated with the need to provide a substrate to these reporters, such as its high cost and non-uniform tissue penetration. In this work we reconstitute a fungal bioluminescence pathway (FBP) in planta using an easily composable toolbox of parts. We demonstrate that the FBP can create luminescence across various tissues in a broad range of plants without external substrate addition. We also show how our toolbox can be used to deploy the FBP in planta to build auto-luminescent reporters for the study of gene-expression and hormone fluxes. A low-cost imaging platform for gene expression profiling is also described. These experiments lay the groundwork for the future construction of programmable auto-luminescent plant traits, such as creating light driven plant-pollinator interactions or light emitting plant-based sensors.

Rapid, raw-read reference and identification (R4IDs): A flexible platform for rapid generic species ID using long-read sequencing technology

<https://www.biorxiv.org/content/10.1101/281048v1>

The versatility of the current DNA sequencing platforms and the development of portable, nanopore sequencers means that it has never been easier to collect genetic data for unknown sample ID. DNA barcoding and meta-barcoding have become increasingly popular and barcode databases

continue to grow at an impressive rate. However, the number of canonical genome assemblies (reference or draft) that are publically available is relatively tiny, hindering the more widespread use of genome scale DNA sequencing technology for accurate species identification and discovery. Here, we show that rapid raw-read reference datasets, or R4IDs for short, generated in a matter of hours on the Oxford Nanopore MinION, can bridge this gap and accelerate the generation of useable reference sequence data. By exploiting the long read length of this technology, shotgun genomic sequencing of a small portion of an organism's genome can act as a suitable reference database despite the low sequencing coverage. These R4IDs can then be used for accurate species identification with minimal amounts of re-sequencing effort (1000s of reads). We demonstrated the capabilities of this approach with six vascular plant species for which we created R4IDs in the laboratory and then re-sequenced, live at the Kew Science Festival 2016. We further validated our method using simulations to determine the broader applicability of the approach. Our data analysis pipeline has been made available as a Dockerised workflow for simple, scalable deployment for a range of uses.

Quantitative, image-based phenotyping methods provide insight into spatial and temporal dimensions of plant disease

<https://www.biorxiv.org/content/10.1101/064980v1>

Plant disease symptoms exhibit complex spatial and temporal patterns that are challenging to quantify. Image-based phenotyping approaches enable multi-dimensional characterization of host-microbe interactions and are well suited to capture spatial and temporal data that are key to understanding disease progression. We applied image-based methods to investigate cassava bacterial blight, which is caused by the pathogen *Xanthomonas axonopodis* pv. *manihotis* (Xam). We generated Xam strains in which individual predicted type III effector (T3E) genes were mutated and applied multiple imaging approaches to investigate the role of these proteins in bacterial virulence. Specifically, we quantified bacterial populations, water-soaking disease symptoms, and pathogen spread from the site of inoculation over time for strains with mutations in *avrBs2*, *xopX*, and *xopK* as compared to wild-type Xam. *avrBs2* and *xopX* both showed reduced growth in planta and delayed spread through the vasculature system of cassava. *avrBs2* exhibited reduced water-soaking symptoms at the site of inoculation. In contrast, *xopK* exhibited enhanced induction of disease symptoms at the site of inoculation but reduced spread through the vasculature. Our results highlight the importance of adopting a multi-pronged approach to plant disease phenotyping

to more fully understand the roles of T3Es in virulence. Finally, we demonstrate that the approaches used in this study can be extended to many host-microbe systems and increase the dimensions of phenotype that can be explored.

Automated Reactive Accelerated Aging for Rapid In Vitro Evaluation of Neural Implants Performance

<https://www.biorxiv.org/content/10.1101/204099v1>

Objective Novel therapeutic applications for neural implants require miniaturized devices. Pilot clinical studies suggest that rapid failure of the miniaturized neural implants in the body presents a major challenge for this type of technology. Miniaturization imposes stricter requirements for reliability of materials and designs. Evaluation of neural implant performance over clinically relevant timescales presents time-and cost-prohibitive challenges for animal models.

OptiJ: Open-source optical projection tomography of large organ samples

<https://www.biorxiv.org/content/10.1101/656488v1>

The three-dimensional imaging of mesoscopic samples with Optical Projection Tomography (OPT) has become a powerful tool for biomedical phenotyping studies. OPT uses visible light to visualize the 3D morphology of large transparent samples. To enable a wider application of OPT, we present OptiJ, a low-cost, fully open-source OPT system capable of imaging large transparent specimens up to 13 mm tall and 8 mm deep with $50 \text{ } \mu\text{m}$ resolution. OptiJ is based on off-the-shelf, easy-to-assemble optical components and an ImageJ plugin library for OPT data reconstruction. The software includes novel correction routines for uneven illumination and sample jitter in addition to CPU/GPU accelerated reconstruction for large datasets. We demonstrate the use of OptiJ to image and reconstruct cleared lung lobes from adult mice. We provide a detailed set of instructions to set up and use the OptiJ framework. Our hardware and software design are modular and easy to implement, allowing for further open microscopy developments for imaging large organ samples.

The OptoGenBox - a device for long-term optogenetics in *C. elegans*

<https://www.biorxiv.org/content/10.1101/2020.01.13.903948v1>

Optogenetics controls neural activity and behavior in living organisms through genetically targetable actuators and light. This method has revolutionized biology and medicine as it allows controlling

cells with high temporal and spatial precision. Optogenetics is typically applied only at short time scales, for instance to study specific behaviors. Behavior controls systemic physiological processes. For example, arousal and sleep affect aging and health span. To study how behavior controls key physiological processes, behavioral manipulations need to occur at extended time scales. However, methods for long-term optogenetics are scarce and typically require expensive compound microscope setups. Small model animals have been instrumental in solving the mechanistic basis of medically important biological processes. We developed OptoGenBox, an affordable and simple-to-use device for long-term optogenetic manipulation of small organisms. OptoGenBox provides a controlled environment and is programmable to allow the execution of complex optogenetic manipulations over long experimental times of many days to weeks. To test our device, we investigated how optogenetically increased arousal and optogenetic sleep deprivation affect survival of arrested first larval stage *C. elegans*. We optogenetically activated the nociceptive ASH sensory neurons using ReaChR, thus triggering an escape response and increase in arousal. In addition, we optogenetically inhibited the sleep neuron RIS using ArchT, a condition known to impair sleep. Both, optogenetically increased arousal as well as optogenetic sleep deprivation reduced survival. Thus, OptoGenBox presents an affordable system to study the long-term consequences of optogenetic manipulations of key biological processes in small animals.

Adaptive diversification of growth allometry in the plant *Arabidopsis thaliana*

<https://www.biorxiv.org/content/10.1101/269498v1>

Seed plants vary tremendously in size and morphology. However, variation and covariation between plant traits may at least in part be governed by universal biophysical laws and biological constants. Metabolic Scaling Theory (MST) posits that whole-organismal metabolism and growth rate are under stabilizing selection that minimizes the scaling of hydrodynamic resistance and maximizes the scaling of resource uptake. This constrains variation in physiological traits and in the rate of biomass accumulation, so that they can be expressed as mathematical functions of plant size with near constant allometric scaling exponents across species. However, observed variation in scaling exponents questions the evolutionary drivers and the universality of allometric equations. We have measured growth scaling and fitness traits of 451 *Arabidopsis thaliana* accessions with sequenced genomes. Variation among accessions around the scaling exponent predicted by MST correlated with relative growth rate, seed production and stress resistance. Genomic analyses indicate that growth allometry is affected by many genes associated with local climate and abiotic stress

response. The gene with the strongest effect, PUB4, has molecular signatures of balancing selection, suggesting that intraspecific variation in growth scaling is maintained by opposing selection on the trade-off between seed production and abiotic stress resistance. Our findings support a core MST prediction and suggest that variation in allometry contributes to local adaptation to contrasting environments. Our results help reconcile past debates on the origin of allometric scaling in biology, and begin to link adaptive variation in allometric scaling to specific genes.

Probing the effect of uniaxial compression on cell migration

<https://www.biorxiv.org/content/10.1101/082461v1>

The chemical, physical and mechanical properties of the extra-cellular environment have a strong effect on cell migration. Aspects such as pore-size or stiffness of the matrix influence the selection of the mechanism used by cells to propel themselves, including pseudopod or blebbing. How a cell perceives its environment, and how such a cue triggers a change in behaviour are largely unknown, but mechanics is likely to be involved. Because mechanical conditions are often controlled by modifying the composition of the environment, separating chemical and physical contributions is difficult and requires multiple controls. Here we propose a simple method to impose a mechanical compression on individual cells without altering the composition of the gel. Live imaging during compression provides accurate information about the cell's morphology and migratory phenotype. Using *Dictyostelium* as a model, we observe that a compression of the order of 500 Pa flattens the cells under gel by up to 50%. This uniaxial compression directly triggers a transition in the mode of migration, from primarily pseudopodial to bleb driven, in less than 30 sec. This novel device is therefore capable of influencing cell migration in real time and offers a convenient approach to systematically study mechanotransduction in confined environments.

Single and population coding of taste in the gustatory-cortex of awake mice

<https://www.biorxiv.org/content/10.1101/575522v3>

Electrophysiological analysis has reveals much about the broad coding and neural ensemble dynamics that characterize gustatory cortical (GC) taste processing in awake rats, and about how these dynamics relate to behavior. With regard to mice, meanwhile, data concerning cortical taste coding have largely been restricted to imaging—a technique that reveals average levels of neural responsiveness, but that (currently) lacks the temporal sensitivity necessary for evaluation of fast response dynamics; furthermore, the few extant studies have thus far failed to provide consensus

on basic features of coding. We have recorded the spiking activity of ensembles of GC neurons while presenting representatives of the basic taste modalities (sweet, salty, sour and bitter) to awake mice. Our first central result is the identification of similarities between rat and mouse taste processing: most mouse GC neurons (~66%) responded distinctly to multiple (3-4) tastes; temporal coding analyses further reveal, for the first time, that single mouse GC neurons sequentially code taste identity and palatability—the latter responses emerging ~0.5s after the former—with whole GC ensembles transitioning suddenly and coherently from coding taste identity to coding taste palatability. The second finding is that spatial location plays very little role in any aspect of taste responses—neither between- (anterior-posterior) nor within-mouse (dorsal-ventral) mapping revealed anatomical regions with narrow or temporally simple taste responses. These data confirm recent results showing that mouse cortical taste responses are not “gustatopic,” but also go beyond these imaging results to show that mice process tastes through time.

Impact of precisely-timed inhibition of gustatory cortex on taste behavior depends on single-trial ensemble dynamics

<https://www.biorxiv.org/content/10.1101/486043v3>

The purpose of perception is the driving of action. During tasting, for instance, every stimulus must be either swallowed or rejected (the latter via a behavior known as “gaping”). Taste responses in the rodent gustatory cortex (GC) span this sensorimotor divide, progressing through a series of firing-rate epochs that culminate in action-related firing. Population analyses reveal this emergence to be a sudden, coherent ensemble transition that, despite varying in latency between trials, reliably precedes gaping onset by 0.2-0.3s. Here, we tested whether this transition drives gaping, by delivering 0.5s GC perturbations at various time-points in tasting trials. Perturbations significantly delayed gaping, but only when they preceded the variably-timed action-related transition - thus, the same perturbation might have an impact or not, depending on the transition latency in that particular trial. Our results suggest a distributed attractor network model of taste processing, and a dynamical role for cortex in driving motor behavior.

Low acetylcholine during early sleep is important for motor memory consolidation

<https://www.biorxiv.org/content/10.1101/494351v3>

The synaptic homeostasis theory of sleep proposes that low neurotransmitter activity in sleep is optimal for memory consolidation. We tested this theory by asking whether increasing acetylcholine

levels during early sleep would disrupt motor memory consolidation. We trained separate groups of adult mice on the rotarod walking and skilled reaching for food tasks, and after training, administered physostigmine, an acetylcholinesterase inhibitor, to increase cholinergic tone in subsequent sleep. Post-sleep testing suggested that physostigmine impaired motor skill acquisition. Home-cage video monitoring and electrophysiology revealed that physostigmine disrupted sleep structure, delayed non-rapid-eye-movement sleep onset, and reduced slow-wave power in the hippocampus and cortex. The impaired motor performance with physostigmine, however, was not solely due to its effects on sleep structure, as one hour of sleep deprivation after training did not impair rotarod performance. A reduction in cholinergic tone by inactivation of cholinergic neurons during early sleep also affected rotarod performance. Administration of agonists and antagonists of muscarinic and nicotinic acetylcholine receptors revealed that activation of muscarinic receptors during early sleep impaired rotarod performance. The experiments suggest that the increased slow wave activity and inactivation of muscarinic receptors during early sleep due to reduced acetylcholine contribute to motor memory consolidation.

Partial-resistance against aphids in wild barley involves phloem and mesophyll-based defences

<https://www.biorxiv.org/content/10.1101/502476v2>

Aphids, including the bird cherry-oat aphid (*Rhopalosiphum padi*), are significant agricultural pests. Aphid populations are typically controlled using insecticides, but there is increasing demand for more sustainable pest management practices. The wild relative of barley, *Hordeum spontaneum* 5 (Hsp5) has been described as partially-resistant to *R. padi*. Partial-resistance is proposed to involve higher thionin and lipoxygenase gene expression. However, the underlying mechanistic processes are unknown. In this study we compared Hsp5 with a susceptible cultivar of barley (Concerto) to test the extent to which partial-resistance affects aphid fitness. We used the electrical penetration graph technique to monitor *R. padi* feeding patterns to elucidate the tissue location of partial-resistance factors alongside molecular and biochemical analyses to identify potential mechanisms. We show that partial-resistance in Hsp5 extends to three aphid species and is mediated by phloem/mesophyll-based factors, leading to a three-fold increase in the time aphids take to establish sustained phloem ingestion. Partial-resistance likely involves elevated expression of defence and phytohormone genes alongside altered phloem amino acid composition. Further work is required to establish the function of these traits, however this study highlights plant tissues which are important

in conferring broad-spectrum partial-resistance against aphids in barley.

Non-linear phenotypic variation uncovers the emergence of heterosis in *Arabidopsis thaliana*

<https://www.biorxiv.org/content/10.1101/404616v1>

Heterosis describes the phenotypic superiority of hybrids over their parents in traits related to fitness. Understanding and predicting non-additive inheritance such as heterosis is crucial for evolutionary biology, as well as for plant and animal breeding. However, the physiological bases of heterosis remain debated. Moreover, empirical data in various species have shown that diverse genetic and molecular mechanisms are likely to explain heterosis, making it difficult to predict its emergence and amplitude from parental genotypes alone. In this study, we evaluated a model of physiological dominance proposed by Sewall Wright to explain the non-additive inheritance of metabolic fluxes at the cellular level. We used 450 hybrids derived from crosses among natural inbred accessions of *Arabidopsis thaliana* to test Wrightâ€™s model for two fitness-related traits at the whole-plant level: growth rate and fruit number. We found that allometric relationships between traits constrain phenotypic variation in hybrids and inbreds to a similar extent. These allometric relationships behave predictably, in a non-linear manner, explaining up to 75% of heterosis amplitude, while genetic distance among parents at best explains 7%. Thus, our findings are consistent with Wrightâ€™s model of physiological dominance on plant performance, and suggest that the emergence of heterosis is an intrinsic property of non-linear relationships between traits. Furthermore, our study highlights the potential of a geometric approach of phenotypic relationships for predicting heterosis of two major components of crop productivity and yield.

The Stress-Chip: A microfluidic platform for stress analysis in *Caenorhabditis elegans*

<https://www.biorxiv.org/content/10.1101/285163v1>

An organismâ€™s ability to mount a physiological response to external stressors is fundamental to its interaction with the environment. Experimental exploration of these interactions benefits greatly from the ability to maintain tight control of the environment, even under conditions in which it would be normal for the subject to flee the stressor. Here we present a nematode research platform that pairs automated image acquisition and analysis with a custom microfluidic device. This platform enables tight environmental control in low-density, single-worm arenas, which preclude animal escape while still allowing a broad range of behavioral activities. The platform is easily scalable, with two 50 arena arrays per chip and an imaging capacity of 600 animals per scanning device.

Validating the device using dietary, osmotic, and oxidative stress indicates that it should be of broad use as a research platform, including eventual adaptation for additional stressors, anthelmintic-drug screening, and toxicology studies.

Early Detection of Apathetic Phenotypes in Huntingtonâ€™s Disease Knock-in Mice Using Open Source Tools

<https://www.biorxiv.org/content/10.1101/208520v1>

Apathy is one of the most prevalent and progressive psychiatric symptom in Huntingtonâ€™s disease (HD) patients. However, preclinical work in HD mouse models tend to focus on molecular and motor, rather than affective, phenotypes. Measuring behavior in mice often produces noisy data and requires large cohorts to detect phenotypic rescue with appropriate power. The operant equipment necessary for measuring affective phenotypes is typically expensive, proprietary to commercial entities, and bulky which can render adequately sized mouse cohorts as cost-prohibitive. Thus, we describe here a home-built open-source alternative to commercial hardware that is reliable, scalable, and reproducible. Using off-the-shelf hardware, we adapted and built several of the rodent operant buckets (ROBucket) designed to test HttQ111/+ mice for attention deficits in fixed ratio (FR) and progressive ratio (PR) tasks. We find that, despite normal performance in reward attainment in the FR task, HttQ111/+ mice exhibit reduced PR performance at 9-11 months of age, suggesting motivational deficits. We replicated this in two independent cohorts, which demonstrates the reliability and utility of both the apathetic phenotype, and these ROBuckets, for preclinical HD studies.

RPW8/HR Repeats Control NLR Activation in *A. thaliana*

<https://www.biorxiv.org/content/10.1101/559864v3>

In many plant species, conflicts between divergent elements of the immune system, especially nucleotide-binding oligomerization domain-like receptors (NLR), can lead to hybrid necrosis. Here, we report deleterious allele-specific interactions between an NLR and a non-NLR gene cluster, resulting in not one, but multiple hybrid necrosis cases in *Arabidopsis thaliana*. The NLR cluster is RESISTANCE TO PERONOSPORA PARASITICA 7 (RPP7), which can confer strain-specific resistance to oomycetes. The non-NLR cluster is RESISTANCE TO POWDERY MILDEW 8 (RPW8) / HOMOLOG OF RPW8 (HR), which can confer broad-spectrum resistance to both fungi and oomycetes. RPW8/HR proteins contain at the N-terminus a potential transmembrane domain,

followed by a specific coiled-coil (CC) domain that is similar to a domain found in pore-forming toxins MLKL and HET-S from mammals and fungi. C-terminal to the CC domain is a variable number of 21- or 14-amino acid repeats, reminiscent of regulatory 21-amino acid repeats in fungal HET-S. The number of repeats in different RPW8/HR proteins along with the sequence of a short C-terminal tail predicts their ability to activate immunity in combination with specific RPP7 partners. Whether a larger or smaller number of repeats is more dangerous depends on the specific RPW8/HR autoimmune risk variant.

EternaBrain: Automated RNA design through move sets and strategies from an Internet-scale RNA videogame

<https://www.biorxiv.org/content/10.1101/326736v3>

Emerging RNA-based approaches to disease detection and gene therapy require RNA sequences that fold into specific base-pairing patterns, but computational algorithms generally remain inadequate for these secondary structure design tasks. The Eterna project has crowdsourced RNA design to human video game players in the form of puzzles that reach extraordinary difficulty. Here, we demonstrate that Eterna participants' moves and strategies can be leveraged to improve automated computational RNA design. We present an eternamoves-large repository consisting of 1.8 million of player moves on 12 of the most-played Eterna puzzles as well as an eternamoves-select repository of 30,477 moves from the top 72 players on a select set of more advanced puzzles. On eternamoves-select, we present a multilayer convolutional neural network (CNN) EternaBrain that achieves test accuracies of 51% and 34% in base prediction and location prediction, respectively, suggesting that top players' moves are partially stereotyped. Pipelining this CNN's move predictions with single-action-playout (SAP) of six strategies compiled by human players solves 61 out of 100 independent puzzles in the Eterna100 benchmark. EternaBrain-SAP outperforms previously published RNA design algorithms and achieves similar or better performance than a newer generation of deep learning methods, while being largely orthogonal to these other methods. Our study provides useful lessons for future efforts to achieve human-competitive performance with automated RNA design algorithms.

Developmental exposure to pesticide contaminated food impedes bumblebee brain growth predisposing adults to become poorer learners

<https://www.biorxiv.org/content/10.1101/690602v1>

Understanding the risk to biodiversity from pesticide exposure is a global priority. For bees, an understudied step in evaluating pesticide risk is understanding how pesticide contaminated foraged food brought back to the colony can affect developing individuals. Provisioning bumblebee colonies with pesticide (neonicotinoid) treated food, we investigated how exposure during two key developmental phases (brood and/or early-adult), impacted brain growth and assessed the consequent effects on adult learning behaviour. Using micro-computed tomography (μ CT) scanning and 3D image analysis, we compared brain development for multiple neuropils in workers 3 and 12-days post-emergence. Mushroom body calyces were the neuropils most affected by exposure during either of the developmental phases, with both age cohorts showing smaller structural volumes. Critically, reduced calycesTM growth in pesticide exposed workers was associated with lower responsiveness to a sucrose reward and impaired learning performance. Furthermore, the impact from brood exposure appeared irrecoverable despite no exposure during adulthood.

PiFlow: A Biocompatible Low-Cost Programmable Dynamic Flow Pumping System Utilizing a Raspberry Pi Zero and Commercial Piezoelectric Pumps

<https://www.biorxiv.org/content/10.1101/192047v5>

With the rise of research utilizing microphysiological systems (MPSs), the need for tools that enable the physiological mimicking of the relevant cellular environment is vital. The limited ability to reproduce crucial features of the microenvironment, such as surrounding fluid flow and dynamic changes in biochemical stimuli, severely limits the types of experiments that can be carried out. Current equipment to achieve this, such as syringe and peristaltic pumps, is expensive, large, difficult to program and has limited potential for scalability. Here, we present a new pumping platform that is open-source, low-cost, modular, scalable, fully-programmable and easy to assemble that can be incorporated into cell culture systems to better recapitulate physiological environments. By controlling two commercially available piezoelectric pumps using a Raspberry Pi Zero microcontroller, the system is capable of producing arbitrary dynamic flow profiles with reliable flow rates ranging from 1 to 3,000 μ L/min as specified by an easily programmable Python-based script. We validated the accuracy of the flow rates, the use of time-varying profiles, and the practicality of the system by creating repeatable dynamic concentration profiles using a 3D-printed static micromixer.

An automated barcode tracking system for behavioural studies in birds

<https://www.biorxiv.org/content/10.1101/201590v1>

Recent advances in technology allow researchers to automate the measurement of animal behaviour. These methods have multiple advantages over direct observations and manual data input as they reduce bias related to human perception and fatigue, and deliver more extensive and complete data sets that enhance statistical power. One major challenge that automation can overcome is the observation of many individuals at once, enabling whole-group or whole-population tracking.

Octopi: Open configurable high-throughput imaging platform for infectious disease diagnosis in the field

<https://www.biorxiv.org/content/10.1101/684423v1>

Access to quantitative, robust, yet affordable diagnostic tools is necessary to reduce global infectious disease burden. Manual microscopy has served as a bedrock for diagnostics with wide adaptability, although at a cost of tedious labor and human errors. Automated robotic microscopes are poised to enable a new era of smart field microscopy but current platforms remain cost prohibitive and largely inflexible, especially for resource poor and field settings. Here we present Octopi, a low-cost (\$250-\$500) and reconfigurable autonomous microscopy platform capable of automated slide scanning and correlated bright-field and fluorescence imaging. Being highly modular, it also provides a framework for new disease-specific modules to be developed. We demonstrate the power of the platform by applying it to automated detection of malaria parasites in blood smears. Specifically, we discovered a spectral shift on the order of 10 nm for DAPI-stained *Plasmodium falciparum* malaria parasites. This shift allowed us to detect the parasites with a low magnification (equivalent to 10x) large field of view (2.56 mm²) module. Combined with automated slide scanning, real time computer vision and machine learning-based classification, Octopi is able to screen more than 1.5 million red blood cells per minute for parasitemia quantification, with estimated diagnostic sensitivity and specificity exceeding 90% at parasitemia of 50/ μ l and 100% for parasitemia higher than 150/ μ l. With different modules, we further showed imaging of tissue slice and sputum sample on the platform. With roughly two orders of magnitude in cost reduction, Octopi opens up the possibility of a large robotic microscope network for improved disease diagnosis while providing an avenue for collective efforts for development of modular instruments.

A closed-loop hand prosthesis with simultaneous intraneuronal tactile and position feedback

<https://www.biorxiv.org/content/10.1101/262741v1>

Current myoelectric prostheses allow upper-limb amputees to regain voluntary motor control of their artificial limb by exploiting residual muscle function in the forearm¹. However, the over-reliance on visual cues resulting from a lack of sensory feedback is a common complaint^{2,3}. Recently, several groups have provided tactile feedback in upper-limb amputees by using implanted electrodes^{4,5,6,7,8}, surface nerve stimulation^{9,10} or sensory substitution^{11,12}. These approaches have led to improved function and prosthesis embodiment^{4,5,6,7,13,14}. Nevertheless, the provided information remains limited to a subset of the rich sensory cues available to healthy individuals. More specifically, proprioception, the sense of limb position and movement, is predominantly absent from current systems. Here we show that sensory substitution based on intraneuronal stimulation can deliver position feedback in real-time and in conjunction with somatotopic tactile feedback. This approach allowed two trans-radial amputees to regain high and close-to-natural remapped proprioceptive acuity, with a median joint angle reproduction accuracy of 9.1° and a median threshold to detection of passive movements of 9.5°, which was compatible with results obtained in healthy subjects^{15,16,17}. The simultaneous delivery of position information and somatotopic tactile feedback allowed both amputees to discriminate object size and compliance with high levels of accuracy (75.5%). These results demonstrate that touch information delivered via somatotopic neural stimulation and position information delivered via sensory substitution can be exploited simultaneously and efficiently by trans-radial amputees. This study paves the way towards more sophisticated bidirectional bionic limbs conveying rich, multimodal sensations.

Cortical circuit alterations precede disease onset in Huntingtonâ€™s disease mice

<https://www.biorxiv.org/content/10.1101/391771v1>

Abstract Huntingtonâ€™s disease (HD) is a devastating hereditary movement disorder, characterized by degeneration of neurons in the striatum and cortex. Studies in human patients and mouse HD models suggest that disturbances of neuronal function in the neocortex play an important role in the disease onset and progression. However, the precise nature and time course of cortical alterations in HD have remained elusive. Here, we use chronic *in vivo* two-photon calcium imaging to monitor the activity of single neurons in layer 2/3 of the primary motor cortex in awake, behaving R6/2 transgenic HD mice and wildtype littermates. R6/2 mice show age-dependent changes in neuronal activity with a clear increase in activity at the age of 8.5 weeks, preceding the onset of

motor and neurological symptoms. Furthermore, quantitative proteomics demonstrate a pronounced downregulation of synaptic proteins in the cortex, and histological analyses in R6/2 mice and HD patient samples reveal reduced inputs from parvalbumin-positive interneurons onto layer 2/3 pyramidal cells. Thus, our study provides a time-resolved description as well as mechanistic details of cortical circuit dysfunction in HD.

The ion channel ppk301 controls freshwater egg-laying in the mosquito *Aedes aegypti*

<https://www.biorxiv.org/content/10.1101/441592v1>

Aedes aegypti mosquitoes are deadly vectors of arboviral pathogens including Zika, dengue, and yellow fever, and breed in containers of freshwater associated with human habitation^{1,2}. Female *Ae. aegypti* lay eggs near freshwater because larval and pupal stages are aquatic³. They use volatile cues to locate water at a distance⁴, while at close-range they contact water to evaluate its suitability for egg-laying^{4–7}. High salinity is lethal to mosquito offspring and therefore correctly laying eggs in freshwater is a crucial parenting decision made by female mosquitoes. Here we show that the DEG/ENaC channel^{8–10} ppk301 is required for mosquitoes to exploit freshwater egg-laying substrates. When ppk301 mutant females contact water, they do not lay eggs as readily as wild-type animals and are more likely to make aberrant decisions between freshwater and saltwater at concentrations that impair offspring survival. We used a CRISPR-Cas9-based genetic knock-in strategy combined with the Q-binary transactivator system¹¹ to build genetic tools for labelling and imaging neurons in the mosquito. We found that ppk301 is expressed in sensory neurons in legs and proboscis, appendages that directly contact water, and that ppk301-expressing neurons project to central taste centres. Using *in vivo* calcium imaging with the genetically-encoded calcium sensor GCaMP6s¹², we found that ppk301-expressing cells respond to water but, unexpectedly, also to salt. This suggests that ppk301 is instructive for egg-laying at low salt concentrations but that a ppk301-independent pathway is responsible for inhibiting egg-laying at high salt concentrations. Water is a key resource for insect survival and understanding how mosquitoes interact with water to control different behaviours is an opportunity to study the evolution of chemosensory systems. The new genetic tools described here will enable direct study of not only egg-laying, but also other behaviours in mosquitoes that influence disease transmission and enable comparative studies of insect biology more broadly.

PhyloPi: an affordable, purpose built phylogenetic pipeline for the HIV drug resistance

testing facility

<https://www.biorxiv.org/content/10.1101/367946v2>

Phylogenetic analysis plays a crucial role in quality control in the HIV drug resistance testing laboratory. If previous patient sequence data is available sample swaps can be detected and investigated. As Antiretroviral treatment coverage is increasing in many developing countries, so is the need for HIV drug resistance testing. In countries with multiple languages, transcription errors are easily made with patient identifiers. Here a self-contained blastn integrated phylogenetic pipeline can be especially useful. Even though our pipeline can run on any unix based system, a Raspberry Pi 3 is used here as a very affordable and integrated solution.

Design principles for open source bioinstrumentation: the poseidon syringe pump system as an example

<https://www.biorxiv.org/content/10.1101/521096v1>

The poseidon syringe pump and microscope system is an open source alternative to commercial systems. It costs less than \$400 and can be assembled in under an hour using the instructions and source files available at <https://pachterlab.github.io/poseidon>. We describe the poseidon system and use it to illustrate design principles that can facilitate the adoption and development of open source bioinstruments. The principles are functionality, robustness, simplicity, modularity, benchmarking, and documentation.

Rapid antibiotic resistance predictions from genome sequence data for *S. aureus* and *M. tuberculosis*

<https://www.biorxiv.org/content/10.1101/018564v1>

Rapid and accurate detection of antibiotic resistance in pathogens is an urgent need, affecting both patient care and population-scale control. Microbial genome sequencing promises much, but many barriers exist to its routine deployment. Here, we address these challenges, using a de Bruijn graph comparison of clinical isolate and curated knowledge-base to identify species and predict resistance profile, including minor populations. This is implemented in a package, Mykrobe predictor, for *S. aureus* and *M. tuberculosis*, running in under three minutes on a laptop from raw data. For *S. aureus*, we train and validate in 495/471 samples respectively, finding error rates comparable to gold-standard phenotypic methods, with sensitivity/specificity of 99.3%/99.5% across 12 drugs. For *M. tuberculosis*, we identify species and predict resistance with specificity of 98.5%

(training/validating on 1920/1609 samples). Sensitivity of 82.6% is limited by current understanding of genetic mechanisms. Finally, we demonstrate feasibility of an emerging single-molecule sequencing technique.

Generalisation behaviour of predators toward warning signals displayed by harmful prey: answers from a videogame played by humans

<https://www.biorxiv.org/content/10.1101/409557v2>

The persistence of several warning signals in sympatry is a puzzling evolutionary question because selection favours convergence of colour patterns among toxic species. Such convergence is shaped by predators' reaction to similar but not identical stimulus, i.e. generalisation behaviour. However, studying generalisation behaviour in complex natural communities of predators is challenging, and is thus generally limited to simple variations of prey colour patterns. Here, we used humans as surrogate predators to investigate generalisation behaviours on two prey communities with different level of warning signals complexity. Humans' generalisation capacities were estimated using a computer game simulating a simple (4 morphs) and a complex (10 morphs) community of defended (associated with a penalty) and palatable butterflies. Colour patterns used in the game are actually observed in natural populations of the defended butterflies *H. numata*, and generalisation behaviour of natural predators' communities on these colour patterns have previously been investigated in the wild, allowing direct comparison with human behaviour. We investigated human predation behaviour by recording attack rates on the different defended and palatable colour patterns, as well as player survival time (i.e. score). Phenotypic similarity among the different colour patterns was precisely quantified using a custom algorithm accounting for both colour and pattern variations (CPM method). By analysing attack behaviours of 491 game players, we found that learning was more efficient in the simple prey community. Additionally, profitable prey gained protection from sharing key visual features with unprofitable prey in both communities while learning, in accordance with natural predator behaviours. Moreover, other behaviours observed in natural predators, such as colour neophobia, were detected in humans and shaped morph vulnerability during the game. Similarities between our results in humans and the reaction of natural predator communities to the same colour patterns validate our video-game as a useful proxy to study predator behaviour. This experimental set-up can thus be compared to natural systems, enabling further investigations of generalisation on mimicry evolution.

Annotation-free Learning of Plankton for Classification and Anomaly Detection

<https://www.biorxiv.org/content/10.1101/856815v1>

The acquisition of increasingly large plankton digital image datasets requires automatic methods of recognition and classification. As data size and collection speed increases, manual annotation and database representation are often bottlenecks for utilization of machine learning algorithms for taxonomic classification of plankton species in field studies. In this paper we present a novel set of algorithms to perform accurate detection and classification of plankton species with minimal supervision. Our algorithms approach the performance of existing supervised machine learning algorithms when tested on a plankton dataset generated from a custom-built lensless digital device. Similar results are obtained on a larger image dataset obtained from the Woods Hole Oceanographic Institution. Our algorithms are designed to provide a new way to monitor the environment with a class of rapid online intelligent detectors.

CropSurveyor: a scalable open-source experiment management system for distributed plant phenotyping and IoT-based crop management

<https://www.biorxiv.org/content/10.1101/451120v2>

Background: High-quality plant phenotyping and climate data lay the foundation of phenotypic analysis as well as genotype-by-environment interactions, which is important biological evidence not only to understand the dynamics between crop performance, genotypes, and environmental factors, but also for agronomists and farmers to monitor crops in fluctuating agricultural conditions. With the rise of Internet of Things technologies in recent years, many IoT-based remote sensing devices have been applied to phenotyping and crop monitoring that generate big plant-environment datasets every day; however, it is still technically challenging to calibrate, annotate, and aggregate big data effectively, especially when they were generated in multiple locations, and often at different scales.

Low-Cost Solution for Rodent Home-Cage Behaviour Monitoring

<https://www.biorxiv.org/content/10.1101/342501v2>

In the current research on measuring complex behaviours/phenotyping in rodents, most of the experimental design requires the experimenter to remove the animal from its home-cage environment and place it in an unfamiliar apparatus (novel environment). This interaction may influence behaviour, general well-being, and the metabolism of the animal, affecting the phenotypic outcome even if the data collection method is automated. Most of the commercially available

solutions for home-cage monitoring are expensive and usually lack the flexibility to be incorporated with existing home-cages. Here we present a low-cost solution for monitoring home-cage behaviour of rodents that can be easily incorporated to practically any available rodent home-cage. To demonstrate the use of our system, we reliably predict the sleep/wake state of mice in their home-cage using only video. We validate these results using hippocampal local field potential (LFP) and electromyography (EMG) data. Our approach provides a low-cost flexible methodology for high-throughput studies of sleep, circadian rhythm and rodent behaviour with minimal experimenter interference.

Short Neurorobotics Workshop for High School Students Promotes Competence and Confidence in Computational Neuroscience

<https://www.biorxiv.org/content/10.1101/597609v1>

Understanding the brain is a fascinating challenge, captivating the scientific community and the public alike. The lack of effective treatment for most brain disorders makes the training of the next generation of neuroscientists, engineers and physicians a key concern. Over the past decade there has been a growing effort to introduce neuroscience in primary and secondary schools, however hands-on laboratories have been limited to anatomical or electrophysiological activities. Modern neuroscience research labs are increasingly using computational tools to model circuits of the brain to understand information processing. Here we introduce the use of neurorobots - robots controlled by computer models of biological brains - as an introduction to computational neuroscience in the K-12 classroom. Neurorobotics has enormous potential as an education technology because it combines multiple activities with clear educational benefits including neuroscience, active learning, and robotics. We describe an introductory neurorobot workshop that teaches high school students how to use neurorobots to investigate key concepts in neuroscience, including spiking neural networks, synaptic plasticity, and adaptive action selection. Our do-it-yourself (DIY) neurorobot uses wheels, a camera, a speaker, and a distance sensor to interact with its environment, and can be built from generic parts costing about \$150 in under 4 hrs. Our Neurorobot App visualizes the neurorobot's visual input and brain activity in real-time, and enables students to design new brains and deliver dopamine-like reward signals to reinforce chosen behaviors. We have tested the Neurorobot Workshop with high school students ($n = 3$ workshops, 9 students total) and have found that students were able to complete all exercises in under 3 hrs. In a post-workshop survey, students reported having gained the ability to develop neural networks that perform specific

functions, including goal-directed behavior and memory. Here we provide DIY hardware assembly instructions, discuss our open-source Neurorobot App and demonstrate how to teach the Neurorobot Workshop. By doing this we hope to accelerate research in educational neurorobotics and promote the use of neurorobots to teach computational neuroscience in high school.

An interactive programming paradigm for realtime experimentation with remote living matter

<https://www.biorxiv.org/content/10.1101/236919v2>

Recent advancements in life-science instrumentation and automation enable entirely new modes of human interaction with microbiological processes and corresponding applications for science and education through biology cloud labs. A critical barrier for remote life-science experimentation is the absence of suitable abstractions and interfaces for programming living matter. To this end we conceptualize a programming paradigm that provides stimulus control functions and sensor control functions for realtime manipulation of biological (physical) matter. Additionally, a simulation mode facilitates higher user throughput, program debugging, and biophysical modeling. To evaluate this paradigm, we implemented a JavaScript-based web toolkit, \sim Bioty \sim TM, that supports realtime interaction with swarms of phototactic Euglena cells hosted on a cloud lab. Studies with remote users demonstrate that individuals with little to no biology knowledge and intermediate programming knowledge were able to successfully create and use scientific applications and games. This work informs the design of programming environments for controlling living matter in general and lowers the access barriers to biology experimentation for professional and citizen scientists, learners, and the lay public.

Open source tools for temporally controlled rodent behavior suitable for electrophysiology and optogenetic manipulations

<https://www.biorxiv.org/content/10.1101/243469v2>

Understanding how the brain controls behavior requires observing and manipulating neural activity in awake behaving animals. Neuronal firing is timed at millisecond precision. Therefore, to decipher temporal coding, it is necessary to monitor and control animal behavior at the same level of temporal accuracy. However, it is technically challenging to deliver sensory stimuli and reinforcers as well as to read the behavioral responses they elicit with millisecond precision. Presently available commercial systems often excel in specific aspects of behavior control, but they do not provide a customizable environment allowing flexible experimental design while maintaining high standards for

temporal control necessary for interpreting neuronal activity. Moreover, delay measurements of stimulus and reinforcement delivery are largely unavailable. We combined microcontroller-based behavior control with a sound delivery system for playing complex acoustic stimuli, fast solenoid valves for precisely timed reinforcement delivery and a custom-built sound attenuated chamber using high-end industrial insulation materials. Together this setup provides a physical environment to train head-fixed animals, enables calibrated sound stimuli and precisely timed fluid and air puff presentation as reinforcers. We provide latency measurements for stimulus and reinforcement delivery and an algorithm to perform such measurements on other behavior control systems. Combined with electrophysiology and optogenetic manipulations, the millisecond timing accuracy will help interpret temporally precise neural signals and behavioral changes. Additionally, since software and hardware provided here can be readily customized to achieve a large variety of paradigms, these solutions enable an unusually flexible design of rodent behavioral experiments.

Rapid Reconfiguration of the Functional Connectome after Chemogenetic Locus Coeruleus Activation

<https://www.biorxiv.org/content/10.1101/527457v1>

The locus coeruleus (LC) supplies norepinephrine (NE) to the entire forebrain, regulates many fundamental brain functions, and is implicated in several neuropsychiatric diseases. Although selective manipulation of the LC is not possible in humans, studies have suggested that strong LC activation might shift network connectivity to favor salience processing. To test this hypothesis, we use a mouse model to study the impact of LC stimulation on large-scale functional connectivity by combining chemogenetic activation of the LC with resting-state fMRI, an approach we term “chemo-connectomics”. LC activation rapidly interrupts ongoing behavior and strongly increases brain-wide connectivity, with the most profound effects in the salience and amygdala networks. We reveal a direct correlation between functional connectivity changes and transcript levels of alpha-1, alpha-2, and beta-1 adrenoceptors across the brain, and a positive correlation between NE turnover and functional connectivity within select brain regions. These results represent the first brain-wide functional connectivity mapping in response to LC activation, and demonstrate a causal link between receptor expression, brain states and functionally connected large-scale networks at rest. We propose that these changes in large-scale network connectivity are critical for optimizing neural processing in the context of increased vigilance and threat detection.

Consistent individual differences drive collective behaviour and group functioning of schooling fish

<https://www.biorxiv.org/content/10.1101/131094v1>

The ubiquity of consistent inter-individual differences in behaviour (â€˜animal personalitiesâ€™TM) 1,2, suggests they may constitute a fundamental component of animal groups that may drive their functioning 3,4. Despite increasing evidence that highlights their importance 5â€“16, we still lack a unified mechanistic frame-work to explain and predict how inter-individual differences may affect collective behaviour. Here we investigate how differences in individual behavioural tendencies affect the group structure, movement dynamics, and foraging behaviour of animal groups using free-swimming stickleback fish (*Gasterosteus aculeatus*). Analysis of high-resolution tracking data of known individuals demonstrates that, across a range of contexts, consistent inter-individual differences in social proximity were strongly linked to speed and, together with boldness predicted spatial positioning and leadership within groups, differences in structure and movement dynamics between groups, as well as individual and group foraging performance. These effects of inter-individual behavioural variation on group-level states emerged naturally from a generic model of heterogeneous, self-organising groups. Our study combines experimental and theoretical evidence for a simple mechanism to explain variation in the emergence of structure, dynamics, and functional capabilities of groups across social and ecological scales. In addition, we show that individual performance was conditional to the group composition, providing a potential basis for social selection driving behavioural differentiation between individuals.

Social behavior and anxiety contribute to nicotine self-administration in adolescent outbred rats

<https://www.biorxiv.org/content/10.1101/257097v1>

Both emotional and social traits interact with genetic factors to influence smoking behavior. We previously established a socially acquired nicotine intravenous self-administration model where social learning of a nicotine-associated odor cue reversed conditioned flavor aversion and promoted nicotine intake. In this study, we first phenotyped ~ 800 adolescent heterogeneous stock rats in open field, novel object interaction, social interaction, elevated plus maze, and marble bury behaviors. These rats were then phenotyped on socially acquired nicotine self-administration. We found 243 significant correlations between different behavioral tests. Principal component regression analysis found that ~ 10–20% of the variance in nicotine-related measures, such as intake during

the first or the last three fixed-ratio sessions, the progressive ratio session, and reinstatement behavior, can be explained by variations in behavioral traits. Factors corresponding to social behavior and anxiety were among the strongest predictors of nicotine intake and reinstatement of nicotine-seeking behavior. We also found many sex differences in behavioral measures. These data indicated that the genetic diversity of this population, in combination with social behavior and anxiety, are significant contributors to the divergent nicotine self-administration behavior and indicated a high probability of discovering sex-specific genetic mechanisms for nicotine intake in future genome-wide association studies.

Wide and Deep Imaging of Neuronal Activities by a Wearable Neurolmager Reveals Premotor Activity in the Whole Motor Cortex

<https://www.biorxiv.org/content/10.1101/434035v2>

Wearable technologies for functional whole brain imaging in freely moving animals would advance our understanding of cognitive processing and adaptive behavior. Fluorescence imaging can visualize the activity of individual neurons in real time, but conventional microscopes have limited sample coverage in both the width and depth of view. Here we developed a novel head-mounted laser camera (HLC) with macro and deep-focus lenses that enable fluorescence imaging at cellular resolution for comprehensive imaging in mice expressing a layer- and cell type-specific calcium probe. We visualized orientation selectivity in individual excitatory neurons across the whole visual cortex of one hemisphere, and cell assembly expressing the premotor activity that precedes voluntary movement across the motor cortex of both hemispheres. Including options for multiplex and wireless interfaces, our wearable, wide- and deep-imaging HLC technology could enable simple and economical mapping of neuronal populations underlying cognition and behavior.

MARGO (Massively Automated Real-time GUI for Object-tracking), a platform for high-throughput ethology

<https://www.biorxiv.org/content/10.1101/593046v1>

Fast object tracking in real time allows convenient tracking of very large numbers of animals and closed-loop experiments that control stimuli for multiple animals in parallel. We developed MARGO, a real-time animal tracking suite for custom behavioral experiments. We demonstrated that MARGO can rapidly and accurately track large numbers of animals in parallel over very long timescales. We incorporated control of peripheral hardware, and implemented a flexible software architecture for

defining new experimental routines. These features enable closed-loop delivery of stimuli to many individuals simultaneously. We highlight MARGOâ€™s ability to coordinate tracking and hardware control with two custom behavioral assays (measuring phototaxis and optomotor response) and one optogenetic operant conditioning assay. There are currently several open source animal trackers. MARGOâ€™s strengths are 1) robustness, 2) high throughput, 3) flexible control of hardware and 4) real-time closed-loop control of sensory and optogenetic stimuli, all of which are optimized for large-scale experimentation.

Ethology as a physical science

<https://www.biorxiv.org/content/10.1101/220855v2>

Behaviour is the ultimate output of an animalâ€™s nervous system and choosing the right action at the right time can be critical for survival. The study of the organisation of behaviour in its natural context, ethology, has historically been a primarily qualitative science. A quantitative theory of behaviour would advance research in neuroscience as well as ecology and evolution. However, animal posture typically has many degrees of freedom and behavioural dynamics vary on timescales ranging from milliseconds to years, presenting both technical and conceptual challenges. Here we review 1) advances in imaging and computer vision that are making it possible to capture increasingly complete records of animal motion and 2) new approaches to understanding the resulting behavioural data sets. With the right analytical approaches, these data are allowing researchers to revisit longstanding questions about the structure and organisation of animal behaviour and to put unifying principles on a quantitative footing. Contributions from both experimentalists and theorists are leading to the emergence of a physics of behaviour and the prospect of discovering laws and developing theories with broad applicability. We believe that there now exists an opportunity to develop theories of behaviour which can be tested using these data sets leading to a deeper understanding of how and why animals behave.

Morphological plant modeling: Unleashing geometric and topological potential within the plant sciences

<https://www.biorxiv.org/content/10.1101/078832v2>

Plant morphology is inherently mathematical in that morphology describes plant form and architecture with geometrical and topological descriptors. The geometries and topologies of leaves, flowers, roots, shoots and their spatial arrangements have fascinated plant biologists and

mathematicians alike. Beyond providing aesthetic inspiration, quantifying plant morphology has become pressing in an era of climate change and a growing human population. Modifying plant morphology, through molecular biology and breeding, aided by a mathematical perspective, is critical to improving agriculture, and the monitoring of ecosystems with fewer natural resources. In this white paper, we begin with an overview of the mathematical models applied to quantify patterning in plants. We then explore fundamental challenges that remain unanswered concerning plant morphology, from the barriers preventing the prediction of phenotype from genotype to modeling the movement of leaves in air streams. We end with a discussion concerning the incorporation of plant morphology into educational programs. This strategy focuses on synthesizing biological and mathematical approaches and ways to facilitate research advances through outreach, cross-disciplinary training, and open science. This white paper arose from bringing mathematicians and biologists together at the National Institute for Mathematical and Biological Synthesis (NIMBioS) workshop titled “Morphological Plant Modeling: Unleashing Geometric and Topological Potential within the Plant Sciences” held at the University of Tennessee, Knoxville in September, 2015. Never has the need to quantify plant morphology been more imperative. Unleashing the potential of geometric and topological approaches in the plant sciences promises to transform our understanding of both plants and mathematics.

Open Design 3D-Printable Adjustable Micropipette that meets ISO Standard for Accuracy

<https://www.biorxiv.org/content/10.1101/109231v1>

Scientific communities are drawn to the open source model as an increasingly utilitarian method to produce and share work. Initially used as a means to develop freely available software, open source projects have been applied to hardware including scientific tools. Increasing convenience of 3D printing has fueled the proliferation of open labware projects aiming to develop and share designs for scientific tools that can be produced in-house as cheap alternatives to commercial products. We present our design of a micropipette that is assembled from 3D-printable parts and some hardware that works by actuating a disposable syringe to a user adjustable limit. Graduations on the syringe are used to accurately adjust the set point to the desired volume. Our open design printed micropipette is assessed in comparison to a commercial pipette and meets ISO 8655 standards.

An arbitrary-spectrum spatial visual stimulator for vision research

<https://www.biorxiv.org/content/10.1101/649566v1>

Visual neuroscientists require accurate control of visual stimulation. However, few stimulator solutions simultaneously offer high spatio-temporal resolution and free control over the spectra of the light sources, because they rely on off-the-shelf technology developed for human trichromatic vision. Importantly, consumer displays fail to drive UV-shifted short wavelength-sensitive photoreceptors, which strongly contribute to visual behaviour in many animals, including mice, zebrafish and fruit flies. Moreover, many non-mammalian species feature more than three spectral photoreceptor types. Here, we present a flexible, spatial visual stimulator with up to 6 arbitrary spectrum chromatic channels. It combines a standard digital light processing engine with open source hard- and software that can be easily adapted to the experimentalistâ€™s needs. We demonstrate the capability of this general visual stimulator experimentally in the *in vitro* mouse retinal whole-mount and the *in vivo* zebrafish. Hereby, we intend starting a community effort of sharing and developing a common stimulator design.

Manipulation of Seedling Traits with Pulsed Light in Closed Controlled Environments

<https://www.biorxiv.org/content/10.1101/674432v1>

There is substantial interest in growing crops in closed controlled environments, yet the energy requirements are high. Energy is required to produce light, but also to remove the heat generated when producing light. The goal of the current work examines a possible approach to decrease the energy requirement. The effect of pulsed light treatments was examined by monitoring seedling traits during early photomorphogenic development. Daily light integral remained unchanged between treatments, but the frequency of the pulses was varied. Developmental traits (such as inhibition of hypocotyl elongation rate) were most conspicuous during a normal photoperiod, as in twelve hours light, twelve hours darkness. Consistent with historical reports, when treatments were delivered in shorter durations (e.g. 1 hour on/off) photomorphogenic development was hindered, with the same daily light integral. However, at even shorter light intervals (e.g. seconds) seedlings developed as if they were provided full 12 h treatments. Extension of the dark period following a 5 s pulse was tested to determine the effect on seedling traits. The results showed that the dark period could be extended to at least 10 s without affecting seedling development, and extension to 20 s only had slight effects on seedling traits. The mechanism of the phenomenon was examined in *Arabidopsis* photosensory mutants, with substantial contributions from the phyA and cry1 pathways. The results suggest that pulsed light with extended dark periods can decrease energy input by at least 30% to >50% without affecting visible seedling traits. These pilot experiments in seedlings demonstrate that

implementation of short-interval, pulsed-light strategies may lower energy requirements for growing crops in artificially illuminated environments.

How to develop objective-driven comprehensive science outreach initiatives aiming at multiple audiences

<https://www.biorxiv.org/content/10.1101/023838v1>

Science outreach has become increasingly important for researchers and needs to be of ever improving quality, although the time available aside our science, teaching and administration activities is steadily decreasing. To square this circle, effective strategies are required. Here we argue that this can be achieved by setting simple but ambitious overarching objectives for comprehensive outreach initiatives which target multiple audiences, supported by cumulative build-up of shared high-quality resources, as well as the exchange and collaboration amongst scientists with a common outreach aim. To exemplify this strategy, we explain the low-budget, yet high-quality outreach initiative of the Manchester Fly Facility which aims to promote public awareness of the importance of the model organism *Drosophila* for biomedical research. (1) This initiative targets the general public at science fairs, through public videos, or through extracurricular activities in schools as well as the development of curriculum-relevant sample lessons for teachers - all supported by a dedicated website. (2) The initiative targets university students: by adapting the public outreach resources for their teaching, and through newly developed advanced training strategies that amalgamate the outreach objectives. (3) It targets fellow scientists through blogs, conference presentations and a second website that provides a one-stop-shop for resources, arguments and strategies. As will be explained, this multi-pronged approach is time-saving in the long run and it is powerful because it reaches a wide range of audiences, helps to gain momentum, to build resource, and to gradually improve quality through cross-fertilisation between different activities, and through exchange within the science community. This helps to build communities, and high-quality outreach will have further important added value: arguments that impress the public, tend to be most effective also with reviewers and grant panel members, and often help to readjust aspects of your own scientific work.

An incremental training method with automated, extendible T-maze for training spatial behavioral tasks in rodents

<https://www.biorxiv.org/content/10.1101/514703v1>

We present a training procedure and a T-maze equipped with sensors and automated feeders for training spatial behavioral tasks in rodents. The maze can be transformed from an enclosed box to a maze of variable dimensions. The modularity of the protocol and setup makes it highly flexible and suitable for training a wide variety of spatial tasks, and facilitates incremental training stages of increasing maze size for more efficient learning. The apparatus, in its software and hardware, is able to adapt to animal performance, adjusting task challenges and difficulty.

Species and habitat mapping in two dimensions and beyond. Structure-from-Motion Multi-View Stereo photogrammetry for the Conservation Community

<https://www.biorxiv.org/content/10.1101/2019.12.16.878033v1>

Structure-from-Motion Multi View Stereo (SfM-MVS) photogrammetry is a technique by which volumetric data can be derived from overlapping image sets, using changes of an objects position between images to determine its height and spatial structure. Whilst SfM-MVS has fast become a powerful tool for scientific research, its potential lies beyond the scientific setting, since it can aid in delivering information about habitat structure, biomass, landscape topography, spatial distribution of species in both two and three dimensions, and aid in mapping change over time – both actual and predicted. All of which are of strong relevance for the conservation community, whether from a practical management perspective or understanding and presenting data in new and novel ways from a policy perspective.

Deep learning-based methods for individual recognition in small birds

<https://www.biorxiv.org/content/10.1101/862557v1>

Individual identification is a crucial step to answer many questions in evolutionary biology and is mostly performed by marking animals with tags. Such methods are well established but often make data collection and analyses time consuming and consequently are not suited for collecting very large datasets.

Presynaptic inhibition of cutaneous afferents prevents chronic itch

<https://www.biorxiv.org/content/10.1101/806976v1>

Chronic itch represents an incapacitating burden on patients suffering a wide spectrum of diseases. Despite recent advances in our understanding of the cells and circuits implicated in the processing

of itch information, chronic itch often presents itself without apparent cause. Here, we identify a spinal subpopulation of inhibitory neurons defined by the expression of Ptfla involved in gating mechanosensory information self-generated during locomotion. These neurons receive tactile and motor input and establish presynaptic inhibitory contacts on mechanosensory afferents. Loss of these neurons leads to increased hairy skin sensitivity and chronic itch, at least partially mediated through the classic GRPR pathway. These findings shed new light on the mechanisms implicated in chronic itch and open novel targets for therapy developments.

Genomic heritability estimates in sweet cherry reveal non-additive genetic variance is relevant for industry-prioritized traits

<https://www.biorxiv.org/content/10.1101/233296v1>

Background Sweet cherry is consumed widely across the world and provides substantial economic benefits in regions where it is grown. While cherry breeding has been conducted in the Pacific Northwest for over half a century, little is known about the genetic architecture of important traits. We used a genome-enabled mixed model to predict the genetic performance of 505 individuals for 32 phenological, disease response and fruit quality traits evaluated in the RosBREED sweet cherry crop data set. Genome-wide predictions were estimated using a repeated measures model for phenotypic data across 3 years, incorporating additive, dominance and epistatic variance components. Genomic relationship matrices were constructed with high-density SNP data and were used to estimate relatedness and account for incomplete replication across years.

Karrikin-sensing protein KAI2 is a new player in regulating root growth patterns

<https://www.biorxiv.org/content/10.1101/195891v1>

Roots form highly complex systems varying in growth direction and branching pattern to forage for nutrients efficiently. Here mutations in the KAI2 (KARRIKIN INSENSITIVE) \pm/f^2 -fold hydrolase and the MAX2 (MORE AXILLARY GROWTH 2) F-box leucine-rich protein, which together perceive karrikins (smoke-derived butenolides), caused alteration in root growth direction (root skewing and waving) of *Arabidopsis thaliana*. This exaggerated root skewing was independent of endogenous strigolactone perception by the D14 \pm/f^2 -fold hydrolase and MAX2. Thus KAI2/MAX2 a^{TM} s regulation of root growth may be through perception of endogenous KAI2-ligands, which have yet to be identified. Degradation targets of the KAI2/MAX2 complex, SMAX1 (SUPPRESSOR OF MAX2-1) and SMXL6,7,8 (SUPPRESSOR OF MAX2-1-LIKE) are also involved in the regulation of root

skewing. Genetic data reveal a new potential target for degradation, as mutation in the SKS3 (SKU5 similar) but not the SKU5/SKS17 root plasma membrane glycoprotein suppresses the exaggerated root skewing induced by the lack of MAX2. In *Arabidopsis thaliana* therefore, the KAI2 karrikin-sensing protein acts to limit root skewing, and we propose a mechanism involving root radial expansion as the mutant's gravitropic and mechano-sensing responses remained largely unaffected.

Strategic adjustment of parental care: life-history trade-offs and the role of glucocorticoids

<https://www.biorxiv.org/content/10.1101/063313v1>

Life history theory predicts that optimal strategies of parental investment will depend on ecological and social factors such as current brood value and offspring need. Parental care strategies are also likely to be mediated in part by the hypothalamic-pituitary-adrenal (HPA) axis and glucocorticoid hormones. Here we present an experiment in tree swallows (*Tachycineta bicolor*), a biparental songbird with wide geographic distribution, asking whether parental care is strategically adjusted in response to signals of offspring need and brood value and whether glucocorticoids are involved in these adjustments. Using an automated playback system, we carried out playbacks of nestling begging calls specifically to females in two populations differing in their brood value: a northern population in Ontario, Canada (relatively high brood value) and a southern population in North Carolina, USA (lower brood value). We quantified female offspring provisioning rates before and during playbacks and plasma corticosterone levels (cort) once during late incubation and once immediately after playbacks. Females in both populations increased feeding rates temporarily during the first two hours of playback but the increase was not sustained for the entire duration of playback (six hours). Cort levels from samples at the end of the playback did not differ between control females and females that received playbacks. However, females that had higher increases in cort between the incubation and nestling period had greater fledging success. These results suggest that females are able to strategically respond to offspring need, although the role of glucocorticoids in this strategic adjustment remains unclear.

An automated, high-throughput method for standardizing image color profiles to improve image-based plant phenotyping

<https://www.biorxiv.org/content/10.1101/354274v1>

High-throughput phenotyping has emerged as a powerful method for studying plant biology. Large

image-based datasets are generated and analyzed with automated image analysis pipelines. A major challenge associated with these analyses is variation in image quality that can inadvertently bias results. Images are made up of tuples of data called pixels, which consist of R, G, and B values, arranged in a grid. Many factors, for example image brightness, can influence the quality of the image that is captured. These factors alter the values of the pixels within images and consequently can bias the data and downstream analyses. Here, we provide an automated method to adjust an image-based dataset so that brightness, contrast, and color profile is standardized. The correction method is a collection of linear models that adjusts pixel tuples based on a reference panel of colors. We apply this technique to a set of images taken in a high-throughput imaging facility and successfully detect variance within the image dataset. In this case, variation resulted from temperature-dependent light intensity throughout the experiment. Using this correction method, we were able to standardize images throughout the dataset, and we show that this correction enhanced our ability to accurately quantify morphological measurements within each image. We implement this technique in a high-throughput pipeline available with this paper, and it is also implemented in PlantCV.

Pesticide exposure affects flight dynamics and reduces flight endurance in bumblebees

<https://www.biorxiv.org/content/10.1101/449280v1>

The emergence of agricultural land use change creates a number of challenges that insect pollinators, such as eusocial bees, must overcome. Resultant fragmentation and loss of suitable foraging habitats, combined with pesticide exposure, may increase demands on foraging, specifically the ability to reach resources under such stress. Understanding the effect that pesticides have on flight performance is therefore vital if we are to assess colony success in these changing landscapes. Neonicotinoids are one of the most widely used classes of pesticide across the globe, and exposure to bees has been associated with reduced foraging efficiency and homing ability. One explanation for these effects could be that elements of flight are being affected, but apart from a couple of studies on the honeybee, this has scarcely been tested. Here we used flight mills to investigate how exposure to a field realistic (10ppb) acute dose of imidacloprid affected flight performance of a wild insect pollinator - the bumblebee, *Bombus terrestris audax*. Intriguingly, initial observations showed exposed workers flew at a significantly higher velocity over the first $\frac{3}{4}$ km of flight. This apparent hyperactivity, however, may have a cost as exposed workers showed reduced flight distance and duration to around a third of what control workers were capable of achieving.

Given that bumblebees are central place foragers, impairment to flight endurance could translate to a decline in potential forage area, decreasing the abundance, diversity and nutritional quality of available food, whilst potentially diminishing pollination service capabilities.

Image-based methods for phenotyping growth dynamics and fitness components in *Arabidopsis thaliana*

<https://www.biorxiv.org/content/10.1101/208512v2>

Background The model species *Arabidopsis thaliana* has extensive resources to investigate intraspecific trait variability and the genetic bases of ecologically relevant traits. However, the cost of equipment and software required for high-throughput phenotyping is often a bottleneck for large-scale studies, such as mutant screening or quantitative genetics analyses. Simple tools are needed for the measurement of fitness-related traits, like relative growth rate and fruit production, without investment in expensive infrastructures. Here, we describe methods that enable the estimation of biomass accumulation and fruit number from the analysis of rosette and inflorescence images taken with a regular camera.

Functional dissection of the ARGONAUTE7 promoter

<https://www.biorxiv.org/content/10.1101/392910v3>

ARGONAUTES are the central effector proteins of RNA silencing which bind target transcripts in a small RNA-guided manner. *Arabidopsis thaliana* has ten ARGONAUTE (AGO) genes, with specialized roles in RNA-directed DNA methylation, post-transcriptional gene silencing, and antiviral defense. To better understand specialization among AGO genes at the level of transcriptional regulation we tested a library of 1497 transcription factors for binding to the promoters of AGO1, AGO10, and AGO7 using yeast 1-hybrid assays. A ranked list of candidate DNA-binding TFs revealed binding of the AGO7 promoter by a number of proteins in two families: the miR156-regulated SPL family and the miR319-regulated TCP family, both of which have roles in developmental timing and leaf morphology. Possible functions for SPL and TCP binding are unclear: we showed that these binding sites are not required for the polar expression pattern of AGO7, nor for the function of AGO7 in leaf shape. Normal AGO7 transcription levels and function appear to depend instead on an adjacent 124-bp region. Progress in understanding the structure of this promoter may aid efforts to understand how the conserved AGO7-triggered TAS3 pathway functions in timing and polarity.

Low-cost, open-access refractive index mapping of algal cells using the transport of intensity equation

<https://www.biorxiv.org/content/10.1101/640755v1>

Phase contrast microscopy allows stain free imaging of transparent biological samples. One technique, using the transport of intensity equation (TIE), can be performed without dedicated hardware by simply processing pairs of images taken at known spacings within the sample. The resulting TIE images are quantitative phase maps of unstained biological samples. Therefore, spatially resolved refractive index information can also be determined.

Affordable and robust phenotyping framework to analyse root system architecture of soil-grown plants

<https://www.biorxiv.org/content/10.1101/573139v1>

The analysis of root system growth, root phenotyping, is important to inform efforts to enhance plant resource acquisition from soils. However, root phenotyping remains challenging due to soil opacity and requires systems that optimize root visibility and image acquisition. Previously reported systems require costly and bespoke materials not available in most countries, where breeders need tools to select varieties best adapted to local soils and field conditions. Here, we present an affordable soil-based growth container (rhizobox) and imaging system to phenotype root development in greenhouses or shelters. All components of the system are made from commodity components, locally available worldwide to facilitate the adoption of this affordable technology in low-income countries. The rhizobox is large enough (~6000 cm² visible soil) to not restrict vertical root system growth for at least seven weeks after sowing, yet light enough (~21 kg) to be routinely moved manually. Support structures and an imaging station, with five cameras covering the whole soil surface, complement the rhizoboxes. Images are acquired via the Phenotiki sensor interface, collected, stitched and analysed. Root system architecture (RSA) parameters are quantified without intervention. RSA of a dicot (chickpea, *Cicer arietinum* L.) and a monocot (barley, *Hordeum vulgare* L.) species, which exhibit contrasting root systems, were analysed. The affordable system is relevant for efforts in Ethiopia and elsewhere to enhance yields and climate resilience of chickpea and other crops for improved food security.

Fast near-whole brain imaging in adult *Drosophila* during responses to stimuli and behavior

<https://www.biorxiv.org/content/10.1101/033803v4>

Whole brain recordings give us a global perspective of the brain in action. In this study, we describe a method using light field microscopy to record near-whole brain calcium and voltage activity, at high speed, in behaving adult flies. We first obtained global activity maps for various stimuli and behaviors. Notably, we found that brain activity increased on a global scale when the fly walked but not when it groomed. This global increase with walking was particularly strong in dopamine neurons. Second, we extracted maps of spatially distinct sources of activity as well as their time series using principal component analysis and independent component analysis. The characteristic shapes in the maps matched the anatomy of sub-neuropil regions and in some cases a specific neuron type. Brain structures that responded to light and odor were consistent with previous reports, confirming the new technique's validity. We also observed previously uncharacterized behavior-related activity, as well as patterns of spontaneous voltage activity.

XRN1 is a Species-Specific Virus Restriction Factor in Yeasts

<https://www.biorxiv.org/content/10.1101/069799v1>

In eukaryotes, the degradation of cellular mRNAs is accomplished by Xrn1p and the cytoplasmic exosome. Because viral RNAs often lack canonical caps or poly-A tails, they can also be vulnerable to degradation by these host exonucleases. Yeast lack sophisticated mechanisms of innate and adaptive immunity, but do use RNA degradation as an antiviral defense mechanism. One model is that the RNA of yeast viruses is subject to degradation simply as a side effect of the intrinsic exonuclease activity of proteins involved in RNA metabolism. Contrary to this model, we find a highly refined, species-specific relationship between Xrn1p and the L-A totiviruses of different *Saccharomyces* yeast species. We show that the gene XRN1 has evolved rapidly under positive natural selection in *Saccharomyces* yeast, resulting in high levels of Xrn1p protein sequence divergence from one yeast species to the next. We also show that these sequence differences translate to differential interactions with the L-A virus, where Xrn1p from *S. cerevisiae* is most efficient at controlling the L-A virus that chronically infects *S. cerevisiae*, and Xrn1p from *S. kudriavzevii* is most efficient at controlling the L-A-like virus that we have discovered within *S. kudriavzevii*. All Xrn1p orthologs are equivalent in their interaction with another virus-like parasite, the Ty1 retrotransposon. Thus, the activity of Xrn1p against totiviruses is not simply an incidental consequence of the enzymatic activity of Xrn1p, but rather Xrn1p co-evolves with totiviruses to maintain its potent antiviral activity and limit viral propagation in *Saccharomyces* yeasts. Consistent with this, we demonstrated that Xrn1p physically interacts with the Gag protein encoded by the L-A

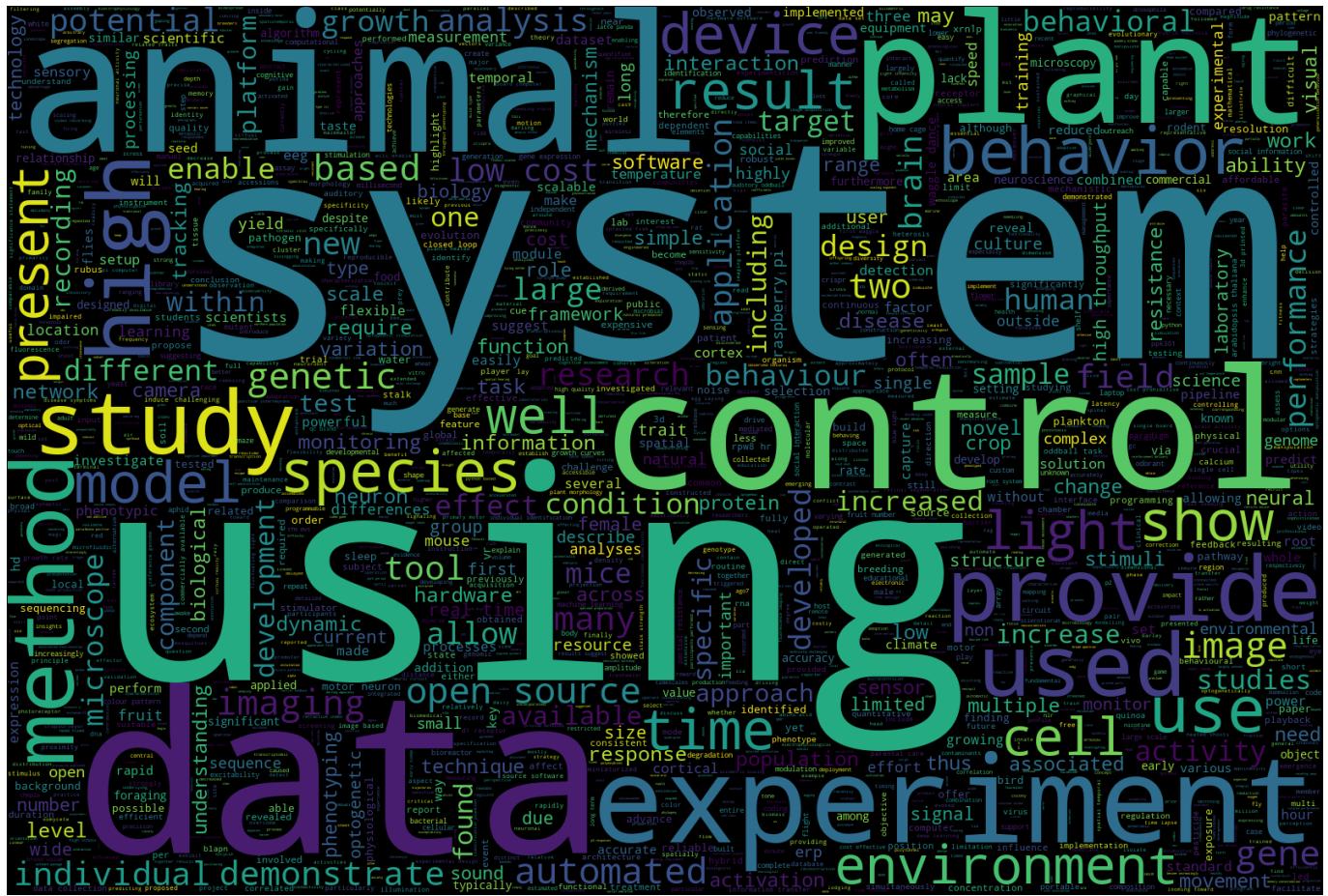
virus, suggesting a host-virus interaction that is more complicated than just Xrn1p-mediated nucleolytic digestion of viral RNAs.

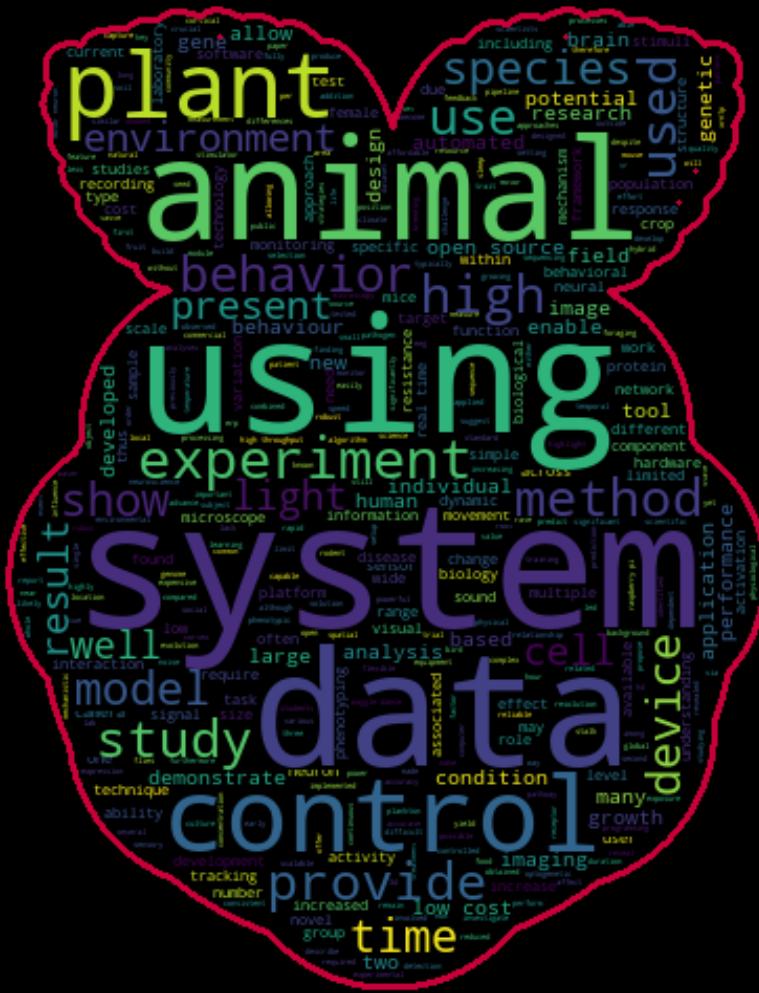
Thinking small: next-generation sensor networks close the size gap in vertebrate biologging

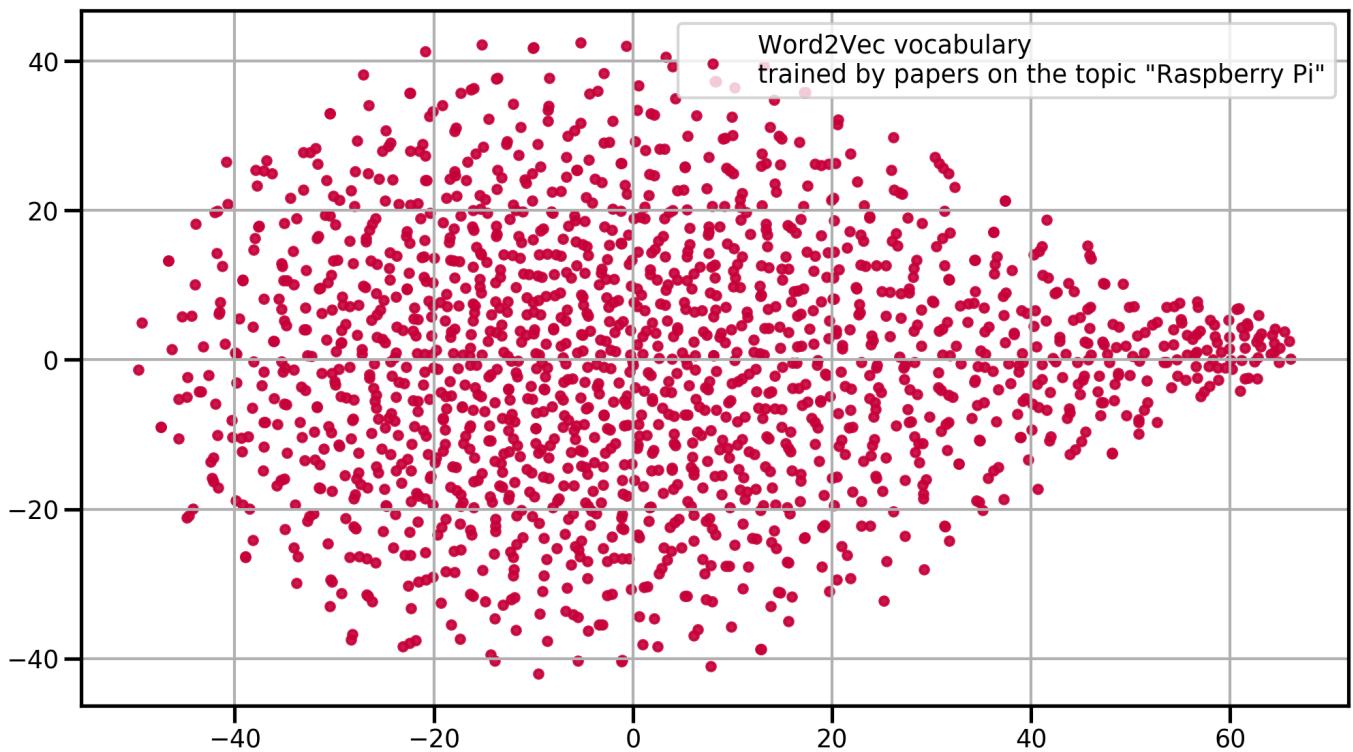
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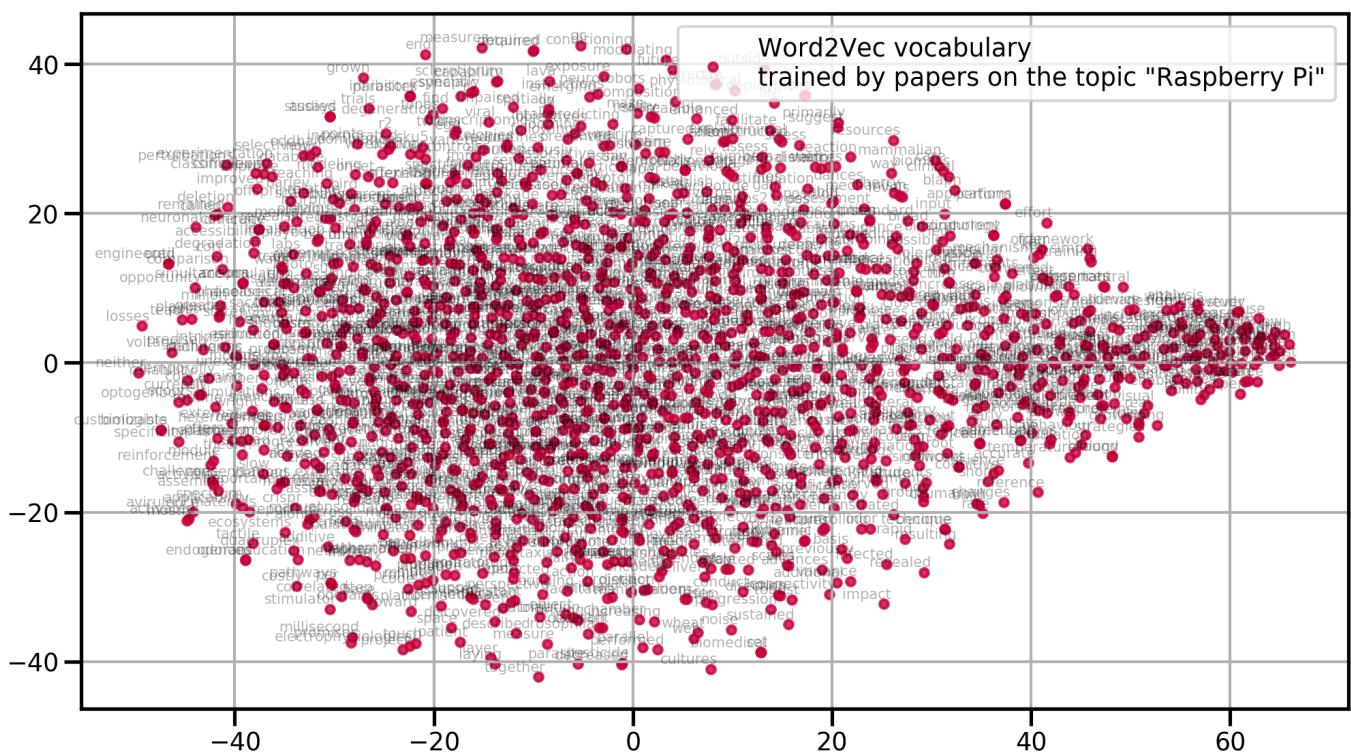
Recent advances in animal tracking technology have ushered in a new era in biologging. However, the considerable size of many sophisticated biologging devices restricts their application to larger animals, while old-fashioned techniques often still represent the state-of-the-art for studying small vertebrates. In industrial applications, low-power wireless sensor networks fulfill requirements similar to those needed to monitor animal behavior at high resolution and at low tag weight. We developed a wireless biologging network (WBN), which enables simultaneous direct proximity sensing, high-resolution tracking, and long-range remote data download at tag weights of one to two grams. Deployments to study wild bats created social networks and flight trajectories of unprecedented quality. Our developments highlight the vast capabilities of WBNs and their potential to close an important gap in biologging: fully automated tracking and proximity sensing of small animals, even in closed habitats, at high spatial and temporal resolution.

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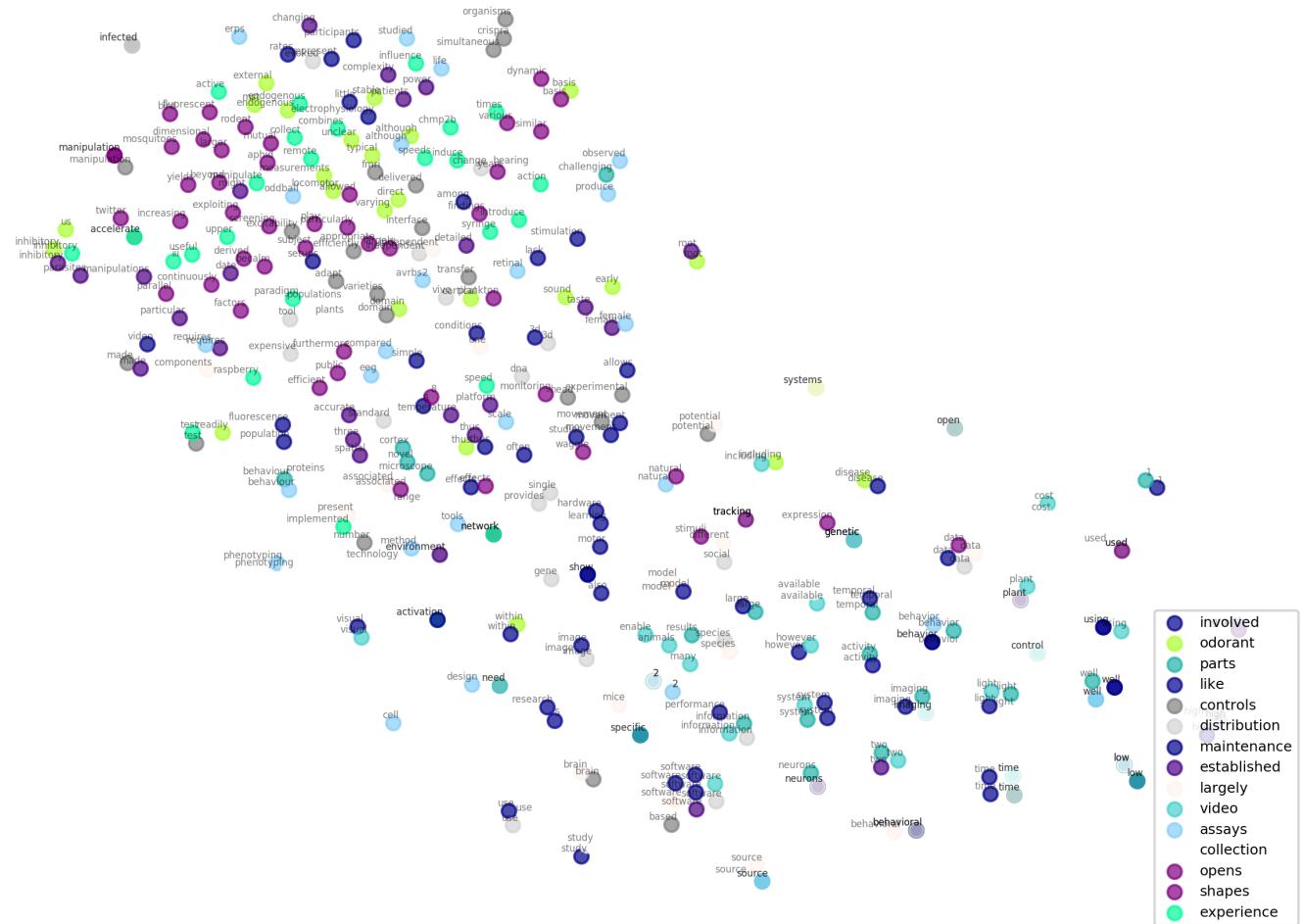








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