Telemetry for small animal physiology

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Animal research is inherently difficult. Living organisms are complicated physiological systems, and collecting data from them is often challenging. The complexity and challenges of *in vivo* animal biology make it an interesting and exciting topic to many researchers, but the intense dedication of time and resources for acquiring data can create a significant bottleneck. Telemetry can offer some relief by allowing researchers to take automated physiological measurements wirelessly from animals, which reduces labor burden and stress on animals. As an added benefit, wireless and automated recordings permit much more extensive data collection over long periods of time and under more natural conditions, ushering in a new era of large data sets and novel insights into animal physiology.

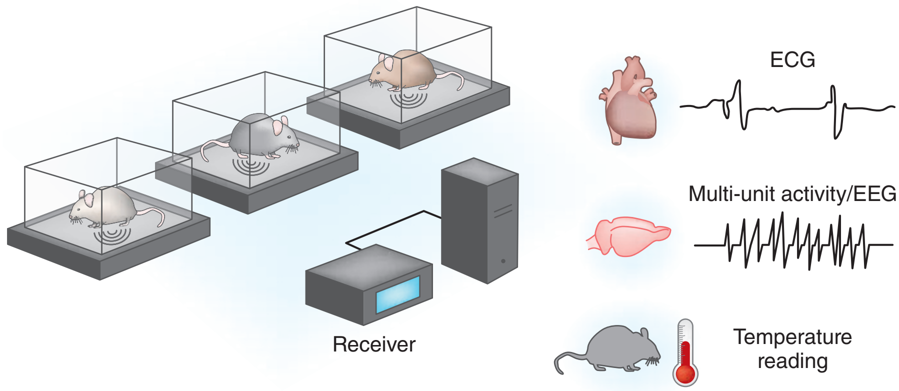

FIGURE 1 | Schematic of a general telemetry setup for wireless and automated measuring of physiological parameters. Illustration by Kim Caesar.

Difficulties in data collection

In vivo physiological measurements are typically taken from animals on an individual basis, which is problematic for several reasons. First, the data collection requires repeated efforts from the researcher taking the measurements. When multiple animals are being used in a study, this process can become very time-consuming. Second, human-induced variability can be introduced when collecting data from each animal one at a time, leading to more data variance and decreased statistical power. Furthermore, the traditional steps of collecting *in vivo* physiological data are highly unnatural for most animals. When an animal is removed from a home cage or enclosure for the taking of measurements, there is often an associated stress response and change in the animal's physiology. In some experiments this state-change might not affect results; however, for many researchers studying natural biology and behaviors, these changes can significantly affect research outcomes. Thus, most investigators hope to minimize such stress responses and the effects of human handling.

One solution for these problems is the use of telemetry for *in vivo* physiological recordings. Telemetry, in laboratory animal science, is a research method whereby small implanted devices permit automated and wireless measurements from small animals, with data then transmitted to a receiver outside the animals' cages[1]. A primary goal of these systems is to provide experimenters with desired physiological data while research animals are conscious and undisturbed. This leads to fast and automated data collection from animals without the need for direct human interaction, streamlining experiments and reducing the typical drawbacks that can occur with conventional methods.

Telemetry systems

After an initial implantation surgery, a typical telemetry device, composed of sensors, a battery and a transmitter, sends out physiological data through radio waves that are detected by a receiver and recorded to the experimenter's computer (**Fig. 1**). By remotely receiving data emission from implanted animals, these systems greatly reduce the amount of human effort required for data collection and also allow for more natural, hands-off measurements in behaving animals.

Sensory devices can range from a simple thermal detector for measuring body temperature to an intricate array of electrodes implanted in the brain[2,3]. Whatever the case, the physiological data is obtained from the animal, encoded and then sent out through a small radio transmitter. This information is then captured and digitized by another receiving device in the general vicinity of the animal, located outside the animal's home cage.

Telemetry in research

Telemetry methods are now being employed in multiple fields of biology and medicine and have already been in use for several years. Researchers have used telemetry to record blood pressure in mice during treadmill exercise[4], to examine brain activity continuously in mouse models of

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epilepsy[5], and even to study cardiovascular measurements using devices implanted in the aortas of rodents[6]. Each of these applications yields data that are collected automatically, without direct human–animal contact during the measurements.

These benefits allow researchers to collect long, uninterrupted datasets from experimental animals during otherwise normal behavioral and physiological states. In one example, researchers implanted devices in the aortas and carotid arteries of mice and examined arterial pressure and heart rate as the animals were fed a high NaCl diet[7]. Telemetry devices allowed 24-h monitoring of these animals, showing the continuous effects of NaCl on heart rate and mean arterial pressure over multiple days. In another study, epilepsy was examined in rats using a continuous telemetry recording from the brain and a simultaneous electromyogram of muscle activity to detect convulsive seizures following drug injections[8]. Once implanted, the animals were allowed to move freely while measurements were taken at frequent or constant intervals. Without telemetry, data like these could not be collected in a normally behaving animal model of disease.

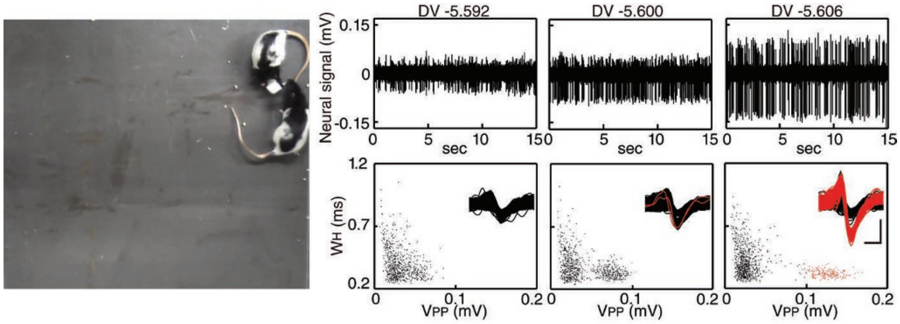

FIGURE 2 | Example single unit recordings collected from a rat's brain during social exploration using wireless telemetry. Rats can be seen (left) interacting naturally during (right) recording of activity in a well-isolated single-unit. Single-unit recordings show raw neural signals and spikes, as well as extracted waveforms overlaid on scatter-plots of spike width (W_H) and spike peak amplitude (V_{PP}). Red waveforms show well-separated spiking activity. These well-isolated recordings let researchers visualize neural activity as freely moving animals interact together. Adapted from *Sci. Rep.* **5**, 7853 (2015).

Naturalistic science

A major benefit of using telemetry in research is that animals are generally unaware that they are being monitored and do not interact directly with researchers. Thus, measurements can be taken during more naturalistic conditions—conditions that closely imitate those occurring in nature—compared with typical laboratory experiments involving human handling. This allows scientists to examine the roles of an animal's immediate environment on its physiology with greater ethological validity and less restriction.

Neuroscience is one discipline that is experiencing particularly large benefits from the application of telemetry methods. This is because the physiology and mechanisms of brain function during natural behavior are still generally unknown. Common research paradigms for measuring neuronal activity in small animals include head-fixed neural recordings and recordings carried out with anesthetized animals in laboratory settings. There are benefits to using these types of studies: by holding an animal still, components of the environment, such as light levels, sounds and smells, can all be carefully controlled. However, neuroscientists are increasingly interested in how brain activity functions in awake behaving animals to produce behavior in less constrained environments. For example, implanted telemetry devices can provide continuous neural measurements while a research animal interacts with other animals (**Fig. 2**; ref. 9), offering an understanding of how brain activity correlates with more complicated animal behaviors, such as socialization or navigation, in settings more enriched than typical laboratory experiments. Data of this kind will be crucial for understanding how brain activity drives more complex and naturalistic behaviors.

The future of wireless physiology

Physiologists who study small animals will clearly benefit from these automated, wireless recording systems. How quickly these devices become ubiquitous tools will likely depend on how quickly their limitations can be overcome. In addition to the financial cost of such devices, their physical size and power requirements also represent hurdles for telemetry equipment[10]. Implanted sensors and transmitters need energy to operate; this typically necessitates that a battery be implanted along with the sensor, which can increase the size of the implant. A less bulky alternative is to use an inductive charger whereby a magnetic field can be applied to power the implant (**Fig. 3**), but this requires animals to be confined during the powering process.

As a prime example of the need to reduce overall implant size, researchers have attempted to take measurements from inside of a rodent heart using telemetry equipment; for this application, they need the power system and data transmitters to be as small as possible[11]. Engineers are working actively to miniaturize telemetry components, with private companies already selling telemetry systems that are specially designed for use with small animals. Future efforts will likely aim to continue reducing the size and complexity of telemetry systems, making them as turnkey and flexible as possible. The merits of telemetry are clear, and assuming that these systems continue to improve, they will likely

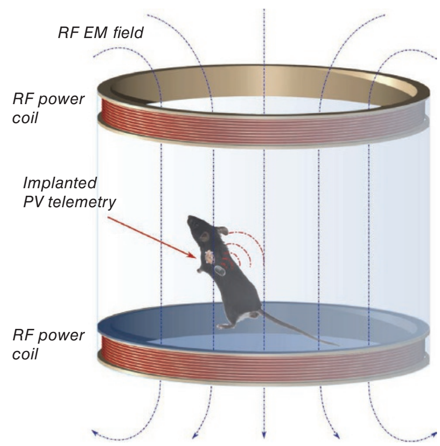

FIGURE 3 | Conceptual schematic of a mouse cage with integrated radio frequency power-generating coils. The electromagnetic fields (blue) enable the implanted telemetry system to be powered without the need for an internal battery. Adapted from *EURASIP J. Embed. Syst.* **2013**, 1 (2013).

become a common and increasingly valuable tool, both in the lab and the vivarium.

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