



How to build a rodent neuro- behavioral core

A practical guide for getting started



*A publication from
Noldus Information Technology*

WELCOME

FOR WHOM IS THIS GUIDEBOOK

This guidebook is designed for researchers and administrators who are considering building a rodent behavioral core, or want to expand their current behavioral testing capacity.

The goal is to provide guidance, information, and tips, based on our extensive experience with building labs and from the contributions of those we interviewed.

ABOUT THE AUTHOR

Jason Rogers received his Ph.D. from the University of Utah under the guidance of Dr. Ray Kesner in the Department of Psychology. His dissertation focused on the neurobiology of learning and memory, specifically the functional and behavioral differences between the hippocampus and parietal cortex. He joined Dr. Ron See's lab as a Post-Doctoral Fellow at the Medical University of South Carolina, focusing on translational models of drug relapse. In 2008, Jason joined Noldus as a Product Specialist and Trainer. Since then, he has had many roles at Noldus, from Account Manager to Lead Consultant and now Senior Research Scientist. He has given training courses, seminars, and spoke at conferences across the globe. A Hoosier by birth, Jason has a passion for playing music, traveling, neuropsychopharmacology, and Star Wars. He also enjoys running, biking, zymurgy, and spending time with his significant other, Dr Candi, daughter Chloe, and two Aussie-doodles, Winston and Albus Doodledore.

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WHY

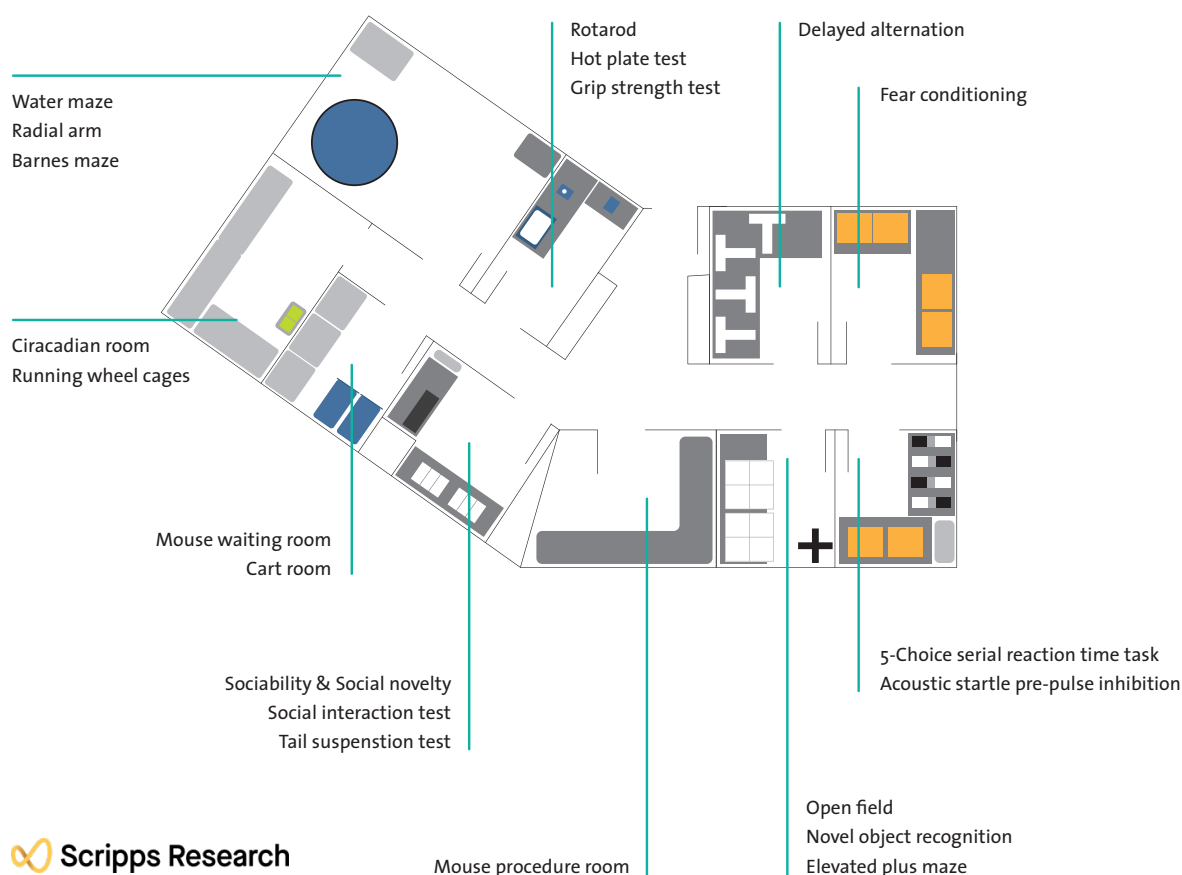
*Three benefits of building
a behavioral core*

WHY BUILD A BEHAVIORAL CORE?

The decision to create dedicated space for behavioral testing is a valuable step for adding a translational link among the cellular/molecular, proteomics, genetics, and imaging cores. There are three main benefits to creating a behavioral core.

CENTRALIZED TESTING LOCATION(S)

An important benefit is to provide a centralized location for equipment, thus saving valuable space and resources. Below, see the floorplan of the behavioral core of Scripps Research as a good example.



TESTING SERVICES THAT EXPAND CAPACITY

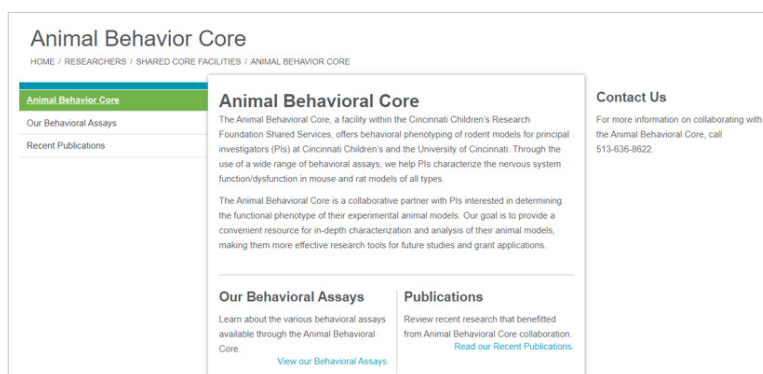
Another benefit is offering testing services that extend or expand the capacity of an individual researcher, lab, or department. For example, this is a list of the behavioral procedures at Perelman, School of Medicine:

- Contextual & Cued fear conditioning
- Barnes maze
- T-maze reward learning
- Y-maze spontaneous alternation
- Spatial object recognition
- Novel object recognition
- Reversal learning & extinction
- Circadian wheel running
- Home cage activity monitoring
- Open field activity/habituation
- Rotarod
- Hole poke exploration
- Social choice
- Social memory
- Resident-intruder/Tube test
- Ultrasonic vocalizations recording
- Elevated zero maze
- Light/dark box
- Acoustic startle response & PPI
- Forced swim test
- Thermal sensitivity
- Grip strength
- Von Frey touch sensitivity
- Gait analysis (ink & paper)
- Marble burying
- Novelty suppressed feeding
- Sucrose & EtOH preference
- Conditioned taste aversion
- Developmental milestone tracking



PROVIDE EXPERTISE

The final benefit is to provide training opportunities, testing services, data analysis, protocol standardization, and/or letters of support for grants specifically for behavioral research. Below the website of Cincinnati Children's, showing their animal behavioral core and its activities.





WHO

Let's build a team

LET'S BUILD OUR TEAM

Your core is as good as the people working there. So, let's discuss who should be in your team:

- Who will manage or lead the core?
- What about the other staff?

WHO WILL MANAGE OR LEAD THE CORE?

Core facilities are, in essence, a non-profit organization within a university. It is the goal of every core to provide a centralized testing location, testing capacities, and expertise, while mitigating as many potential losses as possible. A major expense for any core is the personnel required to manage it. Therefore, the person who will lead your core will depend upon your answer(s) to the following questions:

- Do you expect user fees to pay the salaries of the staff?
- Do you expect grant funding to provide salaries, equipment, etc?

If you expect user fees to recover your losses and provide enough revenue for staff, then it would be best to hire a dedicated manager. This person would be responsible for all the sales and marketing for the core, plus the administrative tasks, such as scheduling, room management, etc. It is imperative that you hire someone with an advanced degree specializing in behavioral science. Before you commit to this role, however, consider the long-term goals of both the core and your manager: is this position a ‘career’ position, meaning you want that person to stay for ten, fifteen, or twenty years? If so, it is essential that you clarify during the hiring process what benefits and/or advancements are in place, otherwise you risk turnover among your staff.

If you expect grant funding to provide salaries, money for equipment, indirects, etc, then it would be best to have a Principle Investigator (PI) lead and manage the facilities. The core should be a part of his/her/their research lab with space large enough for the individual’s research as well as the other core users. If your university is fortunate enough to become an IDRC (see Page 29), then the NIH will provide all the funds necessary and you cannot charge user fees. Before you commit to this type of core, however, consider the demands placed on this PI to ensure that you provide enough time, space, and opportunity to secure funding and continue to produce publishable results.

As such, we found that there are two types of core managers, which will be described on the following pages.

THE DEDICATED MANAGER

Education

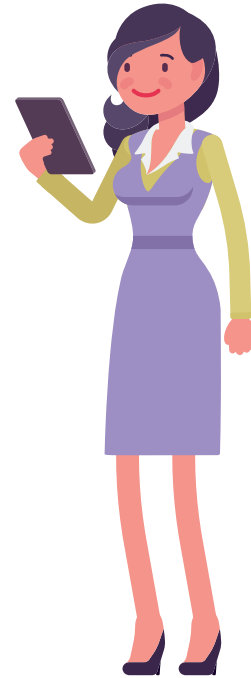
- M.Sc. or Ph.D.
- Trained in behavioral sciences.

Duties and responsibilities

- Manage the core and be responsible for the results.
- Manage, order, and maintain equipment.
- Provide training.
- Write protocols.
- Schedule rooms/services.
- Ability to perform full-service testing.

What to look for in a manager

- Advanced degree (M.Sc. or Ph.D.) with well established experience and expertise in behavioral neuroscience.
- Knowledge of statistics and experience with relevant tools.
- Outstanding interpersonal skills: ability to effectively interact with internal colleagues as well as external collaborators.
- Exceptional verbal and written communication skills, and capability to effectively present scientific results to key stakeholders.
- High levels of motivation, creativity, and independence.
- Remarkable attention to detail with excellent organizational and record keeping skills.
- Strong technical problem-solving skills.



THE PRINCIPLE INVESTIGATOR (PI) LED

Duties and responsibilities

- Manages the lab, but 'does not own the results from the core'.
- Maintains own lab & behavioral core.
- Provides training.
- Writes protocols.
- Consults on experiments.

The difference between a dedicated manager and a PI comes down to time. The dedicated manager is a full-time core position, whereas a PI maintains his/her/their own lab in addition to running the core. The difference is important and will vary by institution and department.

The type of PI to support a core

- Maintains own research track and/or funding.
- Has a collaborative mindset.
- Outstanding interpersonal skills: ability to effectively interact with internal colleagues as well as external collaborators.
- Exceptional teaching skills: able to teach students, technicians, and colleagues.



WHAT ABOUT THE OTHER STAFF?

IMPORTANT STAFF: THE TECHNICIANS

Technicians are the doers. These could be early-to-mid career scientists, typically holding a B.S. or M.Sc. They need to have expertise in techniques such as how to handle the animals and run the behavioral experiments. However, unlike the manager, they don't need to know why an experiment is being conducted or how to analyze or interpret data.

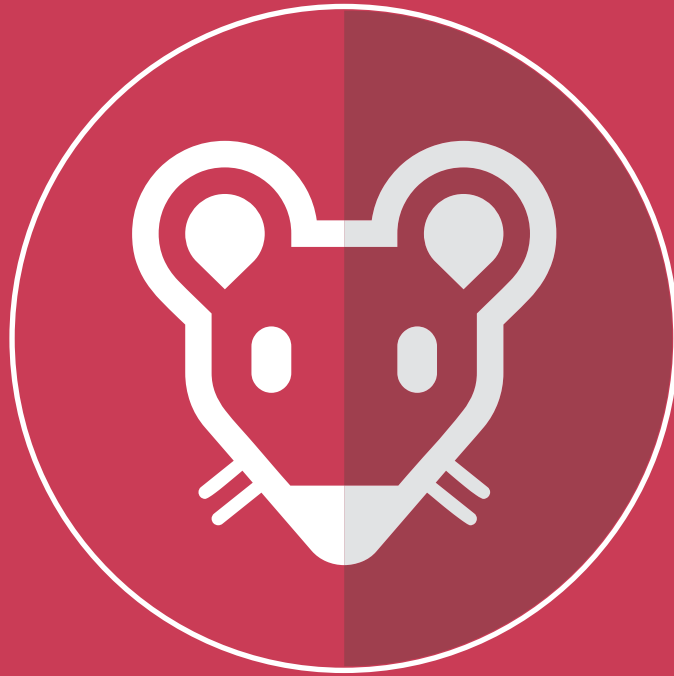
The number of technicians will depend on how busy the core is, how much funding the core receives, etc. There is no standard and it varies by core.



DON'T FORGET YOUR ANIMAL CARE STAFF

Animal care is an often overlooked part of a core, as they aren't paid by the core but are vital to its function. They work with the techs and manager to ensure experiments run smoothly.

Furthermore, working with IACUC (Institutional Animal Care and Use Committee) on your protocols ensures that users have everything they need to properly start their behavioral testing.



WHAT

*Which tests will
you include?*

WHICH TESTS WILL YOU INCLUDE?

In this section we will discuss the which tests you could provide for in your behavioral core:

- Tests, apparatuses, and equipment
- Choosing your tests

TESTS, APPARATUSES, AND EQUIPMENT

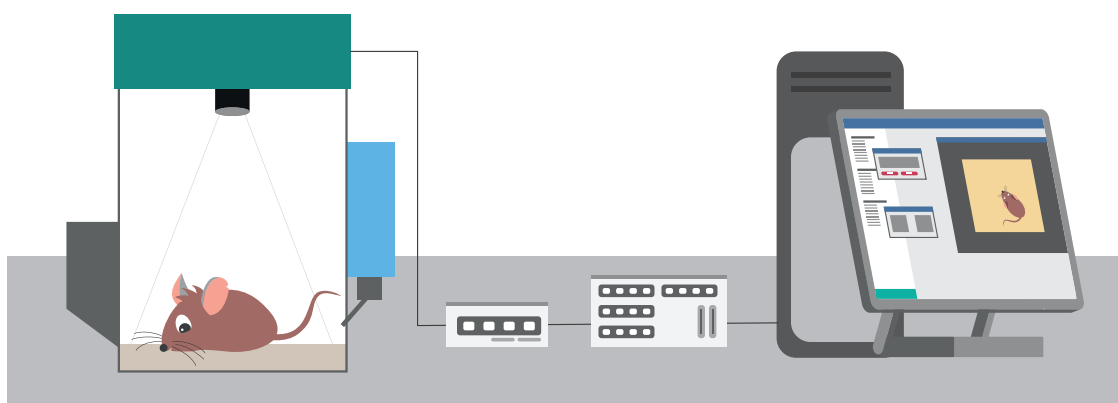
The main function of a behavioral core is to provide equipment for the testing of laboratory animals. The testing apparatuses must be robust, reliable, reproducible, and ideally, automated.

We recommend exploring a few tests from some of the generally recognized standard behavioral categories, which can be divided into six sections: home cage, motor function, pain, anxiety, social interaction, and learning & memory.

HOME CAGE

The first assessment of a behavioral core is the study how the animal lives in its home cage. Behavior of laboratory rodents is often studied in well-controlled, short experiments, in an environment that is separate from the animal's home cage. Handling of the animal, the stress of new surroundings, and the great variety in laboratory environments can make results difficult to interpret and can have a negative effect on animal welfare.

Executing tests in a home cage, like [video tracking](#), provides a solution to these problems. In addition, [automated assessment tools](#) can easily measure activity, feeding, and circadian rhythms.



MOTOR FUNCTION

The assessment of gait and locomotion is important in conditions that affect the central nervous system (CNS), peripheral nervous system (PNS) and skeletal structures or muscles. The tests can be subdivided into two categories (locomotor activity and muscular strength), each with their main tests:



Locomotor activity

Open field, Rotorod, Basso, Beattie, Bresnahan (BBB), free walking (automated or ink & paper), running wheels, or treadmill assessment.



Muscular strength

Rotorod, Grip strength test.

PAIN

The assessment of pain in rodents involves observing surrogate measures of pain and/or using automated tests. The main tests for the assessment of pain are:



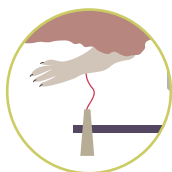
Observational (i.e. grimace scales)

Research has shown that changes in facial expression are not limited to humans but also provide a means of assessing pain in many laboratory species, including rodents.



Gait analysis

The animal's walk, or gait, can be a valuable measurement of its pain. Free-walking gait systems, as well as some treadmill systems, offer automated assessments of pain in rodents.

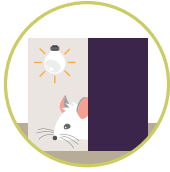


Von Frey hairs

Rodents demonstrate withdrawal reflex when a paw is unexpected touched. A classic test for paw sensitivity, Von Frey hairs use filaments to apply force to a rodent's paw until it bends.

ANXIETY

Many psychiatric illnesses are depression- or anxiety-related disorders. Behavioral tests with rodents are crucial to get insights on the underlying mechanisms and eventually find new treatments. The main tests for anxiety include:



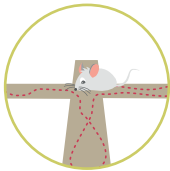
Light-dark box

The light-dark box is used to test the unconditioned anxiety response of rats or mice, based on light and exploratory behavior of rodents.



Open field

The open field test is a straight-forward test to investigate activity, anxiety-related and exploratory behavior of rodents.



Elevated plus maze or zero maze

The elevated plus maze is a well-characterized behavioral paradigm, and is one of the most used tests for anxiety research.

COGNITION & MEMORY

The tests for cognition or learning & memory are the 'classics' when one thinks of a behavioral core. These tests provide the highest translational value and bridge the gap between the cellular/molecular models and the disease states we seek to study.

There are many, many behavioral tests. In fact, there are too many to include here. Below is the list of primary assessments accepted as the norm in behavioral testing:



Water maze

A popular and well-validated test for spatial learning, and one of the most-used behavioral tests in neuroscience research with rat and mouse models.



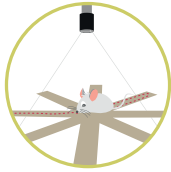
Classical conditioning (i.e. fear conditioning)

Fear conditioning is a form of Pavlovian learning where the subject learns to associate stimuli with a negative (aversive) stimulus or situation.



Novel object recognition

Novel object recognition is a highly validated test for recognition memory, mostly used to test the efficacy of memory enhancing compounds, and other influences on memory.



Radial arm maze or T/Y maze

The radial arm maze is a test for spatial-, working-, and reference-learning and memory in rats and mice, for several sophisticated test protocols.



Barnes maze

The Barnes maze is a paradigm to study spatial learning and memory. It consists of a circular table with holes around the circumference.



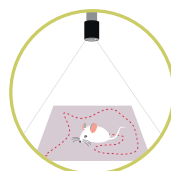
Operant conditioning (self-administration)

This is a learning test used in animal studies to either reinforce or diminish (extinct) certain behaviors.

SOCIAL INTERACTION

Animals display a range of social behaviors, including sexual and mating behavior, agonistic behavior, and maternal behavior. These behaviors can be studied in a pair or group of animals, but researchers can also study how individual animals respond to social stimuli.

In social behavior studies, researchers are often interested in differences between treatment groups or genetic strains. You can use a variety of locations for your research, including an open field or a home cage. The main tests for assessing social behaviors (not related to mating or maternity) include:

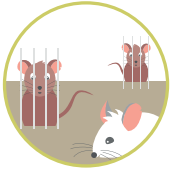


Open field

A straight-forward test to investigate activity, anxiety-related behavior, and exploratory behavior in rodents.

**Resident-intruder**

This test is a standardized method to measure natural offensive and defensive aggression.

**Sociability test**

Designed to test the social behavior or social memory of one individual towards others, this three-chambered cage is used to study the subject's interest in a social stimulus.

CHOOSING YOUR TESTS

There are a lot of tests listed. This isn't a complete list, rather a guide to the standards accepted by the behavioral research community. When designing your core, it is important to choose which tests from these categories you want to use. Your goal is to provide variety and versatility.

CHOOSING YOUR TESTS: GET CATEGORICAL

Start by choosing one or two tasks from each category. For example:

- **Home cage** - Assessment of eating, drinking, and movement
- **Motor function** - Open field and automated free-walking
- **Pain** - Automated free-walking
- **Anxiety** - Elevated plus/zero and open field
- **Learning & memory** - Water maze, novel object recognition, and fear conditioning
- **Social interaction** - Sociability test

SIDE NOTE: ADDING SECONDARY TASKS

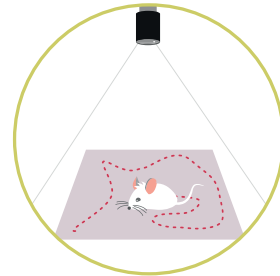
In addition to having versatile, 'primary' behavioral tasks, note the mission and focus of the other cores on campus or your department as a whole. In addition to the tasks listed above, the tasks below may add additional value to your core. Example secondary tasks could include:

- Porsolt/forced swim or tail-suspension
- Marble burying
- Olfactory discrimination

- Acoustic startle
- Ultrasonic vocalizations
- Cincinnati maze

VERSATILITY IN ACTION: THE OPEN FIELD TEST

The open field is the corner piece of any behavioral core. With it, you can assess locomotor activity and anxiety behaviors. Furthermore, you can add objects to conduct the novel object recognition test or put two animals in the arena to assess social behavior. Read more on the versatility of the open field test.





HOW

*Planning, setting up
and maintaining
your core*

THE LOGISTICS OF BUILDING A CORE

In this section we will address the following topics with regards to the logistics of building a core:

- Location, key to success
- Room configuration and lighting
- Scheduling and management
- Financing the core
- Promote your core facility
- Protocols and SOPs
- Accountability

LOCATION, KEY TO SUCCESS

The location of your behavioral core is vital to its success; however, its location is highly dependent upon your available space and your institution's animal housing facility.

Think about your userbase and where they are located. Can your users transport animals across campus and/or through buildings? If not, you run the risk of alienating those users.

A solution would be to offer a temporary housing space near your testing rooms, where outside animals can live during testing. Ideally, your core facilities will be adjacent or exceptionally proximal to your housing facility.



YOU HAVE TO HAVE OPTIONS

No matter where it is located, the core has to provide flexibility in terms of testing space and services.

PLANNING

It's possible that the lab could take months to establish. During that time, you should be interviewing personnel, ordering equipment, negotiating space, etc. You might have to start small or with limited capacity, i.e., one room a few tests, and expand gradually. There is no established protocol for this; it is always university or department specific.

ROOM CONFIGURATIONS & LIGHTING

ROOM CONFIGURATION

In many cases, your core is going to have to work with what is provided. Here are some tips to consider when designing your core layout:

- **Avoid reflection**

Make sure the walls in the testing rooms are not shiny and reflective. This will ensure proper lighting throughout.

- **No windows in your testing rooms**

The worst thing you could do in a core is have windows! Not having windows allows you to control the room lighting and potentially decrease any outside noise.

- **Use negative airflow**

There are many [resources online](#) for establishing negative pressure. It is best to work with your Facilities Management as this will ensure that your testing rooms have no influence upon each other, or that any adjacent office(s) impacts your research.

- **Animal housing**

Include enough space to hold the animal cages of those not undergoing testing. The location of this 'holding room' should be centrally located and not in a testing room itself.

- **Storage**

For extra equipment, cleaning and/or handling supplies, etc.

Depending on the amount of space allocated for your core, the design and room configuration will depend heavily upon the tests you offer. For example, if you want a water maze, try to get a room with a sink and/or drain. It is also likely that this room will only be used for water mazes since it cannot be easily taken down, unlike the open field, elevated plus maze, or Barnes maze, which are more portable and can be placed in your storage room when not used.

Before you place the equipment, check with your potential users to find out which tests are going to be used the most or take the most amount of time to run. This will allow you to configure your testing rooms to maximize space and avoid any unnecessary bottlenecks.

LIGHTING

All testing rooms must be equipped with adjustable lighting; if possible, make the lighting diffuse and arrange your lights around the room. Invest in a lux meter and check the literature for optimal lighting, although expect to see wide ranges (i.e., 2 – 647 lux for the open field).

Even, diffuse lighting is essential if you are using automated tracking. Some cores and researchers suggest including red light into your testing. These lighting variations will differ depending on your particular set of tests. Check with your core's facilities management and, most importantly: do not use overhead fluorescent lighting!

SCHEDULING & MANAGEMENT

Some cores prefer to run everything through the manager, who maintains a schedule using a Google Calendar. It is an easy, zero cost solution. However, if your users want to schedule their own time, consider using scheduling software such as [Stratocore](#) or [iLab Organizer](#). Other cores, such as the genomics or pathology cores, might employ other LIMS (Laboratory Information Management System).

It might be useful to check with the other managers on your campus to see if there are options for your own use.



FINANCING THE CORE

Core facilities are, in essence, a non-profit organization within a university. Based on our research, we discovered that the fee structure of a core is divided into two entities: *cores that charge for usage* and *those that don't*.

CHARGING A FEE

The reason to charge fees is apparent: you have to pay for the staff and for the equipment and space. However, the decision on how much to charge is not easy or standardized in North America. Regardless, the goal of the fee structure is simple: recover as many losses as possible without turning a profit. Therefore, the fee structure is going to depend on your core's operating costs and the amount of time spent using the core.

The standard procedure is to charge hourly; however, per-project charges are also suitable. In addition, your core must consider any capital costs, such as new equipment or the maintenance and upgrades of established equipment.



DETERMINING YOUR FEE STRUCTURE

- **Fixed costs**

Determine your fixed costs, such as salaries, consumables, or any other operational costs.

- **Additional capital costs**

Consider any additional capital costs, such as maintenance contracts, software and hardware upgrades, new equipment, etc.

- **Core usage**

Anticipate your core usage by surveying active, current, or prospective users.

- **Yearly updates**

Your core's fees should be updated yearly to ensure you are not over- or under-charging.

SAMPLE FEE STRUCTURES

The fee structure of many cores is listed on the next page, giving the name of the facility and its manager. Two different rates (in dollars) are given: the staff-run hourly rate (the experiments are performed by the staff of the core) and user-run hourly rate (where the user performs the experiments).

GET A DEDICATED ANALYSIS COMPUTER

Get a separate computer, located outside of the testing area, that is used for analysis only. With this analysis setup, you can charge a minimal amount for use (\$10/h or \$20/h) to cover the cost of the computer and any yearly maintenance fees.

CORES WITH NO FEES

Cores that do not charge fees are subsidized by external funding sources; many of them are funded as a Eunice Kennedy Shriver Intellectual & Developmental Disabilities Research Center (an IDDRC).

Another option, most notable for smaller institutions, is to have users donate equipment purchased through their grants. These types of arrangements are only possible with a manager who also maintains their own funding and operates a space for testing and some education, but cannot offer any full-service testing.

Overview of fee structures at a wide range of behavioral core labs.

Facility/university &	Staff-run (\$/h)	User-run (\$/h)
Albert Einstein college of Medicine <i>Maria Gulinello, Ph.D.</i>	90,-	45,-
Cleveland Clinic <i>Tom Jaramillo, Ph.D.</i>	60,-	25,-
Columbia University <i>Mu Yang, Ph.D.</i>	85,-	40,-
Duke University <i>William Wetsel, Ph.D.</i>	48,-	36,-
Harvard University <i>Barbara Caldarone, Ph.D.</i>	80,-	20,-
New York University <i>Adam Mar, Ph.D.</i>	100,-	variable
Salk Institute <i>Nick Andrews, Ph.D.</i>	60,-	25,-
Scripps <i>Alicia Brantley, Ph.D.</i>	user-run + \$100	variable
Texas A&M <i>Alexandra Trott, Ph.D.</i>	user-run + \$30	variable
Tufts University <i>Andrew Tarr, Ph.D.</i>	75,-	20,-
University of Washington <i>Toby Cole, Ph.D.</i>	0,-	0,-
UC Davis <i>Jill Silverman Ph.D.</i>	63,-	not applicable
UCLA <i>Lindsay Lueptow, Ph.D.</i>	115,-	55,-
UNC, Chapel Hill <i>Sheryl Moy, Ph.D.</i>	40,-	not applicable
University of Houston <i>Colin Haile, Ph.D.</i>	40,-	20,-
University of Kentucky <i>Robert Kline, Ph.D.</i>	40,-	10,-
University of Minnesota <i>Erin Larson, Ph.D.</i>	50,-	10,-
University of Ottawa <i>Kerstin Ure, Ph.D.</i>	30,-	15,-
University of Pittsburg <i>Stacey Rizzo, Ph.D.</i>	70,-	20,-
University of Wisconsin <i>Jules Panksepp, Ph.D.</i>	103,-	23,-
UT Southwestern <i>Shari Birnbaum, Ph.D.</i>	100,-	not applicable
Vanderbilt University <i>Fiona Harrison, Ph.D.</i>	35,-	12,-
Washington University <i>David Wozniak, Ph.D.</i>	45,-	not applicable

PROMOTE YOUR CORE FACILITY

How do you attract users to your core? After all, how can you operate if you have no customers? The key is to demonstrate your value!

- **Spread the word**

It is vitally important that your manager spread the word throughout campus. Give talks to other departments.

- **Online presence**

Create and update your core's website to describe your tests.

Check out these websites to get an idea of how you can communicate your core:

- research.wustl.edu/core-facilities/animal-behavior-core/
- btc.psych.ucla.edu/
- med.umn.edu/neuroscience/research/mouse-behavior-core
- <https://behavior.hms.harvard.edu/>
- einsteinmed.edu/research/shared-facilities/cores/49/animal-behavior-core/

- **Unique Selling Points**

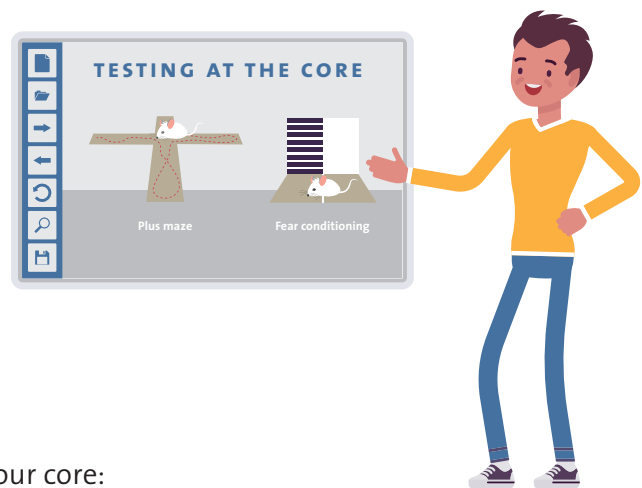
When discussing the core, focus on the possibilities, i.e., what research in the core brings to other users' lives. Demonstrate how you remove barriers and make research-life easier and better (standardized protocols, experts in the field, letters of support with grants, etc.)

- **Networking**

Connect with your vendors and ask them to promote you to other departments on campus or institutions nearby.

- **Organize a party**

Once your core is ready, have a grand opening to raise awareness.



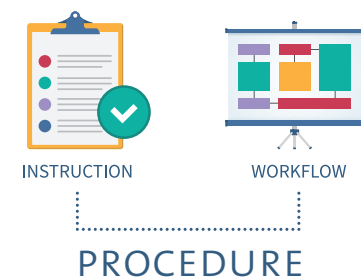
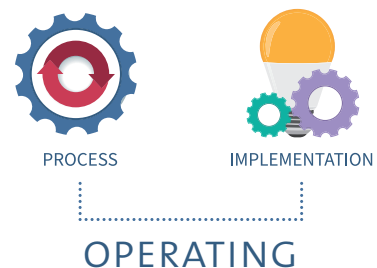
PROTOCOLS AND SOPs

One of the primary goals of this project is to connect core labs throughout North America. Recently, IDDRC core's published a review of data reproducibility using novel object recognition as the paradigm. The field needs more of this! The reason for this need is simple: many standardized tests are not standardized. For example, the size of a mouse open field varies greatly. The 'standard' size varies between 30-40 cm, although there is variation among maze providers: Ugo Basile provides 44x44 cm arenas, whereas, Maze Engineers provides 27x27 cm arenas.

However, with your core, your protocols are the Standard Operating Procedures (SOPs) by which all testing will be done. Your protocols will be approved by IACUC. In turn, you can provide your protocols to your users, who can add it to their own.

When setting up new tests, contact other core managers to ask them what does and does not work. Finally, the more communication with your IACUC or Animal Care, the easier it will be to approve new protocols and ensure no missteps for users.

Testing protocols vary by core and/or institution. If you are interested in obtaining a protocol for any of the behavioral tests listed in this guide, please contact our contributors (listed at the end of the publication).



ACCOUNTABILITY

Focus on providing the best possible space for the animals and the best possible environment to collect quality, reproducible data!

BROKEN OR DAMAGED GOODS

The relationship between the core and its users must rely on trust and open communication.

- **Things in the core will break**
Accidents will happen, regardless of intent.
- **Broken parts must be replaced, and service calls must be made**
Down-time could ruin an experiment, no matter who or what is the cause of the disturbance.
- **Create a forum (online or on paper) for users to report broken/defective items**
When communicating with your users, focus on the functionality of the equipment and the safety of the animals, not the intent of the users or who was to blame!

SUPERVISING USERS

Cleanliness must prevail. Sometimes this means reminding students not to wear heavily scented lotions or perfumes. Other times it means communicating with a PI on what it means to clean the testing area after all the animals have been run for a day.

If at all possible, make your rooms require badge access, creating a digital record of every person in or out of the core. This will create transparency among the users and hold them accountable.





SUMMARY

*Building a
behavioral core*

SUMMARY

The goal of the core is to provide flexible testing space and services. Focus on providing the best possible space for the animals and the best possible environment to collect quality, reproducible data.



Why

- House a centralized testing facility.
- Offer expanded testing services.
- Provide training and expertise.



Who

- Your core will need a team, led by either a PI or a manager.
- Don't forget the technicians and animal care staff.



What

- Choose primary tasks that assess a wide variety of standardized behaviors.
- Have secondary tasks that add additional value to your core.



How

- The location of your behavioral core is vital to its success.
- Create a space that is easy to use, and manage and control.
- Get a scheduling system, set your fees appropriately, and hold users accountable.



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BUTORS

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