RCR AND SRR AT PENN

NEW STUDENT WELCOME AND ORIENTATION 2023

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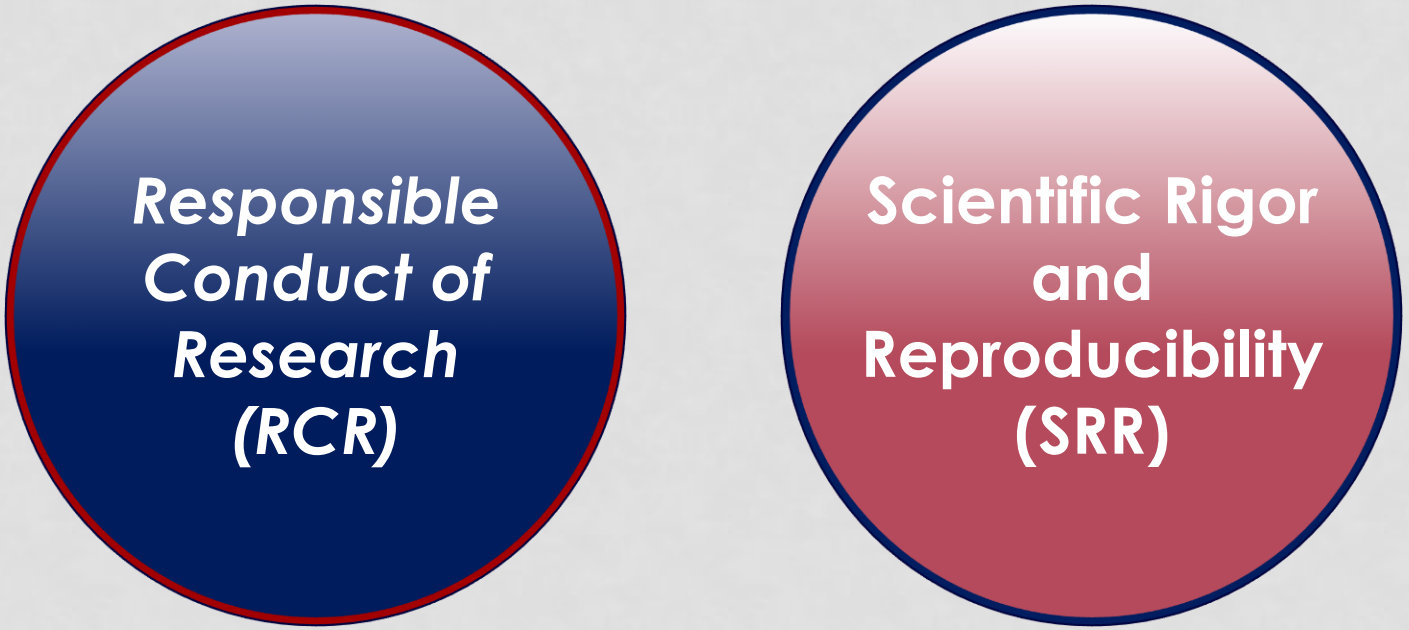
TWO SIDES OF SAME COIN
- EITHER SIDE YOU WIN -



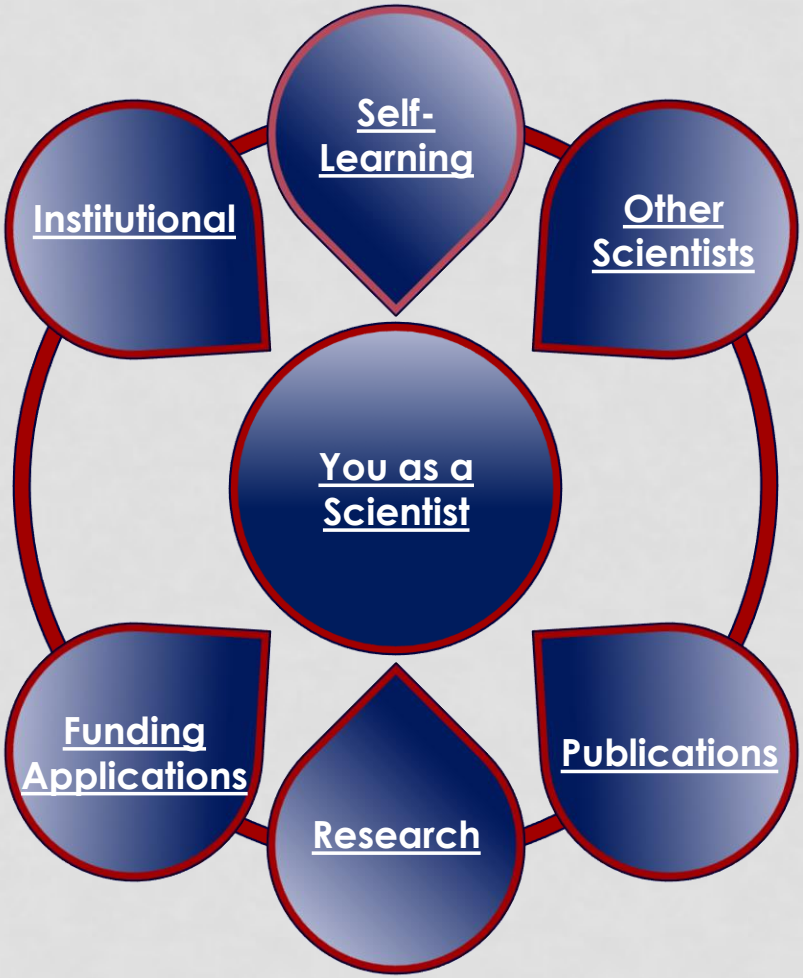
Mandate that research be ethically sound and of rigorous methodological quality.

GOALS FOR TODAY

Develop an **awareness** of best scientific practices.

Provide you with a basic set of **resources and tools** to promote your use of best scientific practices during your training, research, and career.

YOU AS A SCIENTIST



WHAT ARE YOUR PRIMARY GOALS?

- **DO GOOD SCIENCE**
- **KNOW HOW TO IDENTIFY GOOD SCIENCE**
- **HELP OTHERS IDENTIFY AND DO GOOD SCIENCE**
- **All, as you CREATE YOUR 'PROFESSIONAL SELF'!**

Other scientists will know you first from quality of your work – that is your 'professional self'.

RESEARCH INTEGRITY

SHARED VALUES IN SCIENTIFIC RESEARCH

*STENECK, N. H. 2007. *ORI - Introduction to the Responsible Conduct of Research*

, Washington D.C. , U.S. Government Printing Office, p.3

RESEARCH MISCONDUCT

- Fabrication
- Falsification
- Plagiarism

RESEARCH MISCONDUCT

- Serious deviation from accepted practices

RESEARCH MISCONDUCT

- Fabrication
- Falsification
- Plagiarism
- Serious deviation from research practices

Does not include honest error, differences of opinion

UNRELIABLE RESEARCH …

Which reward system leads to misconduct and questionable research practices?

Survival

- Publish lots of papers
- Get lots of citations
- Acquire funding
- Get promoted

Good Research Practices

- Rigor/reproducibility
- Scientific collaboration
- Unrestricted access
- Freely sharing data

Value constancy of results with the goal of building reliable knowledge about the world.

TRAGEDIES

Temptation
Getting my name on this article would look really good on my CV.

Rationalization
It's only a few data points, and those runs were flawed anyway.

Ambition
The better the story we can tell, the better a journal we can go for.

Group and Authority Pressure
The PI's instructions don't exactly match the protocol approved by the ethics review board, but she is the senior researcher.

Entitlement
I've worked so hard on this, and I know this works, and I need to get this publication.

Deception
I'm sure it would have turned out this way (if I had done it).

Incrementalism
It's only a single data point I'm excluding, and just this once.

Embarrassment
I don't want to look foolish for not knowing how to do this.

Stupid Systems
It counts more if we divide the manuscript into three submissions instead of just one.

AREAS THAT REQUIRE RESPONSIBLE CONDUCT

Acquisition and Management of Data
Collaborative Science
Conflicts of Interest and Time
Mentoring
Peer Review
Research Misconduct
Responsible Authorship and Publication
Scientists as Responsible Members of Society
Use of Animals in Research
Use of Humans in Research

Provide you with **resources and tools** to promote best practices

TRAINING IN RCR/SRR

Your training in RCR/SRR is continual.

Why?
See concepts several times; In different **contexts**

= they are "sticky"!

- On-line instruction ('Knowledge Link') KNOWLEDGELINK
- Workshop-based using 'Case Studies'
- RCR-focused lab meetings

NIH RCR RESOURCES

Responsible Conduct of Research Training

"…applies to all NIH Institutional Research Training Grants, Individual Fellowship Awards, Career Development Awards (Institutional and Individual), Research Education Grants, Dissertation Research Grants, or other grant programs with a training component …"

OFFICE of the VICE PROVOST for RESEARCH
UNIVERSITY of PENNSYLVANIA

RESEARCH RESOURCE HUB

- Hub Home
- Initializing Research
- Research Team Management
- Research Design Tools
- Rigor and Credibility
- Electronic Notebooks
- Data, Analysis, and Management
- Dissemination: Presentation and Publication
- Commercialization for Societal Impact
- Connecting to the Community

Responsible Conduct of Research (RCR) – scientific rigor and reproducibility, research integrity, stewardship

https://research.upenn.edu/resources/hub/

Biomedical Graduate Studies

Responsible Conduct of Research (RCR) and Scientific Rigor and Reproducibility (SRR)

https://www.med.upenn.edu/bgs-rcr-exdesl

BGS RCR/SRR WEBSITE

Biomedical Graduate Studies

Responsible Conduct of Research (RCR) and Scientific Rigor and Reproducibility (SRR)

- Overview
- Responsible Conduct of Research (RCR)
- Scientific Rigor and Reproducibility (SRR)
- PhD Student Requirements
- MD/PhD Student Requirements
- Faculty Requirements
- Faculty Reporting

Overview

BGS requires all of its predoctoral students to be trained in i) Responsible Conduct of Research (RCR), and ii) Scientific Rigor and Reproducibility (SRR).

Training in RCR is achieved through lecture, web-based programs, small group workshops, and RCR-focused lab meetings. Training places an emphasis on the involvement of faculty and satisfies requirements set by the NIH for individual fellowships and training grants.

Training in SRR is achieved through lecture and SRR-focused lab meetings. Training similarly places an emphasis on the involvement of faculty and satisfies requirements set by the NIH for individual fellowships and training grants.

Students and faculty share responsibility in complying with required training. It is imperative to understand that failure to comply with training puts funding for training, and consequently research in general, at serious risk at Penn. BGS requires and actively monitors compliance.

CASE STUDIES

- You will read ‘Case Studies’ often
- These are a source for discussion
- In small groups to promote comfortable discussion
- Each group has a ‘facilitator’
  - One who guides, not lectures
  - (for some topics) there will be no perfect answer

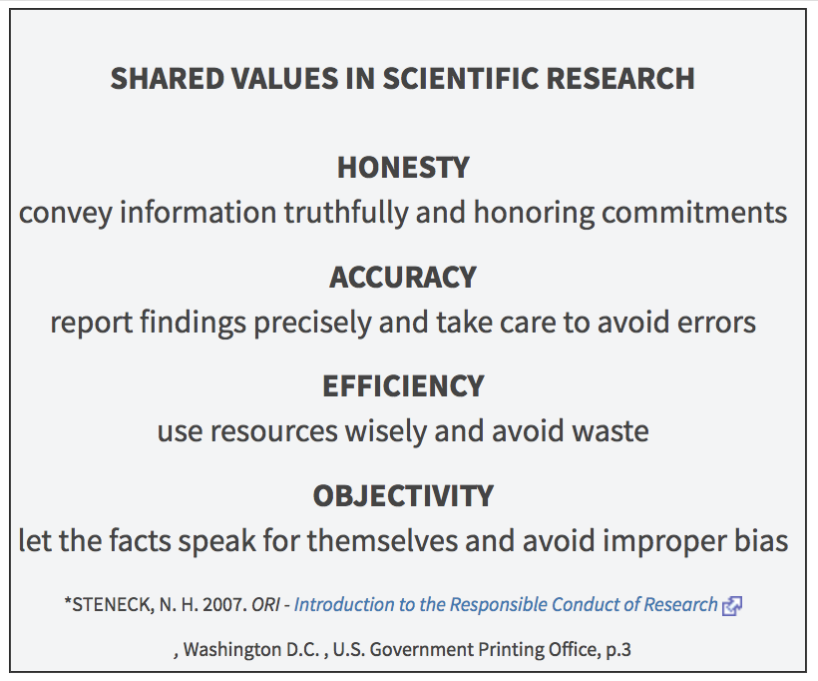
CASE STUDY

The researcher rationalizes that 2 of the runs were flawed, and only reports the single "best" run during a lab meeting.

The result excites the PI so much they include it as a figure in a submitted grant proposal.

CASE STUDY

How do you rate this researcher in terms of



What about the PI? What is/was their role?

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CASE STUDY

You seek out your mentor who encourages you to quantify the outcomes. You find a result that, although statistically insignificant, appears highly reproducible.

You are unsure how to proceed as the result really does not answer your original question and is not significant anyways.

CASE STUDY

What would you do in this case?

It is significant that a result is repeatable especially with working controls and a quantified outcome!

It is often worth re-thinking both the design and premise of your experiment in these cases.

Perhaps there is some critical uncontrolled variable or there are multiple underlying causative factors.

There may be an exciting discovery that is distinct from the original question!

RCR TAKEAWAYS

RCR TAKEAWAYS

If you observe misconduct or feel you are being pressured to perform misconduct, seek out a colleague who you trust and can assist you.

- PI, senior lab member, faculty advisor, program administrator
- Go up the chain step-by-step

Science self-corrects so give involved scientists chances to remedy any disagreement.

RCR TAKEAWAYS

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READY, SET, EXPERIMENT!

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Penn Biomedical Graduate Studies

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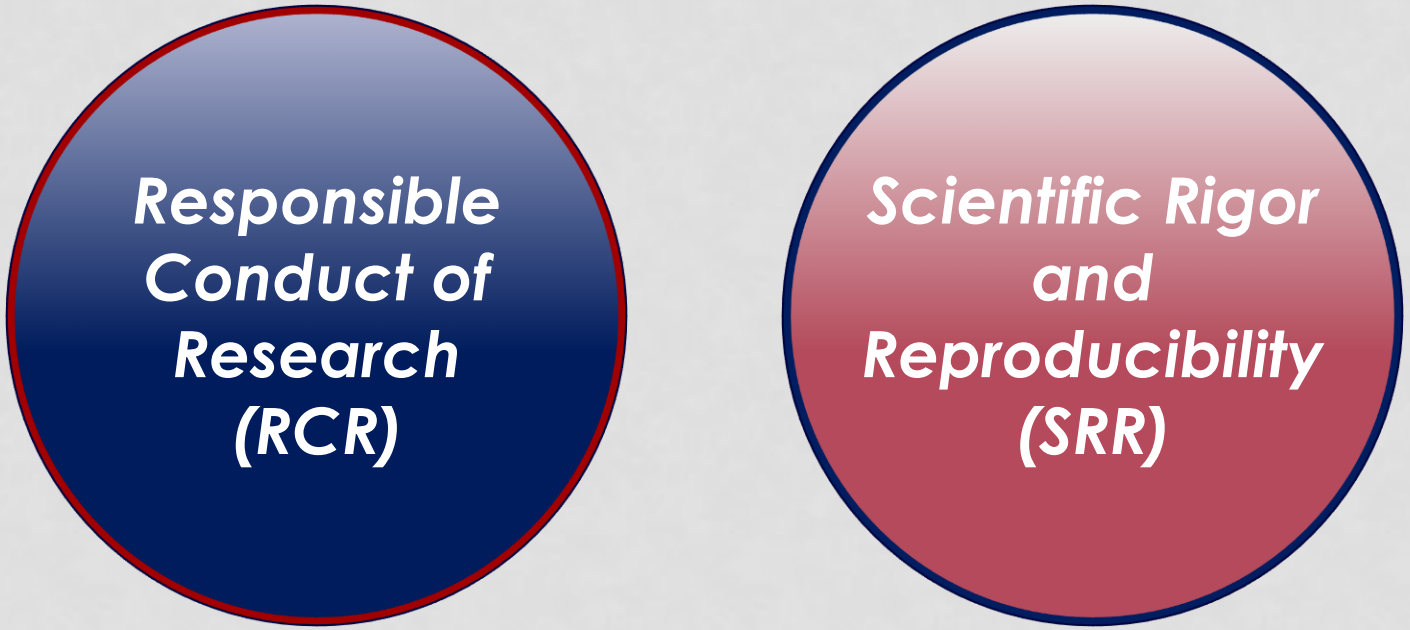


Mandate that research be ethically sound and of rigorous methodological quality.

REPRODUCIBILITY IS FOUNDATIONAL BUT DIFFICULT TO ACHIEVE

eLife

Investigating the replicability of preclinical cancer biology

Timothy M Errington[1]*, Maya Mathur[2], Courtney K Soderberg[1], Alexandria Denis[1†], Nicole Perfito[1‡], Elizabeth Iorns[3], Brian A Nosek[1,4]

REPRODUCIBILITY IN CANCER BIOLOGY

Challenges for assessing replicability in preclinical cancer biology

TIMOTHY M ERRINGTON*, ALEXANDRIA DENIS†, NICOLE PERFITO‡, ELIZABETH IORNS AND BRIAN A NOSEK

46% replication rate

FACTORS THAT AFFECT REPRODUCIBILITY

Technical

- Unvalidated reagents
  - antibodies, cell lines
  - RNAi
- Contaminated cell lines
- Batch effects
- Sophisticated techniques
- Natural variability

Experimental Design

- Study design flaws
  - small sample size
  - non-validated system
- Inappropriate statistics
- HARKing
- P-hacking/multiple testing
- Confirmation bias

Human

- Inadequate method reporting
- Poor archiving
  - Reagents, data, code
- Mistakes/fraud (minor)

Culture

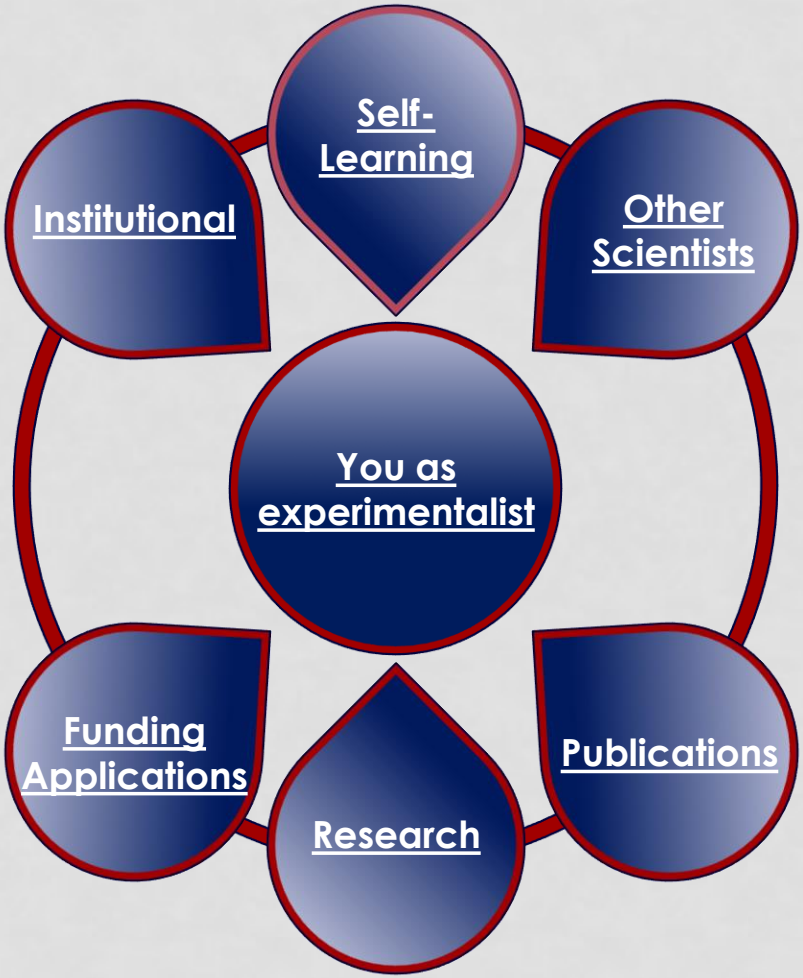
- Publication bias
- Novelty over replication
- Lack of incentives
- Hyper competitiveness

SCIENCE SELF-CORRECTS IN THE LONG TERM BUT NOT SHORT TERM

What short-circuits self-correction?

- **Poor Training in Experimental Design/Statistics**
- **Lack of Openness/Transparency**
- **Publication Practices – Blind to negative data**
- **Culture – "Survival" reward system**

YOU AS EXPERIMENTALIST



A GOOD EXPERIMENTALIST…

Designs non-biased, effective experiments using a well-conceived plan

Produces results with

-high reproducibility

-high predictive value

Key concepts:

- **AWARENESS of different frameworks**
  - **hypothesis, model, question**
- **Parameters defined PRIOR to experimentation**
- **AVOID biases and inappropriate data filters**

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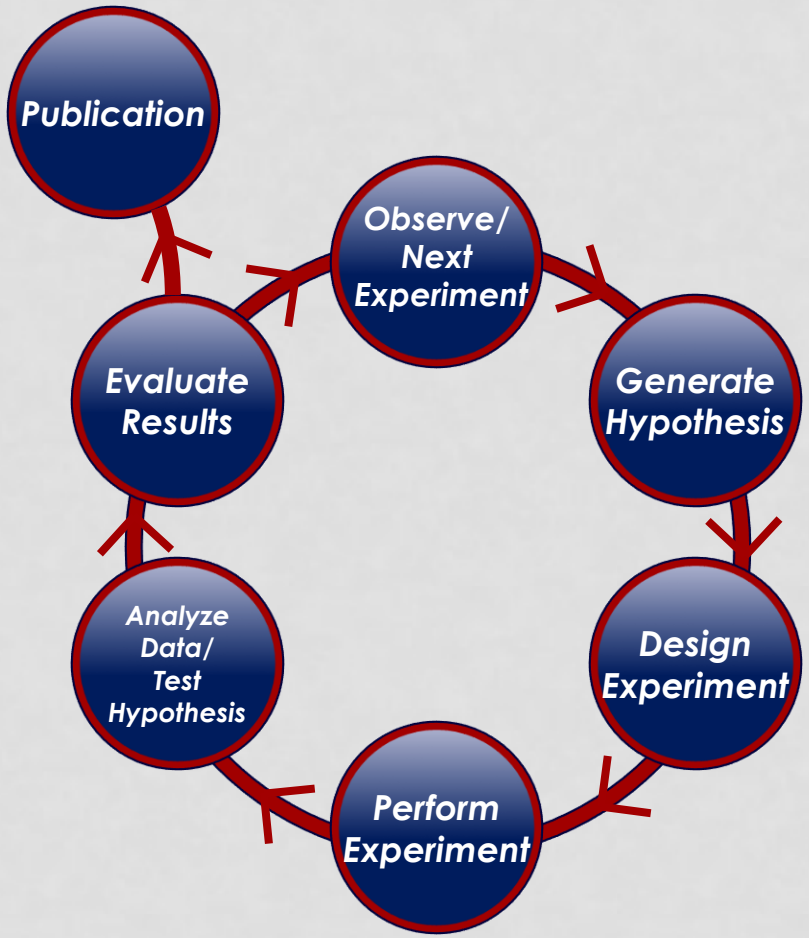
EXPERIMENTS ARE WELL-CONCEIVED PLANS

- **Experiment is: the whole**
- **Experimental design**
  - Clearly-defined hypothesis including statistical procedures
  - System validation
- **Data collection**
- **Analysis**
- **Interpretation**



GOOD EXPERIMENTALISTS ARE AWARE OF TRAPS

Poor Reporting
Non-transparent/ Poor data visualization

Publication bias

Failure to control for bias

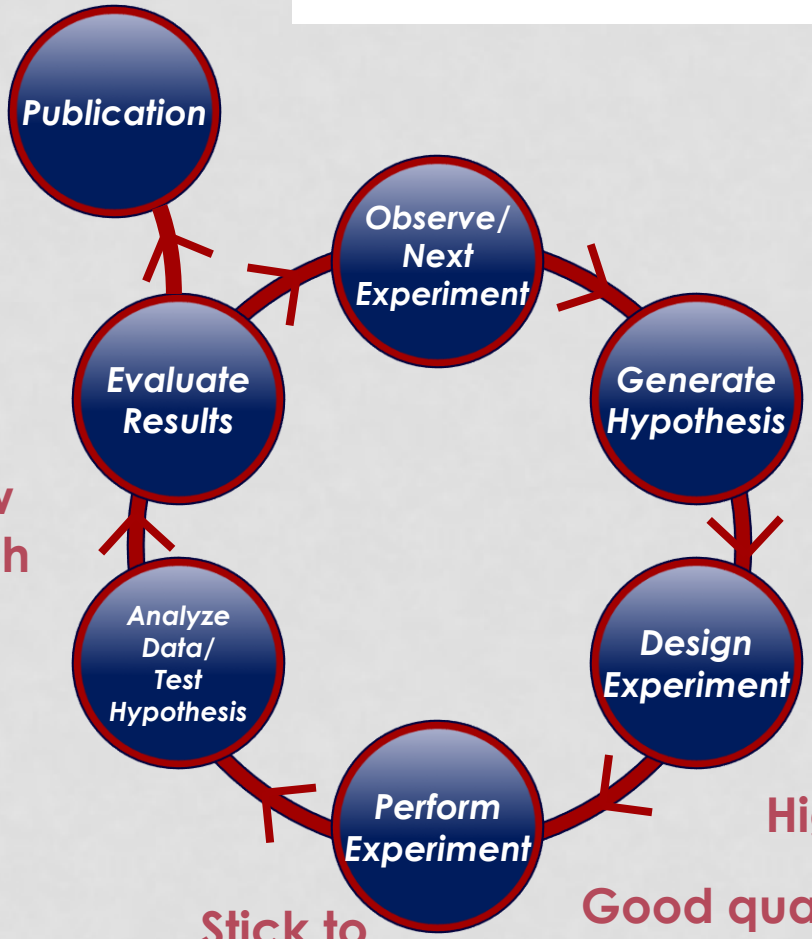
Poor statistics/ Low statistical power

Poor quality control

***P*-hacking**

GOOD EXPERIMENTALISTS AVOID TRAPS

Transparent/
Informational data
figures



Reward
reproducibility
Balance with
novelty/impact

Follow
through

Controlled
for bias

Correct statistics/
High statistical power

Good quality
control

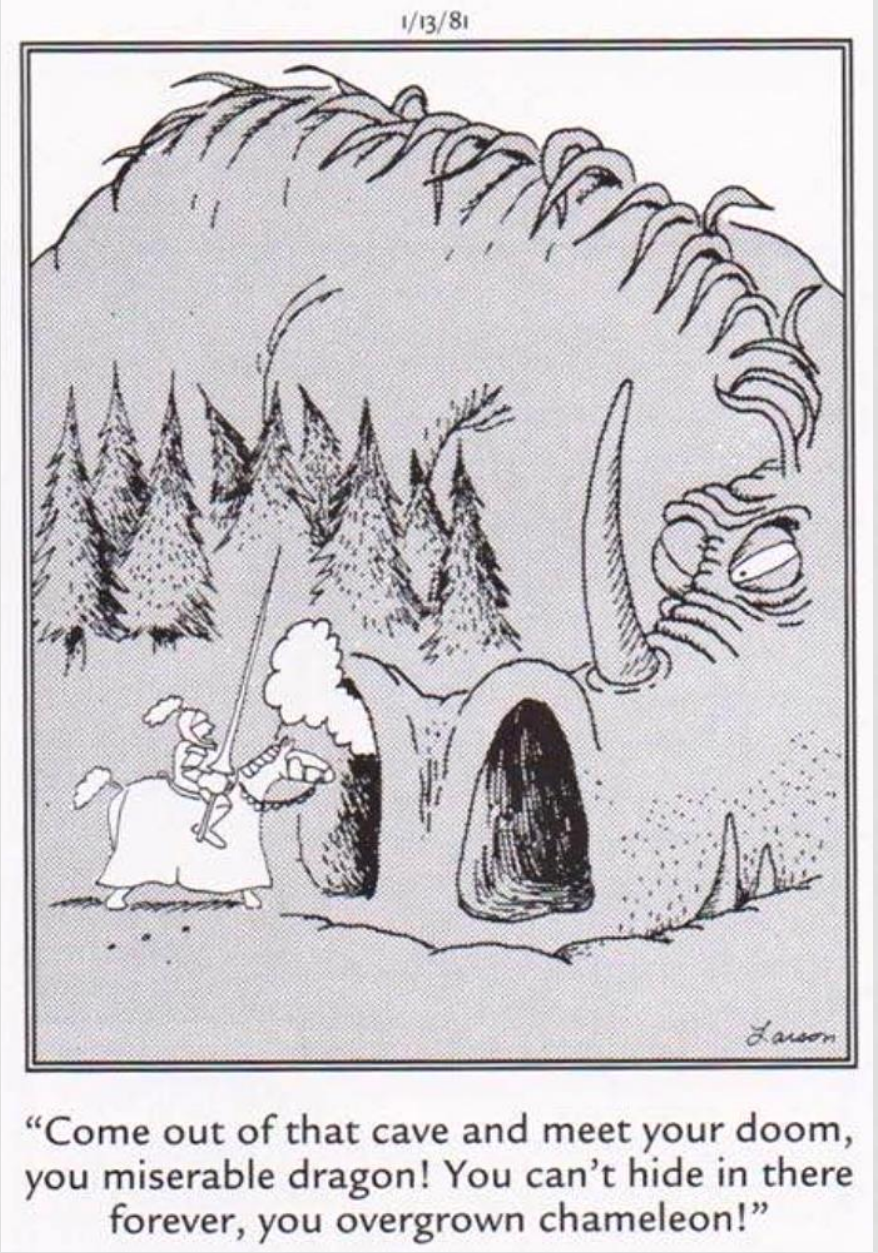
Stick to
the plan

Be aware: Opportunities for deception are plentiful.

Your expectations can influence what you see.

It is easy to be fooled!

Good experimentalists are aware of these traps.



Far Side, Gary Larson

WHAT'S IN IT FOR YOU?

Promotes experimental quality: ***learn something new every experiment***

Facilitates reproducibility

Avoids bias

Saves time, resources, and avoids frustration

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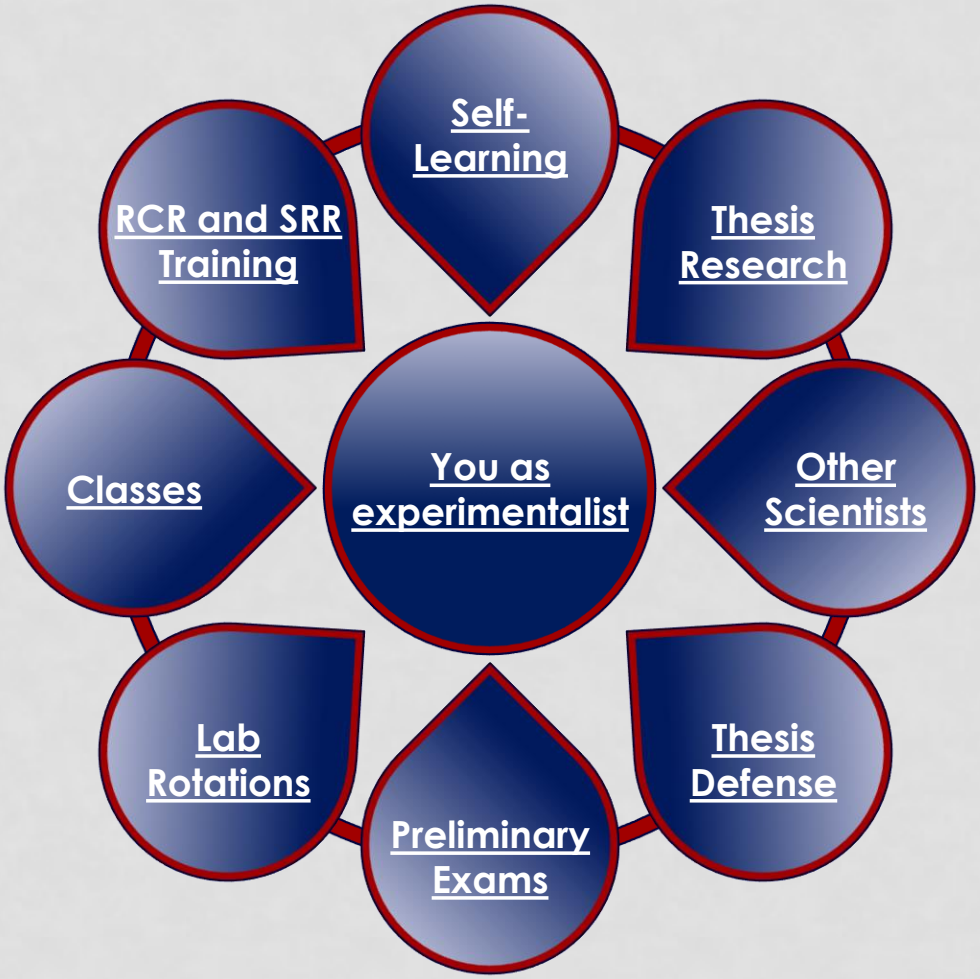
EXPERIMENTAL DESIGN WITHIN BGS



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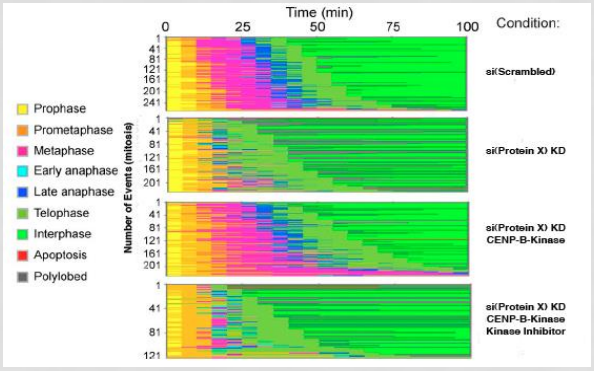
COURSES

You will be asked about the experimental basis of knowledge!

BIOM 5550 Regulation of the Genome
NGG 5730 Systems Neuroscience CAMB 7060 MVP Core
GCB 5360 Fundamentals of Computational Biology
IMUN 5070 Immunopathology
PHRM 5320 Human Physiology GCB 5340 Experimental Genome Science
NGG 6050 NeuroCore: Quantitative Rigor and Reproducibility in Neuroscience
BMB 5100 Data Analysis and Scientific Inference
CAMB 6050 CAMB First Year Seminar GCB 5330 Statistics for Genomics and Biomedical Informatics
PHRM 6230 Fundamentals of Pharmacology
PHRM 5990 PGG Journal Club
BSTA 6300 Statistical Methods and Data Analysis I
EPID 7010 Introduction to Epidemiologic Research CAMB 6100 Molecular Basis of Genetic Therapies
BIOM 6000 Cell Biology and Biochemistry
IMUN 5060 Immune Mechanisms
BSTA 6600 Design of Observational Studies
NGG 5720 Electrical Language of Cells
IMUN 6010 Molecular Immunology
BSTA 6200 Probability I BSTA 6610 Design of Interventional Studies
BMB 5080 Macromolecular Biophysics
BMB 5090 Structural and Mechanistic Biophysics
EPID 6000 Data Science for Biomedical Informatics
CAMB 5120 Cancer Biology and Genetics
PHRM 6240 Medical Pharmacology
BIOM 6100 Foundations in Statistics

Example Exam Question



Given an observation

- describe/interpret data
- formulate a hypothesis
- describe experiments to test the hypothesis
- describe controls
- make predictions
- summarize the results and analysis
- make own conclusions

LABS PERFORM SCIENCE DIFFERENTLY

- Alternative hypotheses/interpretations considered or hypothesis myopia?
- Raw data with all controls shown to the PI? Other senior lab member(s)?
- Equipment/protocols/workflows validated to answer a scientific question? Are there checks embedded to maintain rigor/reproducibility?
- Statisticians/data analysts consulted before experiments?
- Data/code organized, archived and open to all?

CANDIDACY EXAMS

Two years from now you will face your preliminary exam where you will submit and defend a detailed plan about research.

What will you do?
Why will you do it?
Where will you do it?
Who will help you?
How will you do it?
How well do you have to do it?
When will you do it?
How many times will you do it?
How will you interpret the data?
What will happen if you see only a slight difference?

EXPERIMENTAL DESIGN…

requires a detailed plan and sticking to it!

How EXACTLY is the experiment performed?
What EXACTLY is measured?
What EXACTLY will you learn?

Details are critical and we want to hear them!

TAKEAWAYS

- The main goal of a good experimentalist: perform non-biased, effective experiments using a well-conceived plan.

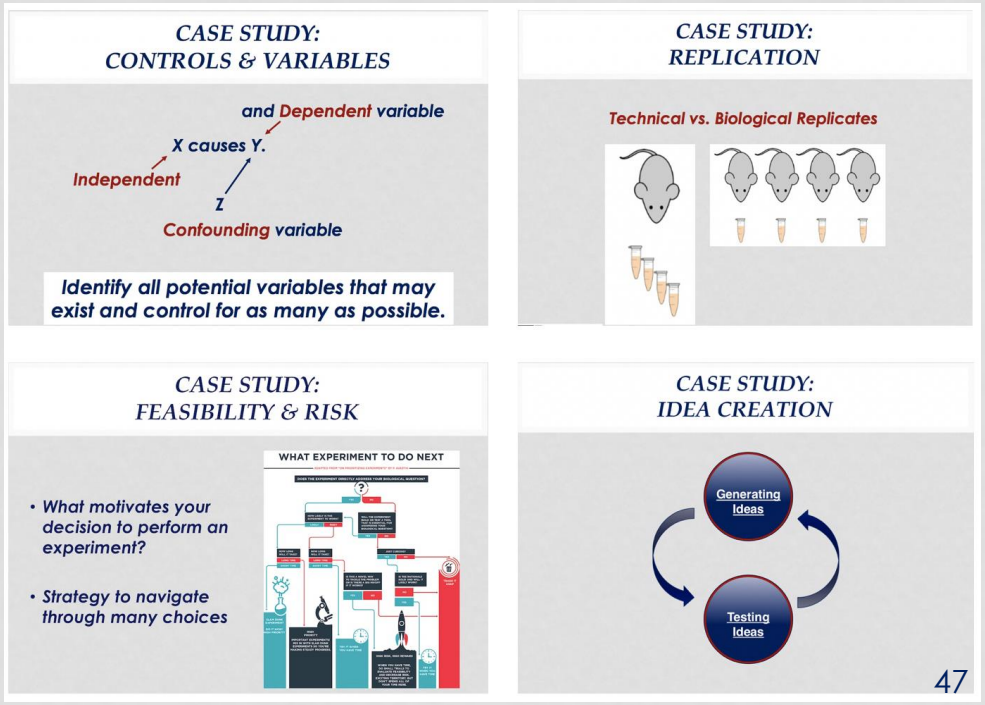
- Design experiments so that you learn something each time.

SCIENCE DELIVERS!
PERFORM EXPERIMENTS!

Give the data the final word!

CASE STUDIES

- ***Controls and variables***
- ***Replication***
- ***Feasibility and risk***
- ***Idea Creation***



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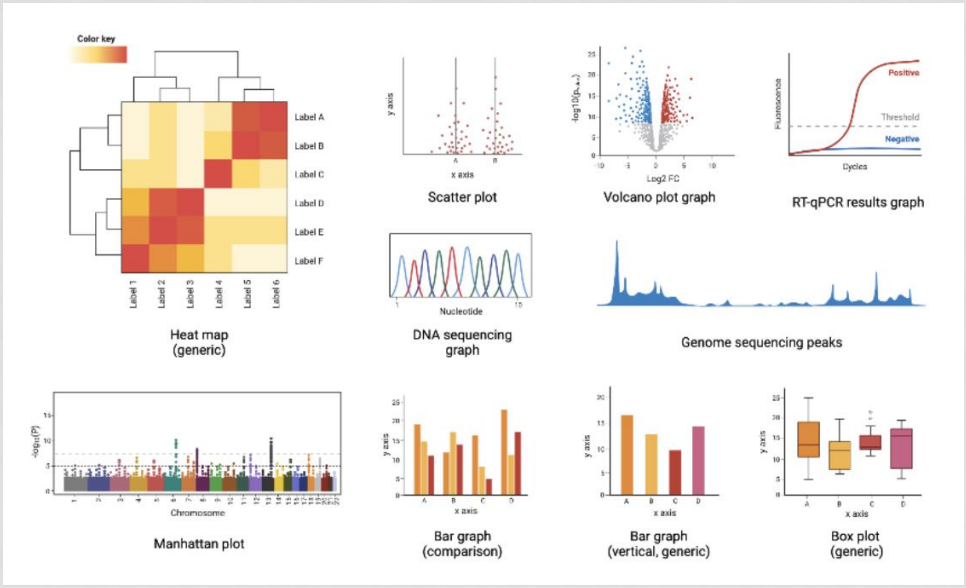
SMALL GROUPS



Groups 1 - 4 251 BRB
Groups 5 – 9 252 BRB
Groups 10-16 BRB Lob
Group 17 253 BRB
Group 18 BRB Lob
Group 19 BRB Aud

Spillover BRB Lobby

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RESOURCE

LET'S EXPERIMENT:
A GUIDE FOR SCIENTISTS WORKING AT THE BENCH

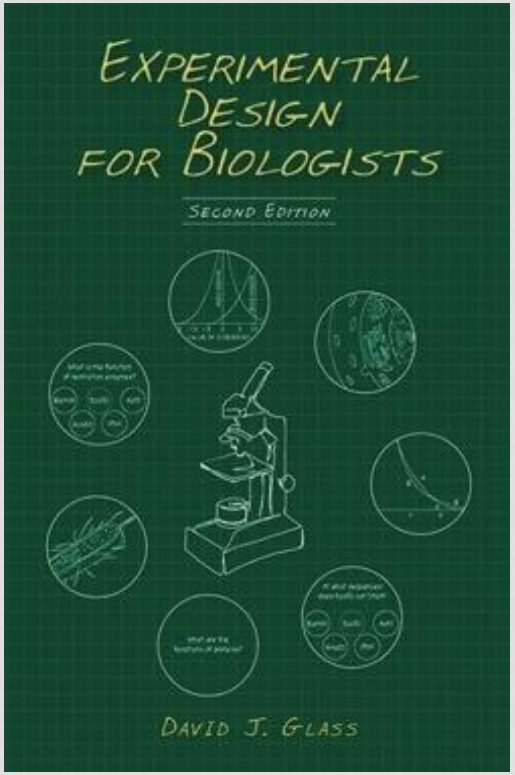
- **Free online course available self-paced, anytime**
- **Tailored for students BEFORE stepping into the lab**

iBiology courses

https://courses.ibiology.org/courses

RESOURCE

- **Based on Experimental Design for Biologists by David J. Glass**
- **2nd ed. 2014. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press.**



BGS RCR/SRR WEBSITE