Research Skills

Week 2

Module Introduction and The Scientific Method & Experimental design

25 Jan 2024

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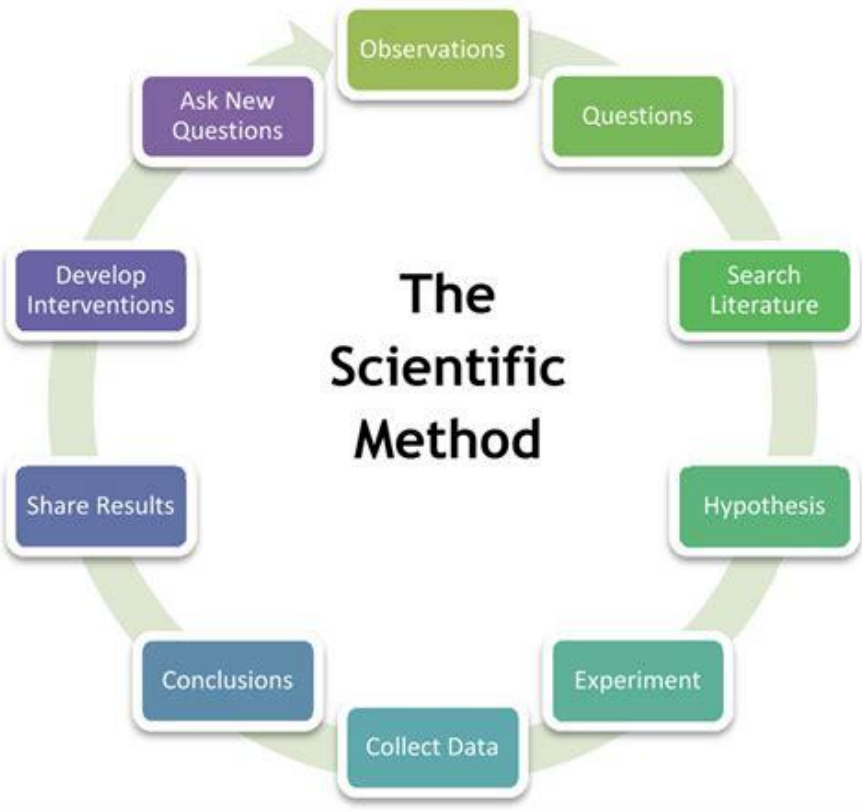

Module Content (summary)

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Experimental Design and Analysis

Week 2 Scientific process part 1

Week 3 Scientific process part 2

Week 4 Research Design: Controls and experimental setup

Week 5 Statistics and calculations

Week 6 Data presentation and interpretation (stats tutorial)

Lab Practicals & results analysis

Week 5 Online Lab, H&S etc.

Week 6 Basic laboratory skills

Weeks 7-9 Laboratory assays

Week 10 Troubleshooting and Excel workshop

Introductions to Research Areas

Week 8

Molecular Biology and Bioinformatics

Week 9

Molecular Modelling

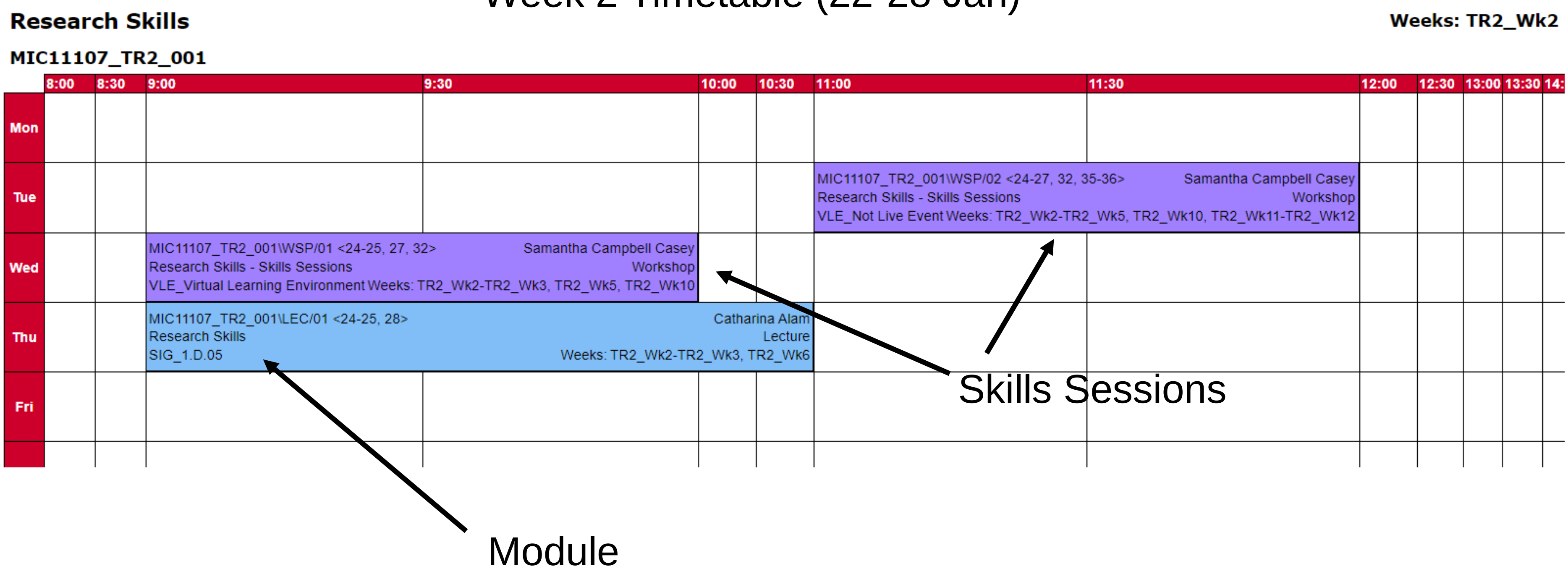
Weeks 11 and 12

Scientific Seminars: Research at Napier

Research Skills module schedule and ‘Research Skills – Skills Sessions’

Please note that the ‘Skills Sessions’ are not directly part of the module and only need to be attended by new students starting their MSc this trimester (not PAS students or Sept starts)

Week 2 Timetable (22-28 Jan)



Module Assessment Structure

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Component 1 (40%)

- Critically interpret and review 2 given data sets and improve the experimental design
- Lectures in week 2-6 will cover topics related to this
- 1200 words total
- DL Monday week 8

Component 2 (60%)

- Write a report on the results from the lab experiments you do in weeks 7-9.
- 4 report sections: Summary, Raw data, Results table/figure and Discussion
- 1000 words total
- DL Monday week 13

Module Learning Outcomes

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This module will provide skills and tools to:

- Understand the Research process
- Critically review research data and interpret results
- Plan (robust) research experiments
- Understand limitations of the research process and (your) experimental data, troubleshoot
- Present data
- Write a scientific summary and discussion

LOs for Today's lecture

After this lecture, you should be able to:

- Explain the process of the Scientific Method
- State some limitations of the Scientific Method
- Understand some possible sources of errors
- Formulate predictions, questions and hypotheses and consider how you could test the hypotheses.

What is science?

- **Science is an organized way of using evidence to learn about the natural world.**
- The goal of science is to investigate and understand the natural world, to explain events in the natural world, and to use those explanations to make useful predictions.
- A way of investigating the world in order to form general rules about why things happen.
- Science is a way of knowing based on experimental or observational evidence and its interpretation.
- Scientists collect and organize information in a careful, orderly way, looking for patterns and connections between events; and they propose explanations that can be tested by examining evidence.
- Science is a discipline largely defined by its primary method – the **scientific method**.

The Scientific Method

- The scientific method is a way to solve a problem

- This is the method on which all projects should be based.

Think Like a Scientist: <u>ASK QUESTIONS</u>

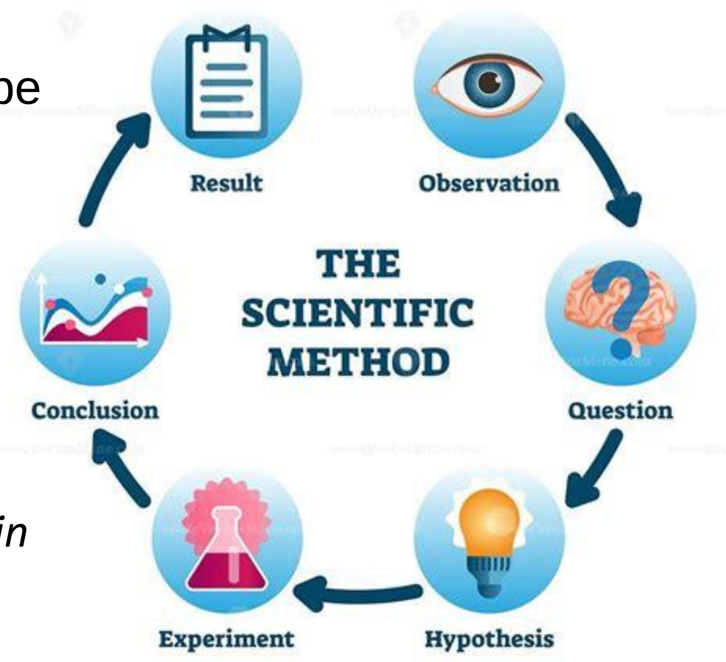
But also: <u>Question the answers</u>

- **Pure Science** - pursuit of knowledge

Example: A study examining the role of a specific protein kinase in cell growth

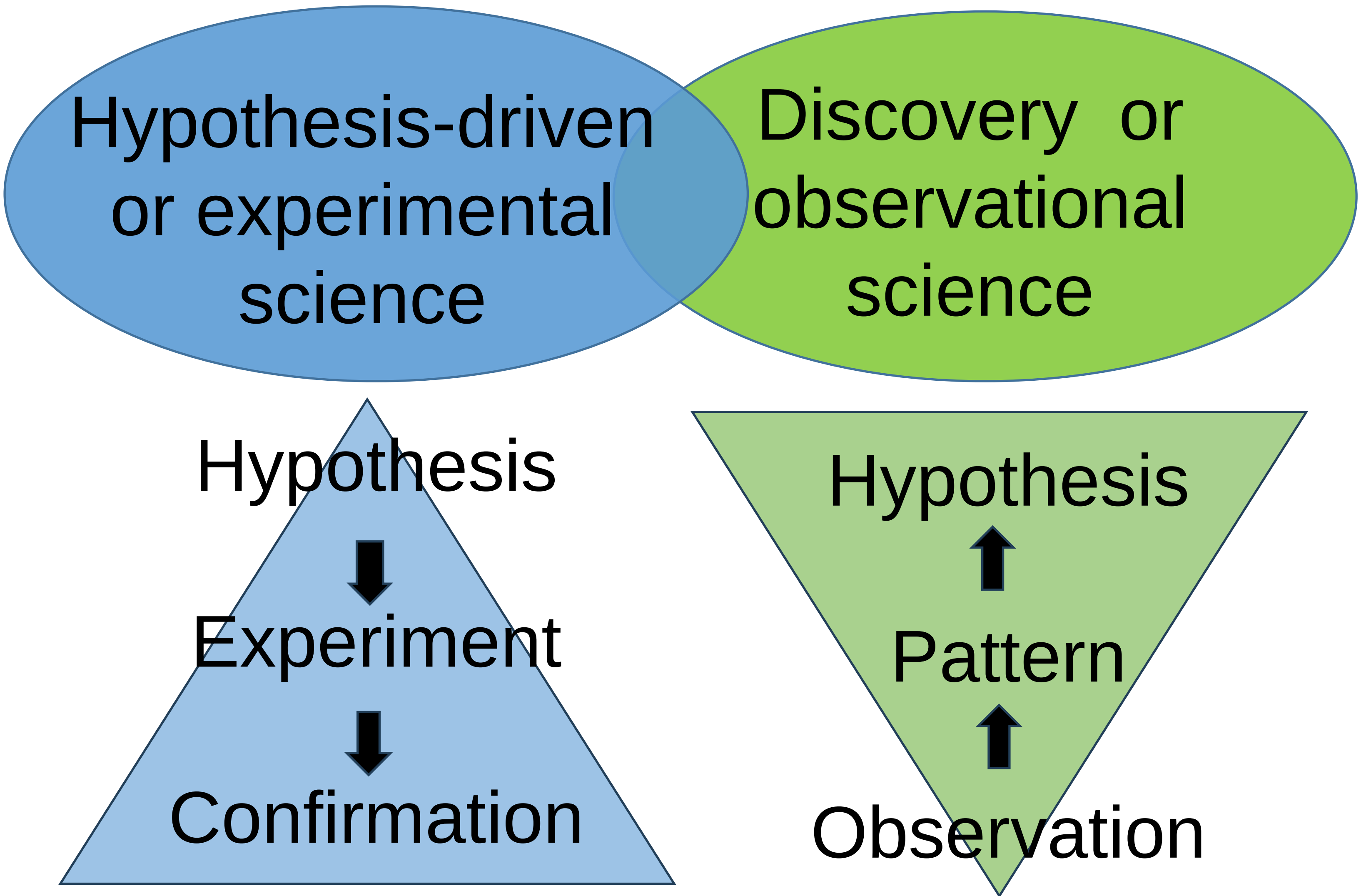
- **Applied Science**- search for practical uses of scientific knowledge

Example: A study examining whether inhibiting the above kinase could be used as a cancer therapeutic, to stop cancer cell growth



Scientists test ideas

Two Primary Approaches to Science:



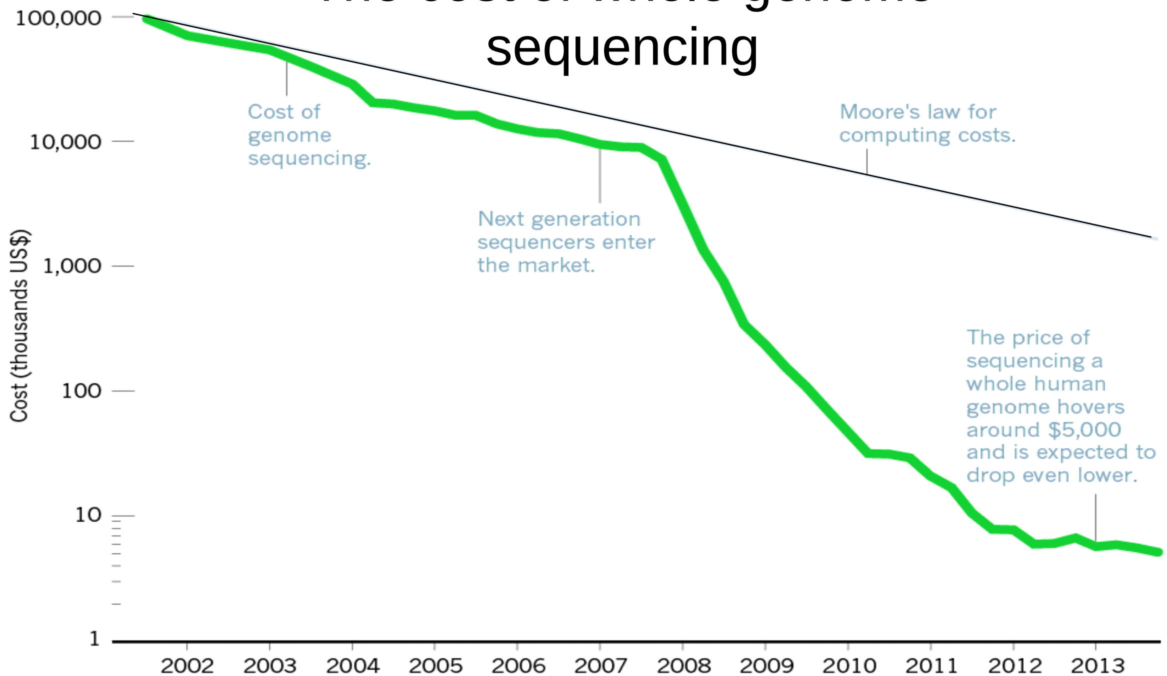
Scientific progress

- Most often, science progresses in small steps
- Although sometimes, specific discoveries or inventions bring about giant leaps and fast progress

The genomics era: Large leaps

1968: one base per month

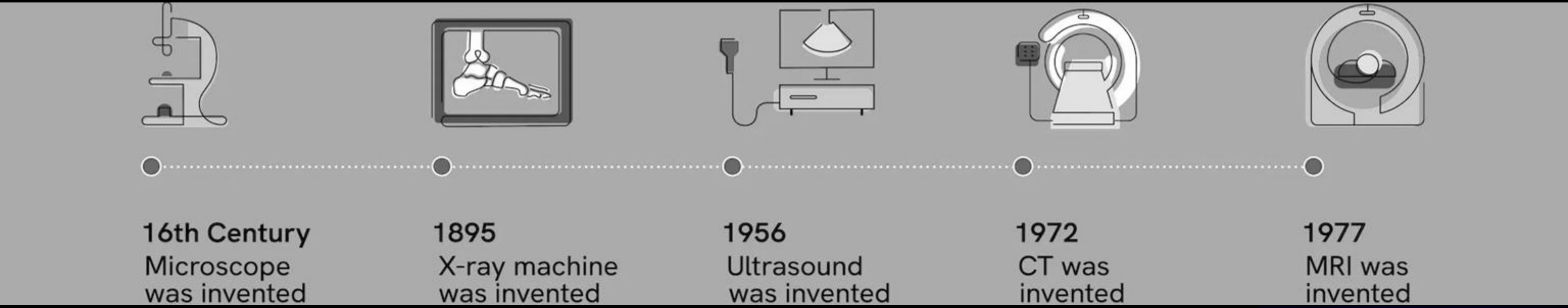
The cost of whole genome sequencing

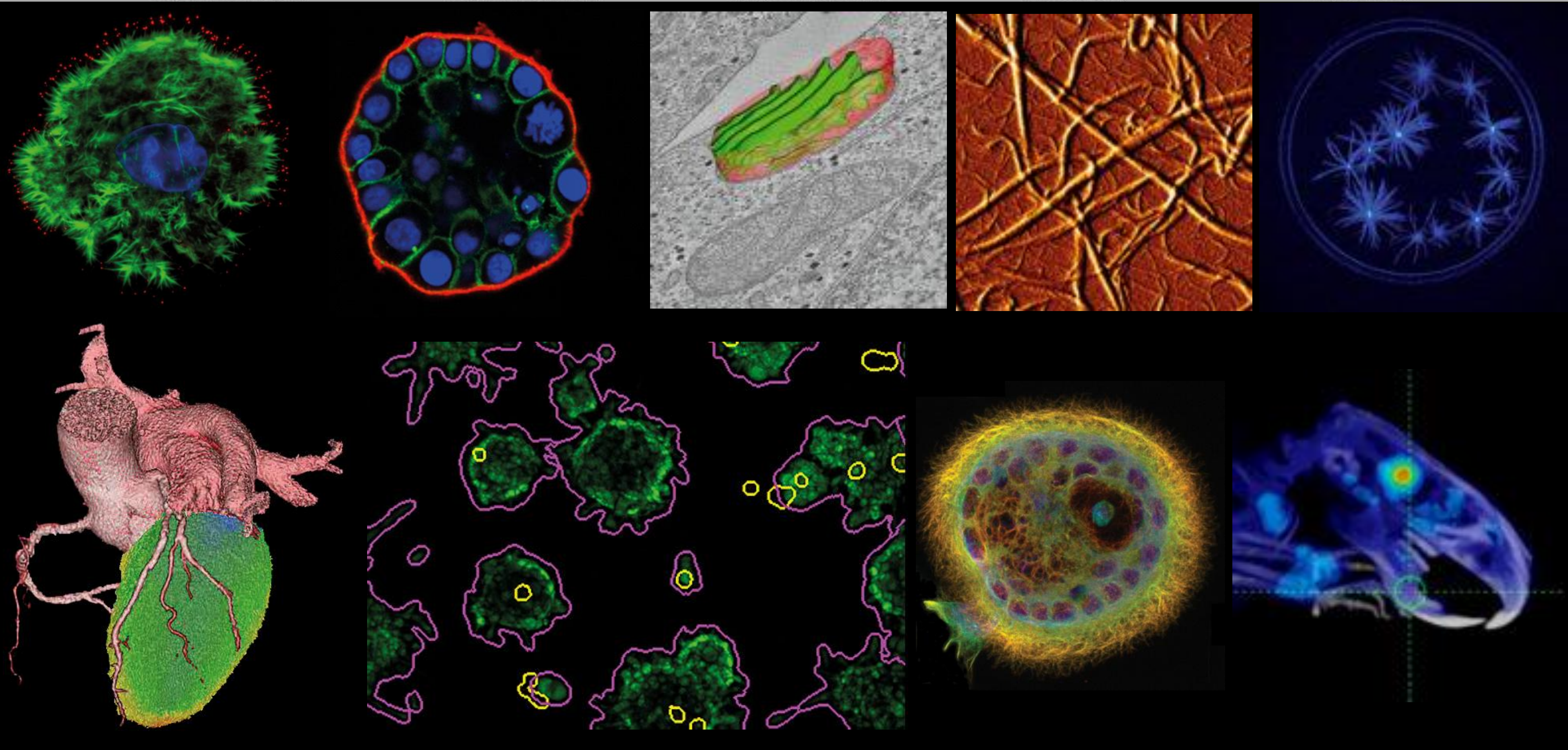


Present day: entire human genome can be sequenced within a few hours

HiSeq X Ten, Illumina

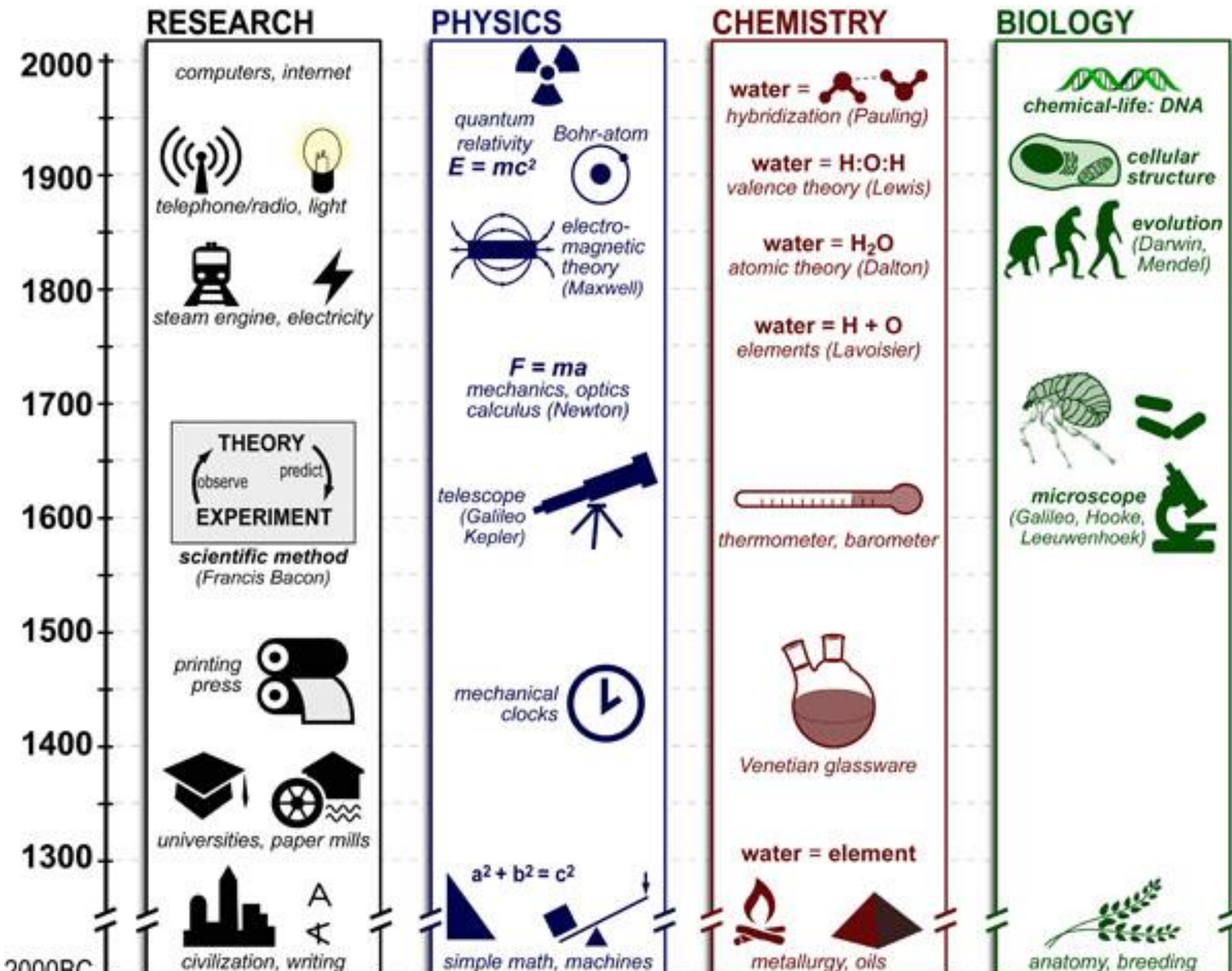
Bioimaging: Large leaps





Progress in Science through time…

…a Eurocentric perspective



Centuries of Scientific discoveries outside Europe!

Progress in Science while Europe was in the Dark Ages

Jabir Bin Hayan (721-815 AD)

- Born in Iraq and practiced in medicine.
- He introduced experimental chemistry and also wrote number of booKs on plants and animals.
- Books are “Al-Nabatat” and “Al-Hayawan”

Bu Ali Sina (980-1037):

- He was born near Bukhara (Uzbekistan).
- He is known as father of modern medicine.
- He was expert in Mathematics, Astronomy, Physics and Paleontology.
- He worked on structure and function and diseases of eyes.
- He described 130 diseases of eye in his book.
- l-Qanun-fil-Tibb ***(The canon of*** ***nedicine)*** was translated into many uropean languages.

Al-Khwarizmi

The word algebra stems from the Arabic word al-jabr, which has its roots in the title of a 9th century manuscript

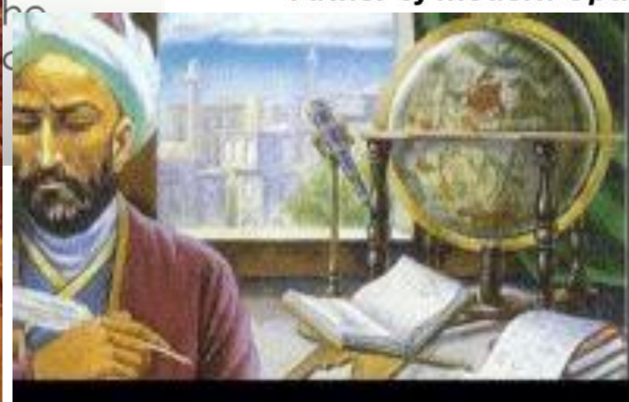
Ibn-ul-Haitham (965-1039):

- He was born in Basra (Iraq).
- He was one the outstanding biologist of Muslim world. He referred sometime as ***“Father of modern Optics”***

mologist.

concept of

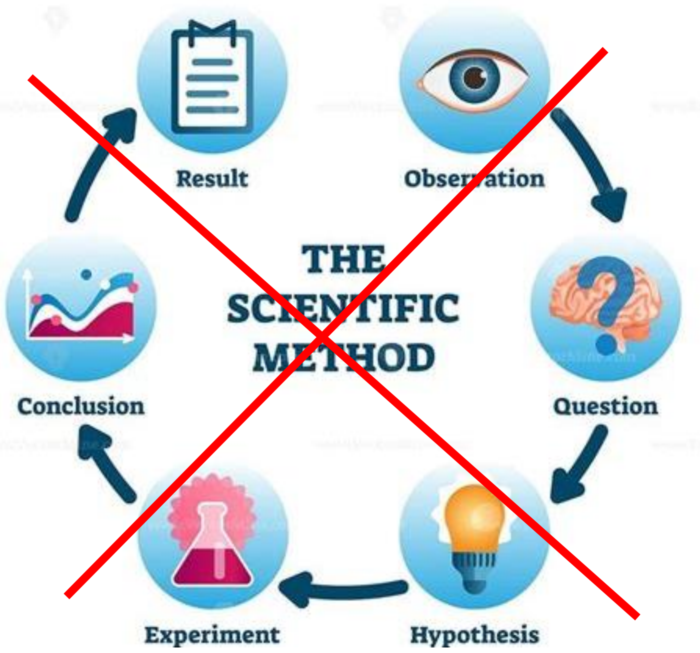
lizanul Hikma”
n, Hebrew,
languages.



Nasir al-Din al-Tusi, a Medieval Persian scholar, put forward the basic theory of evolution 600 years before Darwin was born.

What Science is and is not Activity

- In groups of four or five, propose an explanation for why it rains, without including any scientific thinking in your explanation.
- A member of the group will present its explanation to the class.
- Suppose someone does not believe your explanation, could you supply evidence to support your explanation? Why not?



‘Trust me Bro Science, ‘pseudoscience’ or just plain bad science?

Appears scientific,

- Uses scientific sounding jargon
- Appears to conduct research
- Usually more rhetoric than data: questions
- Fails to follow scientific methods
- Often faults “established scientific community” or claims a conspiracy against revealing “the truth”.

Pseudoscience / Bad science

Pseudoscience is not necessarily fraud; just bad science.

- Extraordinary claims
- Claims usually lack substance
- Practices bias confirmation
- Often pushes particular agenda
- Ignores contrary data
- Value of data often exaggerated

Scientific Explanations

- Science is empirical. It relies on observation and experience.
- The phenomenon studied must be measurable.
- Phenomenon that cannot be measured directly:
    - Subjective questions: Is this painting beautiful?
    - Meta-physical phenomena
- It must be consistent with known natural laws and well-established, well-documented existing theories.
- It must be derived objectively from independently confirmable observations.
- <u>All scientific knowledge must be regarded as tentative</u>.
- Scientific statements must be testable and reproducible (i.e., valid & reliable).

The Scientific Method

Involves the following steps:

- Making **observations** (think of a question)
- Formulating a **hypothesis**
- Designing a **controlled experiment** (variables)
- **Collecting and interpreting data** (conduct experiment)
- Forming a **conclusion** (does this answer your question)
- **Comparing** the conclusion **with existing knowledge**
- **Reporting and publishing** the results
- Developing theories and principles (if new knowledge)

Defining some terms

Hypothesis - "An educated guess"; A testable explanation for an observation a tentative explanation of phenomena. You predict what you think the answer to your question might be based on prior knowledge, logical reasoning and informed, creative imagination.

A hypothesis must be proposed in a way that enables it to be tested.

Theory - A widely accepted explanation of natural phenomena; has stood up to thorough & continual testing. (Big bang theory, theory of general relativity etc.)

Unifying explanations for a broad range of observations

Based on testing a collection of related hypotheses

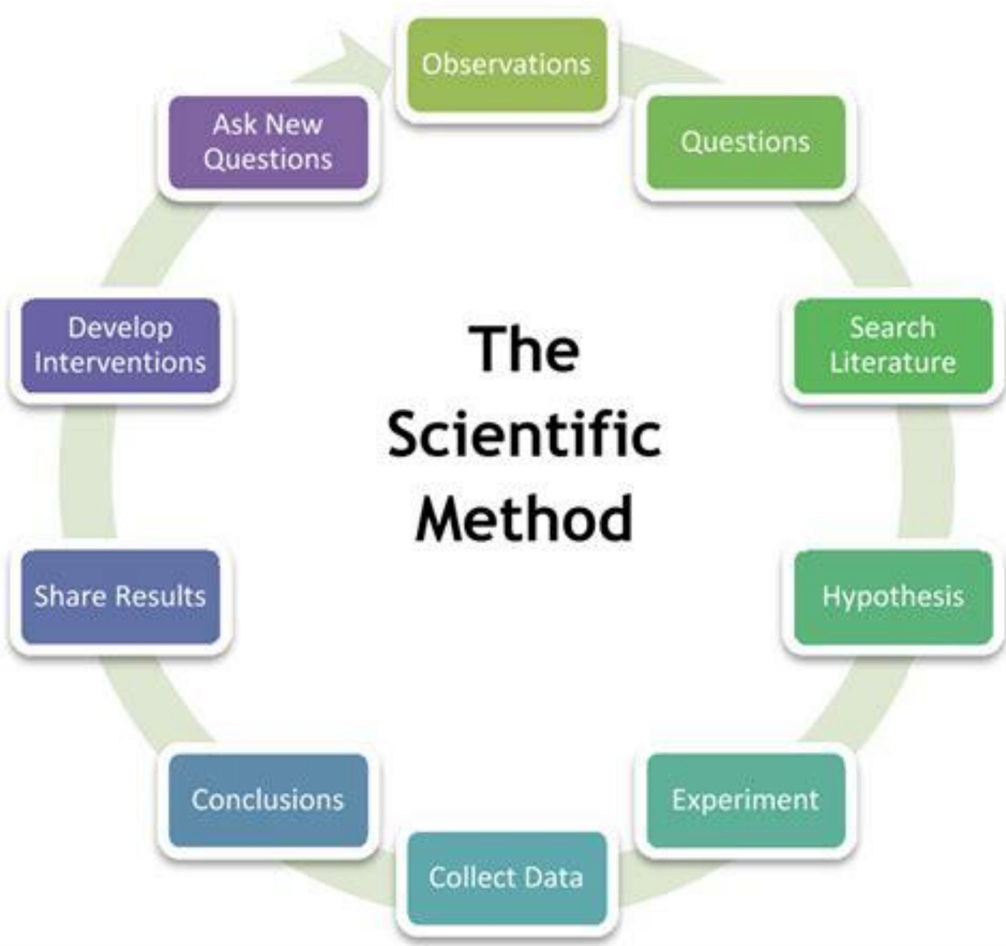
Can be revised given new evidence

Law - A statement of what always occurs under certain conditions. (Law of thermodynamics, Newton's law of motion, Mendelian inheritance etc.)

But remember: All scientific knowledge must be regarded as tentative

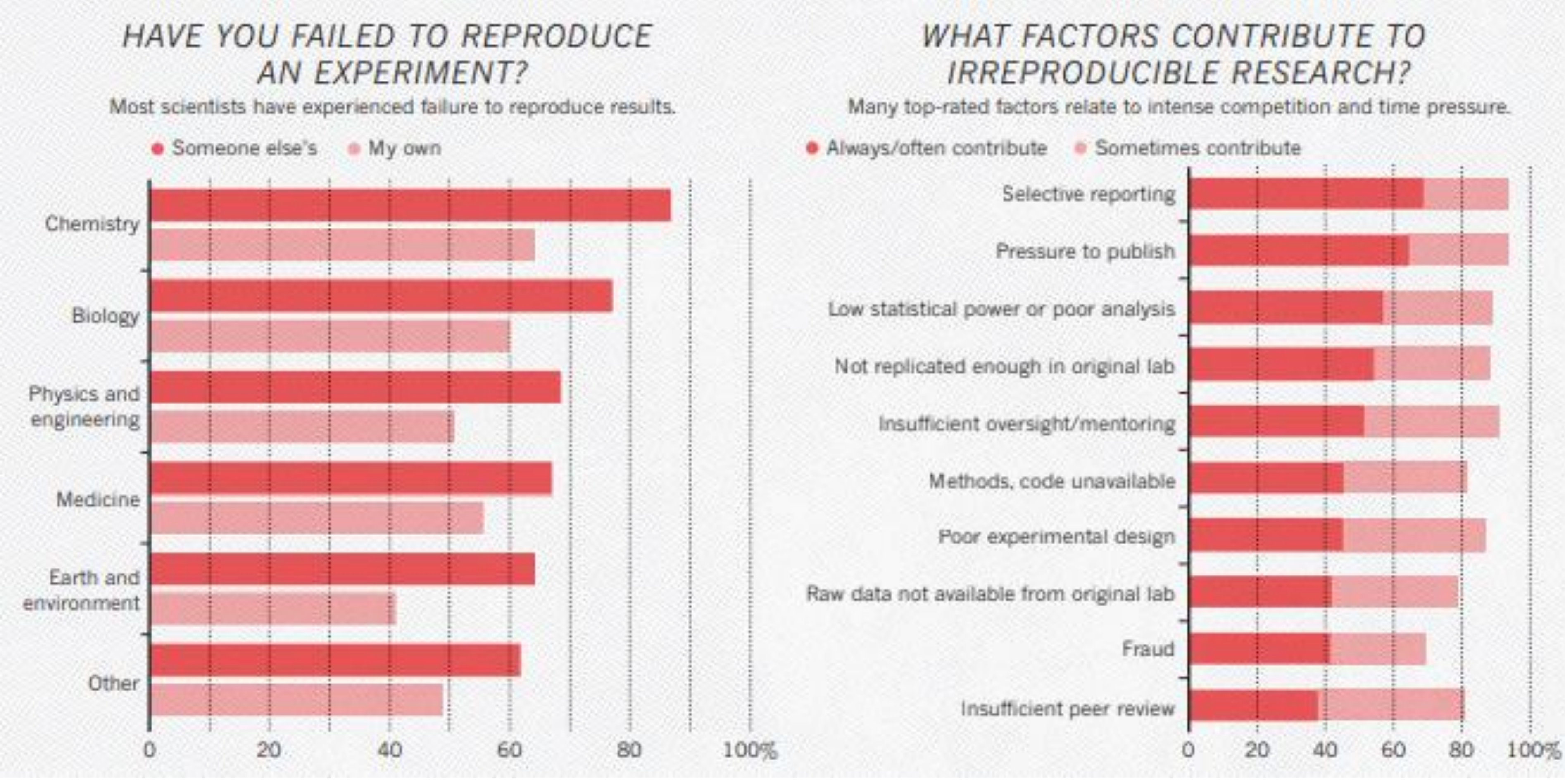
Where do we start?

1. An observation that prompts you to ask a question.
2. Forming a hypothesis based on the question/observations
3. Testing the hypothesis by designing one or more experiments
4. Analysing the results
5. Interpreting and evaluating the results. Can you prove or disprove your hypothesis? Or do you need to modify the experiment, look at a new hypothesis etc? if so, go back to step 2…
6. Draw conclusions



A good experiment should be repeatable by others, and should be designed to directly test the hypothesis, whilst minimising bias, errors and confounding variables

Nature survey on reproducibility in science: https://www.nature.com/articles/d41586-019-00067-3



Baker, M(2016). Is there a reproducibility crisis? *Nature,* 533, 452-454.

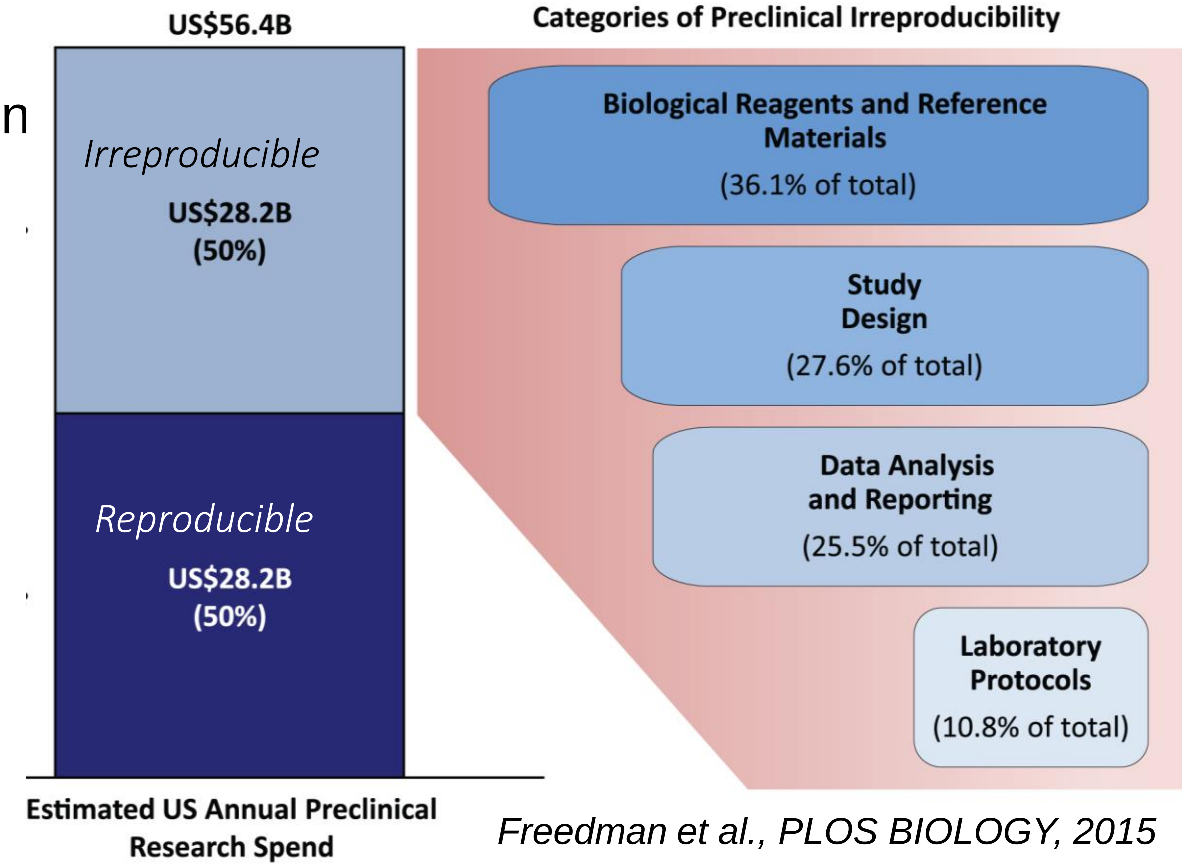
The costs of poor design!!!

Experiments that are badly designed…

– Provide limited or no returns on the effort and resources invested!!!
– Waste resources and money
– Need to be repeated
– Collect incorrect information

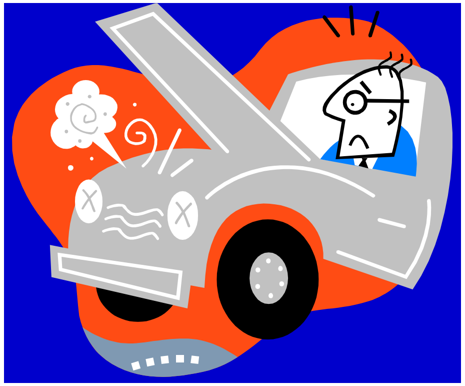
An estimated 28,2 billion USD is spent on irreproducible science annually in the US

Time spent planning and designing at the start will save time and money in the long run



Freedman et al., PLOS BIOLOGY, 2015

Hypothesis building - Let’s test this out



Observation: The car won’t start when I turn the ignition.

Question: Why won’t the car start, something must be faulty?

Hypothesis: A component of the ignition system has failed and so is preventing the car from starting.

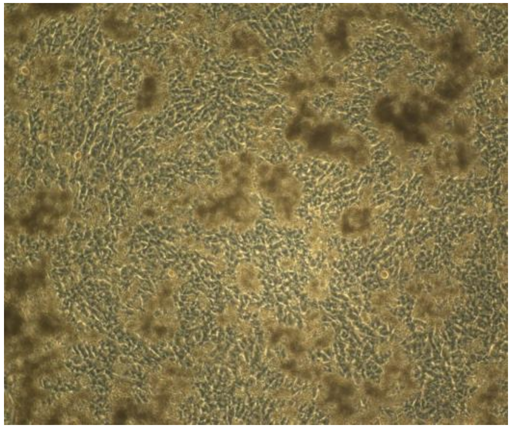
Test hypothesis: Examine the components of the ignition system to identify faulty component

Analyze Results: Data indicates that all components of the ignition system are working normally.

Draw Conclusion: A component other than within the ignition system must be at fault.

New hypothesis: Another component within the car has failed?
The car run out of petrol?

Hypothesis building - Cell Culture example



Observation: My cell culture looks odd…

Question: Why is there floating debris in my cell culture??!

Hypothesis: **?**

Test hypothesis:

Analyze Results:

Draw Conclusion:

New hypothesis:

What is an experiment?

1. An experiment is a <u>**controlled**</u> test of a hypothesis or prediction by gathering data under controlled conditions.

2. Only **one** variable should be changed at a time.

   a. Independent variable – changed by the experimenter. (Hint: ***I*** change the ***I***ndependent variable)

   b. Dependent variable (Responding) – the effect.

3. <u>**Constants**</u> do not change.

4. <u>**Controlled variables**</u> are those which could change, but are not allowed to.

5. Usually there are at least two parts to an experiment:

   a. <u>**Control group**</u> – normal conditions.

   b. <u>**Experimental group(s)**</u> – variables are changed.

6. Goal of the experiment is to test the hypothesis.

An example of an experiment

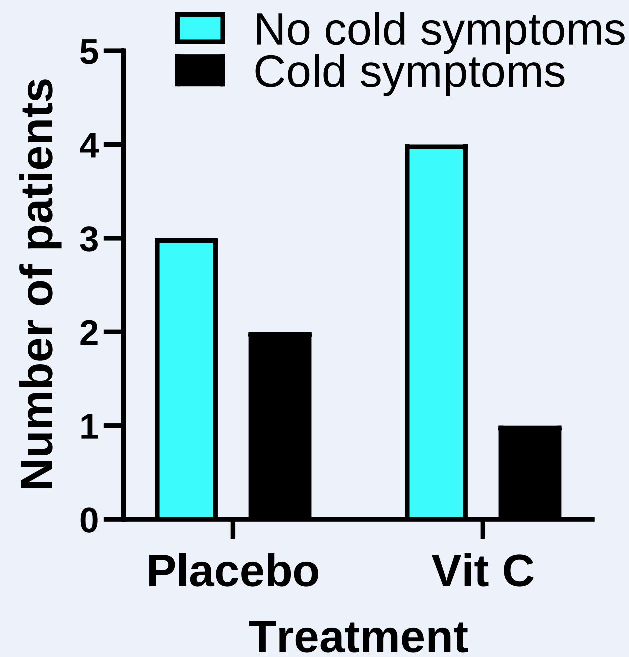
Observation: people who take a daily Vitamin C supplement don’t seem to catch as many colds.

Hypothesis: Vitamin C protects against the common cold virus

Experiment design: Ten females aged 30-40 years, who are friends of the investigator were chosen to test whether vitamin C protected against catching a cold over a 1 week period.

5 were given 1000mg of vitamin C, daily; the other 5 were given a placebo.

Results:



Conclusion:

Vitamin C protects against getting a cold.

Is this a good experiment? Do you trust the conclusions?

Problems with this experiment

This will be discussed in class

A Good Experiment

Should

- Have only one variable
- Control for all other (confounding) variables
- Use a (sufficiently) large number of samples
- Use random (unbiased) selection
- Be repeated/repeatable
- Use double blind testing

Some points to note about designing experiments

- Good experiments are comparative, ideally, the experimental group is compared to **concurrent controls** i.e. controls running at the same time (rather than to historical controls).
- **Randomisation** helps to reduce the effect of uncontrolled variation (increases precision) and gives a solid foundation for statistical analysis.
- **Stratification** is the process of dividing subjects/ samples into homogeneous subgroups before sampling.
- We can sometimes learn more by looking at multiple factors in an experiment rather than just one factor at a time

Some points to note about designing experiments

- Blinding
  - To reduce unconscious biases.
  - Ideally, dissections and measurements should be made without knowledge of the treatment applied.
- Appropriate controls
  - Internal controls: e.g. response before vs. after treatment in the same subject
  - Negative / positive controls
  - Assay controls
  - Why? Increased precision, reducing confounding factors.
- Representativeness
  - Are the subjects/tissues you are studying really representative of the population you want to study?
  - Ideally, your study material is a random sample from the population of interest.

Experimental error

- No experiment is ever perfect
- Human error
- Equipment error
- Poor experimental design
- Incorrect analysis
- Environmental factors (e.g.temperature changes in the lab
- Factors out with the control of the experiments (e.g. powercut)

The limitations of the Scientific Method

Is limited by

- the extent of our basic knowledge
- our ability to interpret the results
- what can be observed with the five senses e.g., what existed prior to the Big Bang and the known universe is outside of the realm of science to investigate
- the changes in the natural world
- tells us “how” a process works, not “why” e.g., does not really explain why the Universe exists
- inability to answer value-based questions involving “should”
- may be affected by the emotional involvement of investigator
- may be affected by time pressure for results

The limitations of the Scientific Method

- inability to capture the full richness and complexities of the phenomenon being studied
- limitations of our measurement instruments
- ethical and legal responsibilities
- we can never be sure *all* untested variables are controlled
- scientists sometimes make mistakes
- accidents, lucky guesses, intellectual powers, and controversies with others contribute strongly to scientific advances
- conclusions based on the experimental data must remain tentative!
- Scientific dogmas

'DISRUPTIVE' SCIENCE HAS DECLINED — EVEN AS PAPERS PROLIFERATE

The proportion of publications that send a field in a new direction has plummeted since the 1940s.

By Max Kozlov

The number of science and technology research papers published has skyrocketed over the past few decades — but the 'disruptiveness' of those papers has dropped, according to an analysis of how radically papers depart from the previous literature[1].

Data from millions of manuscripts show that, compared with mid-twentieth-century research, that done in the 2000s was much more likely to push science forward incrementally than to veer off in a new direction and render previous work obsolete. Analysis of patents from 1976 to 2010 showed the same trend.

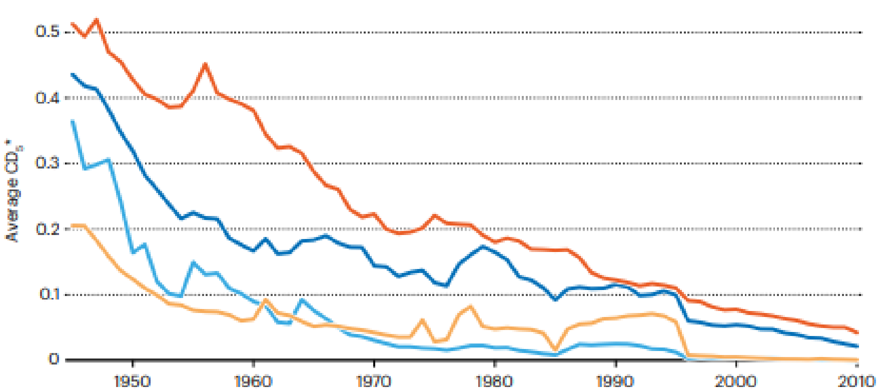
"The data suggest something is changing," says Russell Funk, a sociologist at the University of Minnesota in Minneapolis and a co-author of the analysis, which was published on 4 January in *Nature*. "You don't have quite the same intensity of breakthrough discoveries you once had."

Telltale citations

The authors reasoned that if a study was highly disruptive, subsequent research would be less likely to cite the study's references, and instead would cite the study itself. Using the citation data from 45 million manuscripts and 3.9 million patents, the researchers calculated a measure of disruptiveness, called the CD index,

DISRUPTIVE SCIENCE DWINDLES

To quantify how much a paper shakes up a field, researchers used a metric called a CD index, which ranges from 1 for the most disruptive papers to −1 for the least disruptive. Analysis of millions of papers shows that disruptiveness has fallen over time in all analysed fields.



*Average CD_5 is the CD index five years after a paper's publication.

It's great to see this [phenomenon] documented in such a meticulous manner," says Dashun Wang, a computational social scientist at Northwestern University in Evanston, Illinois, who studies disruptiveness in science. "They look at this in 100 different ways, and I find it very convincing overall."

Other research[2] has suggested that scientific innovation has slowed in recent decades, too, says Yian Yin, also a computational social scientist at Northwestern. But this study offers a "new start to a data-driven way to investigate how science changes", he adds.

Disruptiveness is not inherently good, and incremental science is not necessarily bad, says Wang. The first direct observation of gravitational waves, for example, was both revolutionary and the product of incremental science, he says.

The ideal is a healthy mix of incremental and disruptive research, says John Walsh, a specialist in science and technology policy at the Georgia Institute of Technology in Atlanta. "In a world where we're concerned with the validity of findings, it might be a good thing to have more replication and reproduction," he says.

Why the slide?

The drastic change might stem in part from changes in the scientific enterprise. For example, large research teams have become more common, and Wang and his colleagues have found[3] that big teams are more likely to produce incremental than disruptive science.

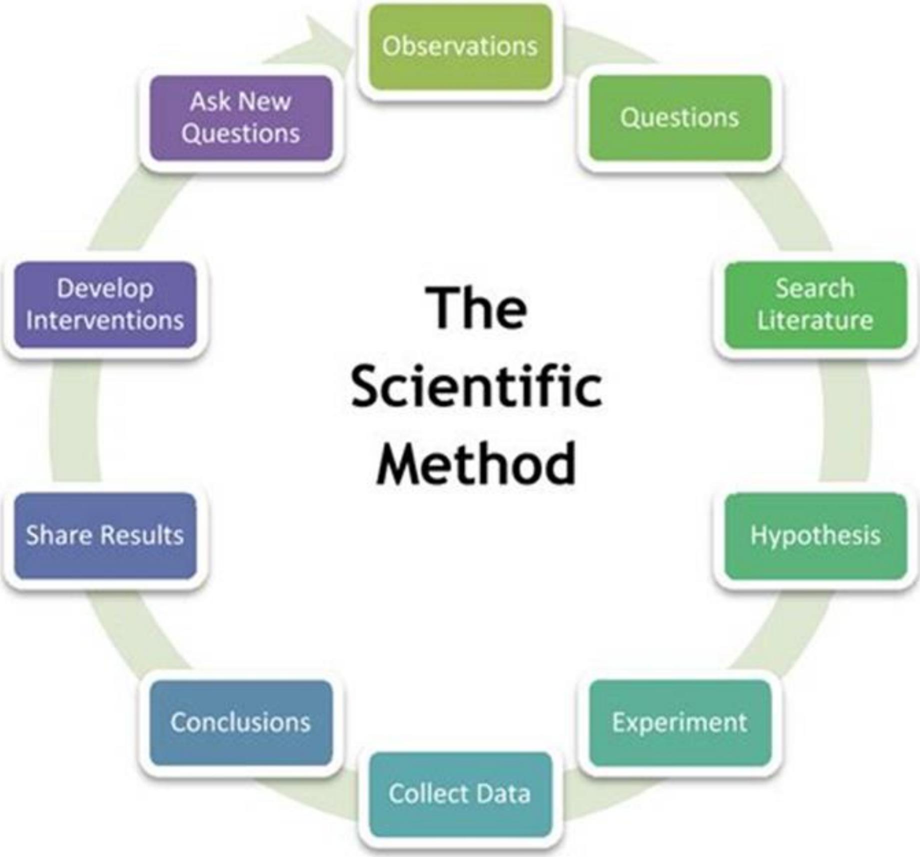
Finding an explanation for the decline won't be easy, Walsh says. Although the proportion of disruptive research dropped significantly between 1945 and 2010, the number of highly disruptive studies has remained about the same. The rate of decline is also puzzling: CD indices fell steeply from 1945 to 1970, then more gradually from the late 1990s to 2010. "Whatever explanation you have for disruptiveness dropping off, you need to also make sense of it levelling off" in the 2000s, he says.

1. Park, M., Leahey, E. & Funk, R. J. *Nature* **613**, 138–144 (2023).
2. Cowen, T. & Southwood, B. Preprint at SSRN http://doi.org/10.2139/ssrn.3822691 (2019).
3. Wu, L., Wang, D. & Evans, J. A. *Nature* **566**, 378–382 (2019).

Link to online paper: https://www.nature.com/articles/d41586-022-04577-5

Recap on designing an experiment

1. Observation / Question / Problem
2. Hypothesis
3. Design an experiment to test the hypothesis
4. Collect and analyse data
5. Interpret results
6. Draw conclusions: can you accept or reject your hypothesis?
7. If you cannot answer the hypothesis, design a new (better) experiment and repeat steps 4 to 6
8. Report and evaluate your results
9. Make new observations and repeat the cycle



Questions?

Revision questions

- Explain the difference between a hypothesis, a theory and a law in scientific terms.
- What are the key stages in the scientific method?
- Explain some essential characteristics of a good experiment
- Explain the difference between an independent and a dependent variable in an experiment.
- Why might randomisation be important in a scientific experiment?

What are the three most important points from this lecture?