2012: https://www.youtube.com/watch?v=ubyWe0bJ41s

Nature Reviews Molecular Cell Biology | AOP, published online 10 April 2008; doi:10.1038/nrm2389

PERSPECTIVES

ESSAY

How to succeed in science: a concise guide for young biomedical scientists. Part I: taking the plunge

Jonathan W. Yewdell

and investigate natural phenomena by formulating and rigorously testing hypotheses. The origins of the scientific method date back at least 1,000 years, and it is arguably the most important invention of civilized man. Armed with the scientific method, we can explore and understand nature to the limits of our intelligence. As a high priest of 'Scientific Methodism', you will be equipped for success not only in science and its allied occupations, but in virtually any career that requires rational decision making (and in

PERSPECTIVES

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How to succeed in science: a concise guide for young biomedical scientists. Part II: making discoveries

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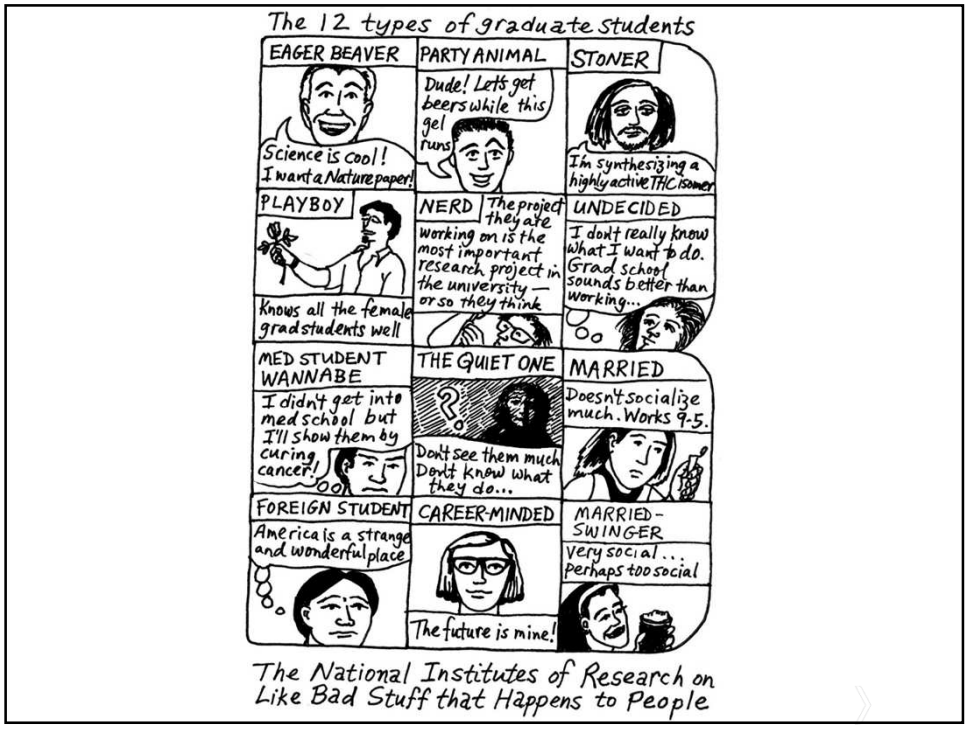
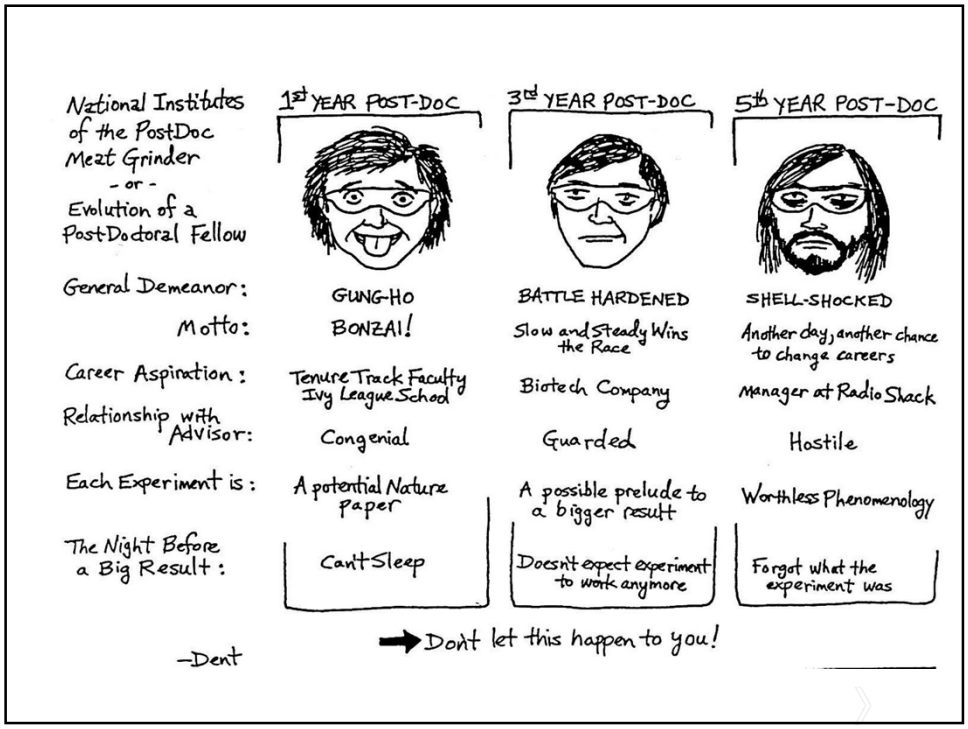
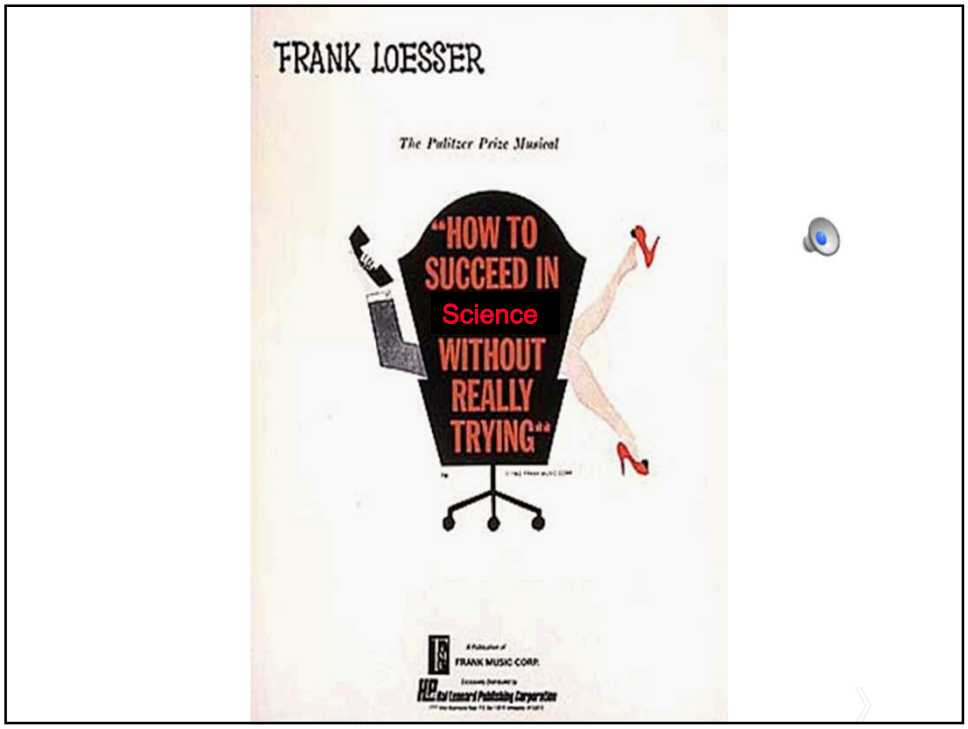
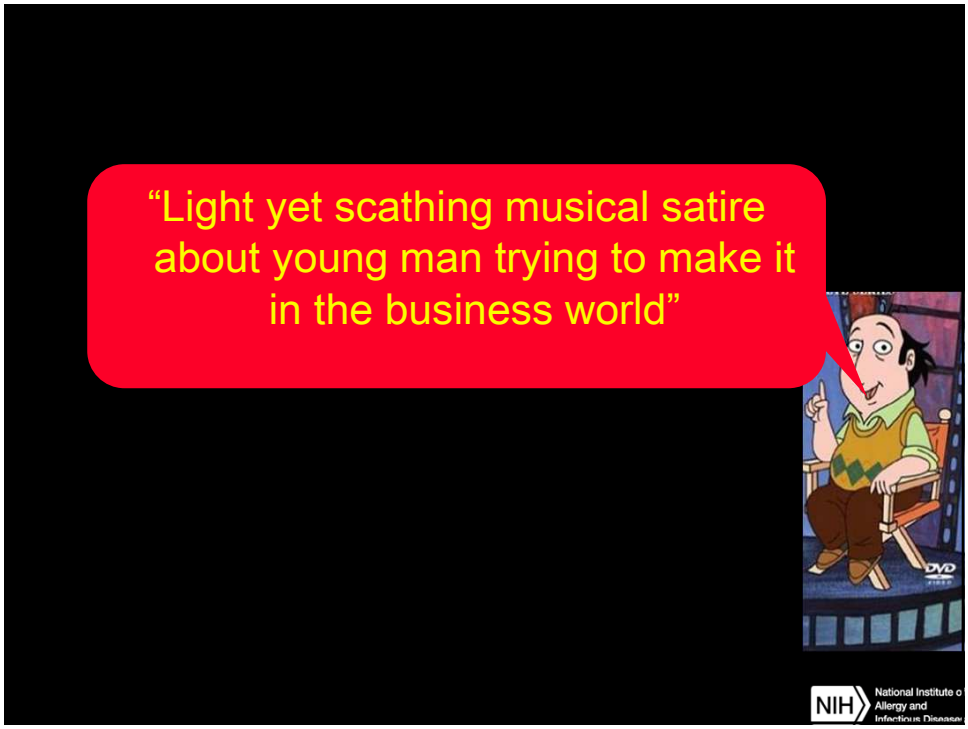
the expertise of neighbouring laboratories. Imagine, for example, that your institution has a first-rate confocal microscope facility, but that confocal microscopy has never been applied to the major research interest of your own laboratory, even though it has a number of obvious applications. Should you take advantage of the situation? Of course! An extreme example to be sure, but many projects have foundered before they started because of the sheer impossibility of gaining


The 12 types of graduate students
EAGER BEAVER
Science is cool! I want a Nature paper!
PARTY ANIMAL
Dude! Lets get beers while this gel runs
STONER
Im synthesizing a highly active THC isomer
PLAYBOY
Knows all the female grad students well
NERD
The project they are working on is the most important research project in the university — or so they think
UNDECIDED
I dont really know what I want to do. Grad school sounds better than working...
MED STUDENT WANNABE
I didn't get into med school but I'll show them by curing cancer!
THE QUIET ONE
Dont see them much Dont know what they do...
MARRIED
Doesn't socialize much. Works 9-5.
FOREIGN STUDENT
America is a strange and wonderful place
CAREER-MINDED
The future is mine!
MARRIED-SWINGER
very social... perhaps too social
The National Institutes of Research on Like Bad Stuff that Happens to People


Nztional Institutes of the PostDoc Meat Grinder
- or -
Evolution of a PostDoctoral Fellow
1st YEAR POST-DOC
3rd YEAR POST-DOC
5th YEAR POST-DOC
General Demeanor:
GUNG-HO
BATTLE HARDENED
SHELL-SHOCKED
Motto:
BONZAI!
Slow and Steady Wins the Race
Another day, another chance to change careers
Career Aspiration:
Tenure Track Faculty Ivy League School
Biotech Company
Manager at Radio Shack
Relationship with Advisor:
Congenial
Guarded
Hostile
Each Experiment is:
A potential Nature Paper
A possible prelude to a bigger result
Worthless Phenomenology
The Night Before a Big Result:
Can't Sleep
Doesn't expect experiment to work anymore
Forgot what the experiment was
Don't let this happen to you!
-Dent


THE SUN'LL COME OUT... TOMORROW!
NIH
National Institute o
Allergy and
Infectious Disease


FRANK LOESSER
The Pulitzer Prize Musical
"HOW TO SUCCEED IN
Science
WITHOUT REALLY TRYING"
FRANK MUSIC CORP.


"Light yet scathing musical satire about young man trying to make it in the business world"
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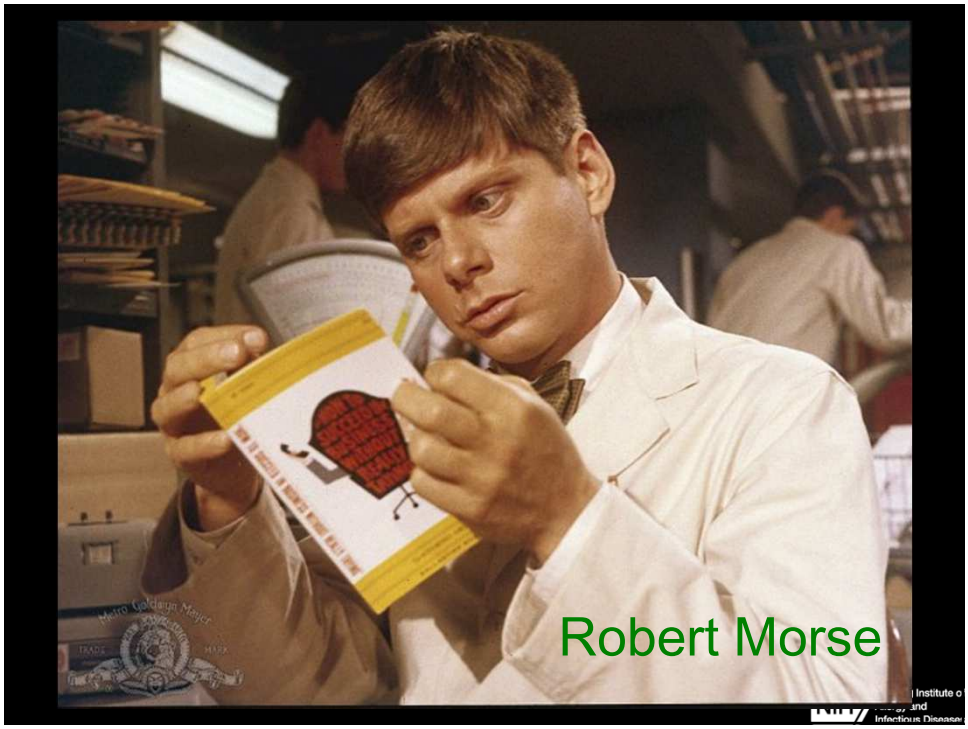
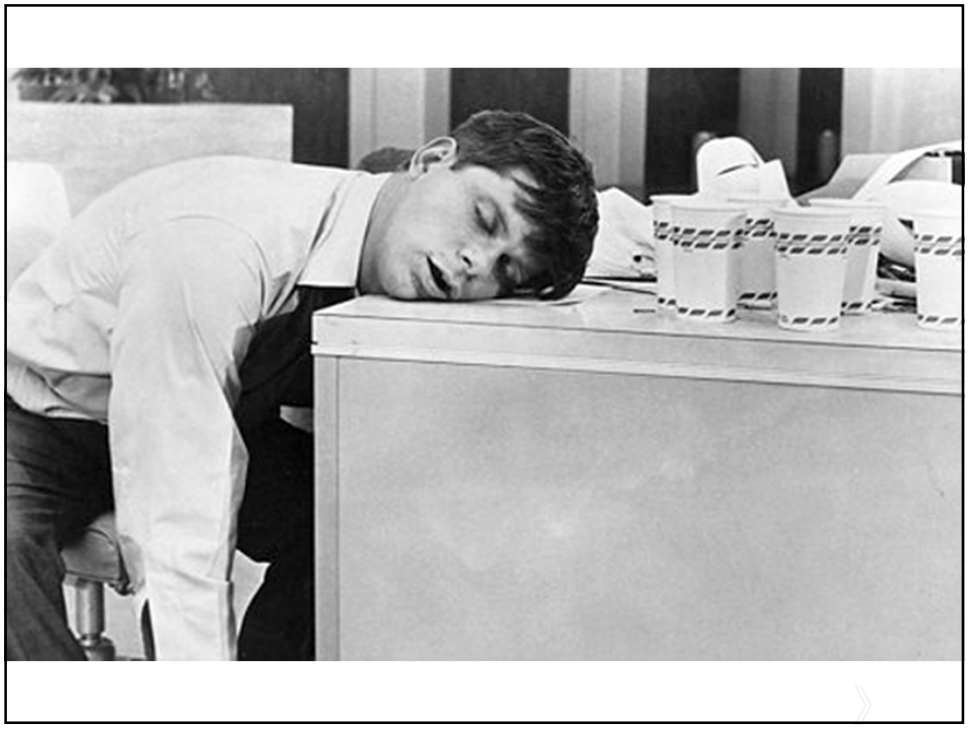

Robert Morse




Bulldogs, Bulldogs: Bow, Wow, Wow
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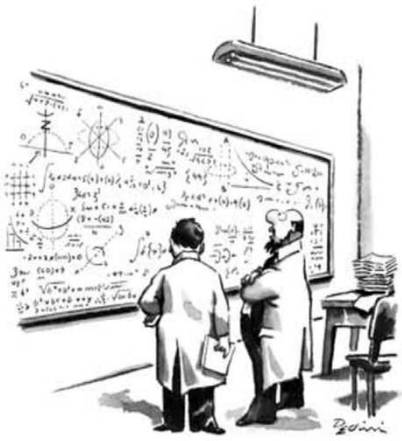
THE COMPLETE CARTOONS OF THE NEW YORKER

1986



"This is fine as far as it goes. From here on, it's who you know."

You Can't

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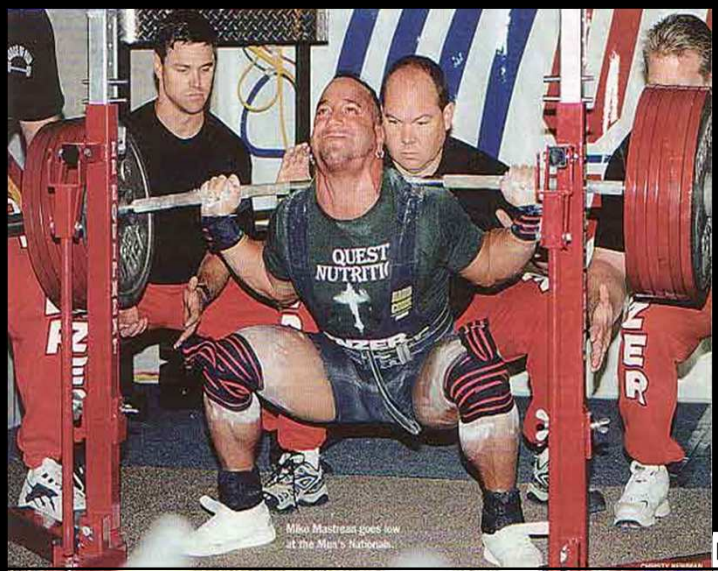
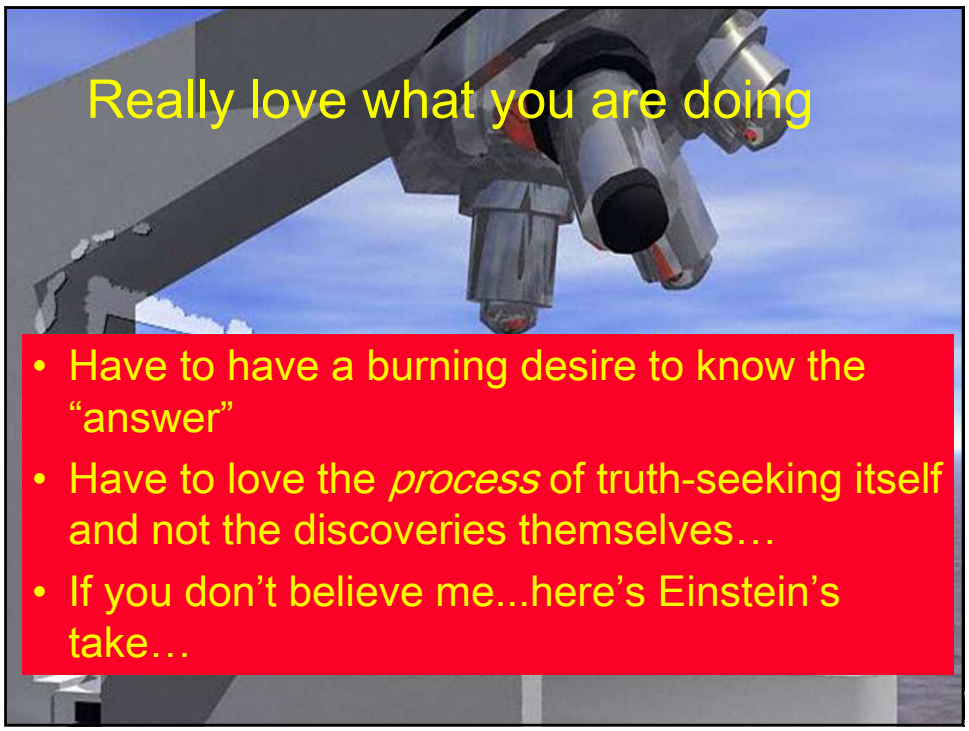
Infectious Disease

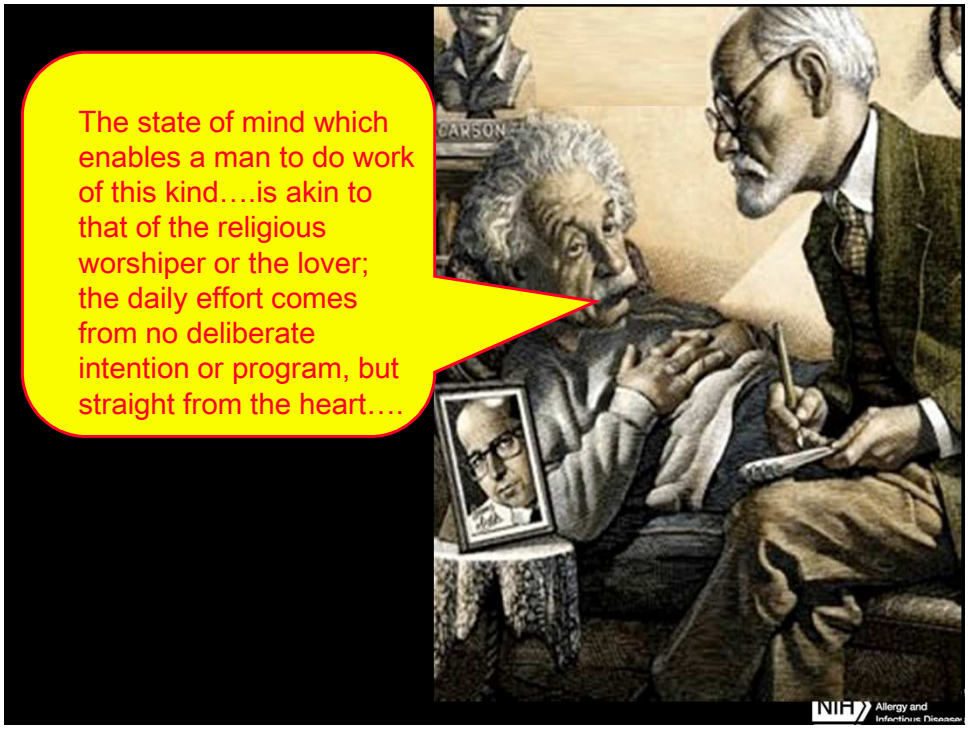
In fact, you've *really* got to try

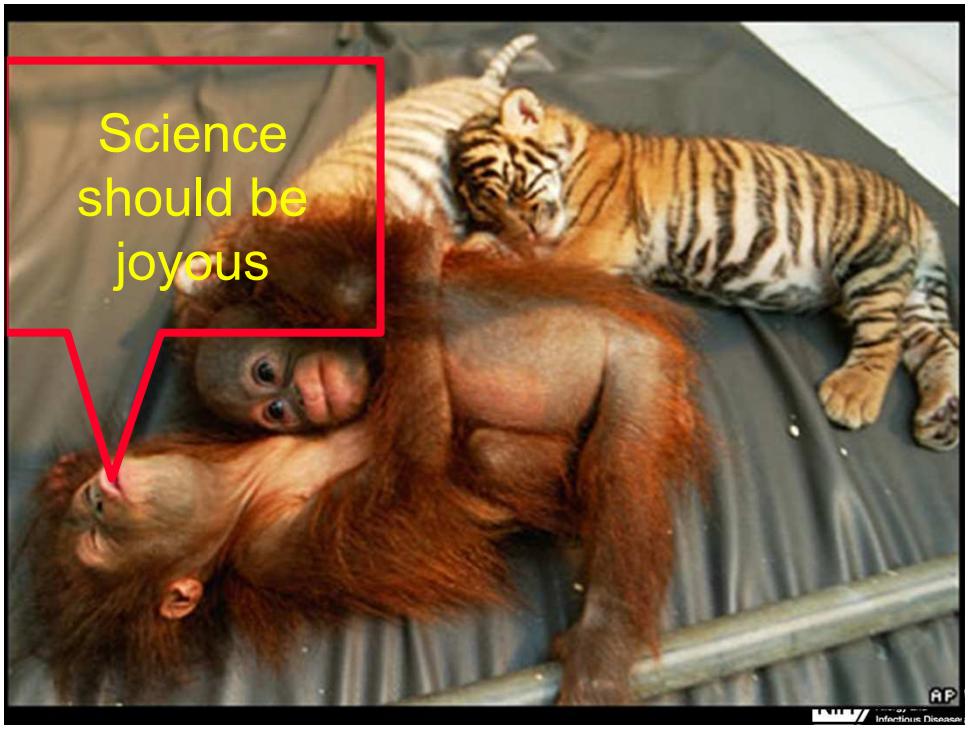


Philosophical Issues

Most Important thing…




The state of mind which enables a man to do work of this kind….is akin to that of the religious worshiper or the lover; the daily effort comes from no deliberate intention or program, but straight from the heart….
CARSON
NIH Allergy and


Science should be joyous
AP

Life is mostly about attitude…

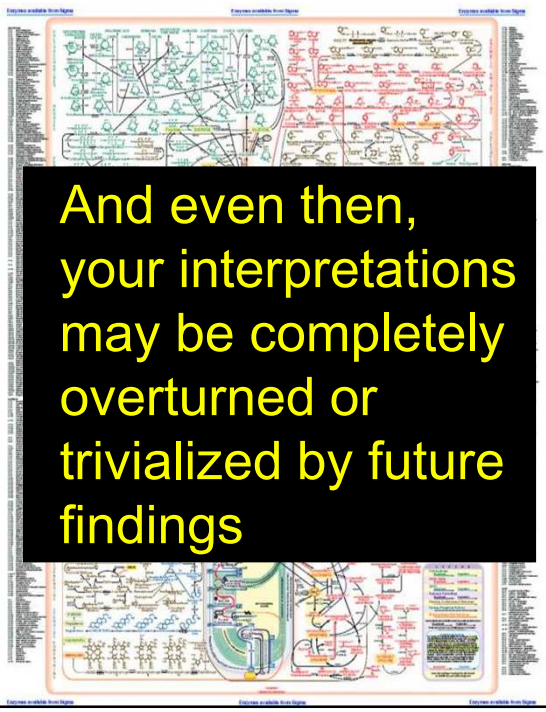
Honoring the *Scientific Method* is More Important than Any Discoveries You Will Make

The ends *never* justify the means in science

Because, among other things

- Trust demands integrity
- Opponents of science exploit every opportunity to discredit scientists
- Your work is not *that* important: if you don't discover it, someone else will
- In fact even if you are wildly successful…

Your life's work will be reduced to a line or two (or ten) of the giant chart of life that future students will terribly resent memorizing…
……

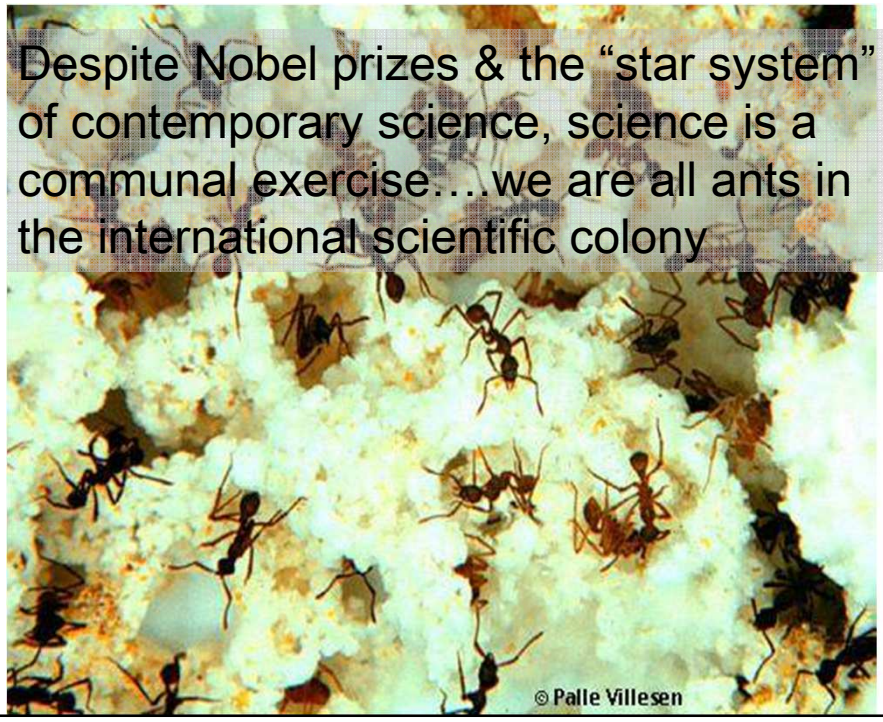


And even then, your interpretations may be completely overturned or trivialized by future findings

In any event, striving to achieve fame as a scientist is futile ….

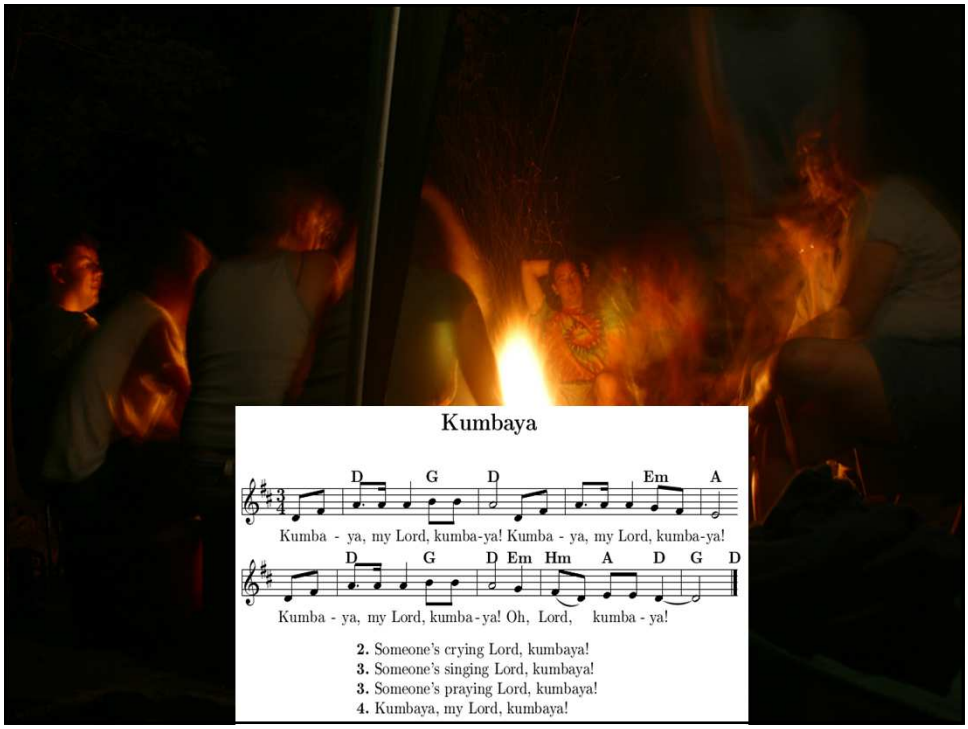
Shouldn't he have a bigger monument? After all, he did invent fire and the wheel.

Despite Nobel prizes & the “star system” of contemporary science, science is a communal exercise….we are all ants in the international scientific colony



The International Nature of Science Should be Cherished

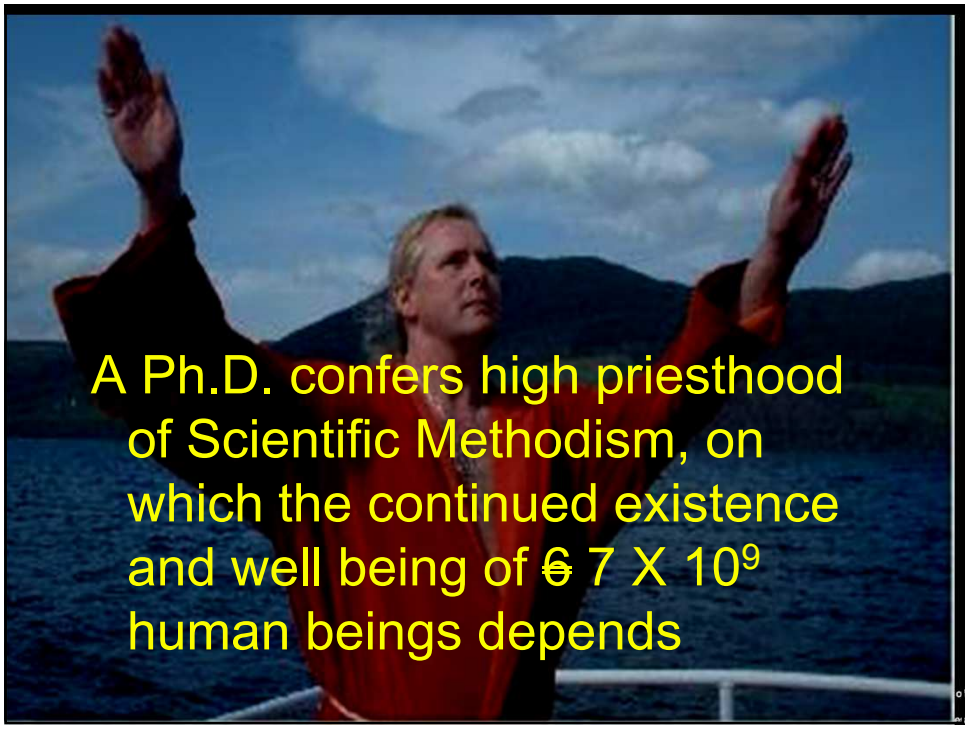
- It is nearly unique among careers
- It is a force for world peace and understanding



You are an important member of a noble enterprise that began in the renaissance

The scientific method forms the foundation of modern society, both technologically and politically

The General Case for Science



Our most important job is to pass the torch of the Scientific Method to the next generation

Getting More Practical

How to make discoveries

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Cross-pollination between fields pays huge dividends

- ❖Attend Seminars in Other Fields
- ❖Talk to your colleagues
- ❖Collaborate!!
- ❖Read Widely
  - But not necessarily deeply

Be the BEE

Too much knowledge about what you are doing can be counter-productive!

If you are really keen on doing an experiment….

Just Do it

To make a discovery, you have to do an experiment[1]

[1]Unless you are a bioinformaticist, of course

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The Best Students

"You really think this will work?"

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Yewdell's Doability (D) Equation

$D = I^2/E$

I=Interest
E=Effort

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Work on Something Interesting or Important

- It's no harder than working on something uninteresting or unimportant
- Select a fundable project
- But do something original
- Exploit your strengths and surroundings

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THE COMPLETE CARTOONS OF THE NEW YORKER

"I'm into stone. There's a hell of a lot of it around."

Exploit your strengths and surroundings

- If your lab has special expertise in a technique, learn it whether or not you immediately need to use it…

How to make discoveries: Work on Something Interesting or Important

- Don't underestimate the value of basic research
- Basic research is always interesting
- Basic research is the golden egg laying goose
- We need to constantly remind ourselves of this fact

Translational research

- Yes, yes, it is crucial to help humanity and to propel the entire research enterprise
- Typically, it does not require excessive creativity
- Or reward creativity
- Most things don't work
- Remember, companies exist for one reason…

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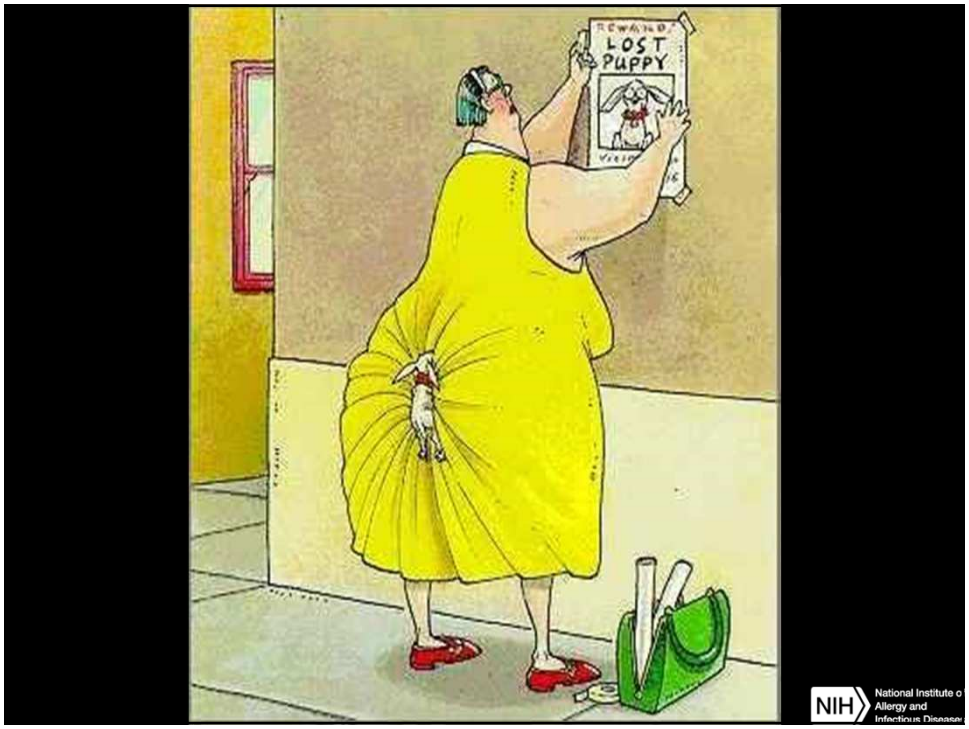
"For goodness' sake get hep, Schwartz! We're not trying to do away with the common cold."

How to Make Discoveries: Interpreting your Data

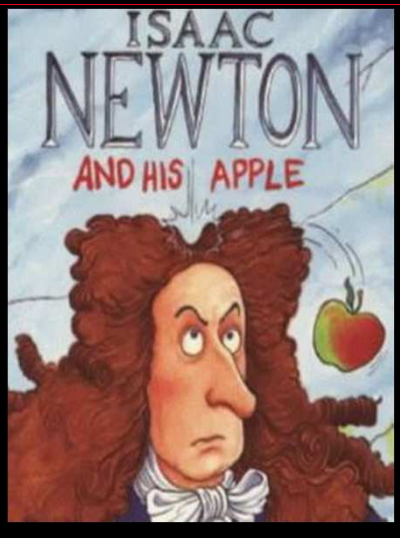
Think out of the box

- What is the most interesting possible interpretation of your data?



Think BIG

Don’t be afraid to make an important discovery



You should be the world's expert

If you don't believe that you are capable of making a significant discovery, don't do basic research

It's OK to Get Sidetracked

If its something really interesting

EMBRACE SERENDIPITY!

SERENDIPITY: from a former name of Sri Lanka. A word coined by Horace Walpole, who says that he had formed it upon the title of a fairy tale called «The Three Princes of Serendip», the heroes of which ' were always making discoveries, by accidents and sagacity, of things they were not in quest for.'

Serendipity is looking for a needle in a haystack and finding the Farmer's Daughter

Julius Comroe

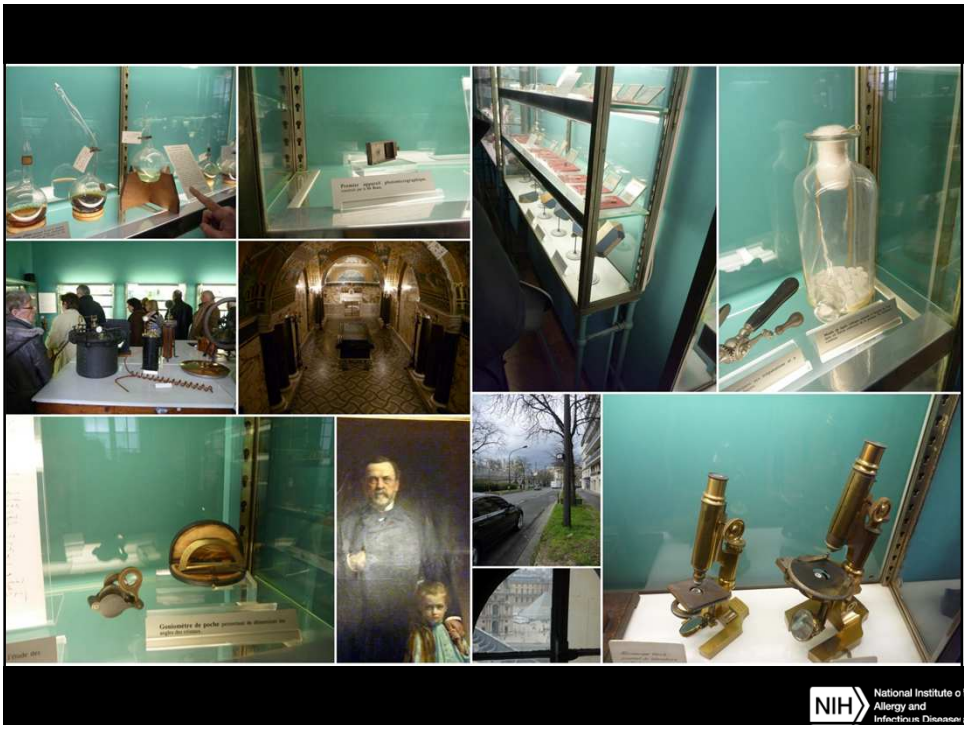
THE COMPLETE CARTOONS OF THE NEW YORKER

1957

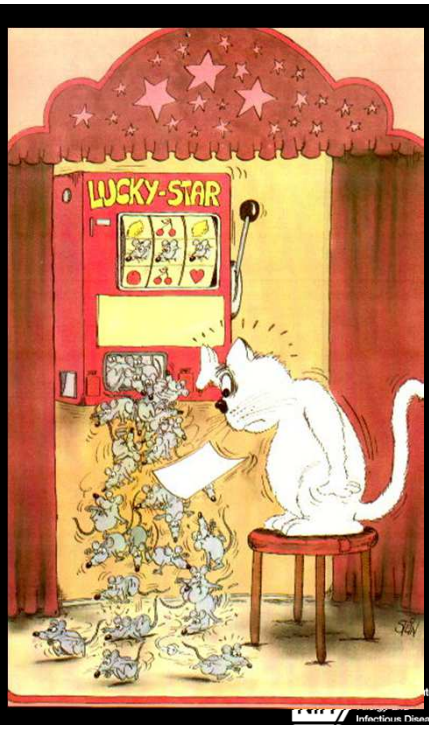
"That's Dr. Arnold Moore. He's conducting an experiment to test the theory that most great scientific discoveries were hit on by accident."

How to be lucky

Dans les champs de l'observation le hasard ne favorise que les esprits préparés



And… you will be luckier if you pull the lever more times…

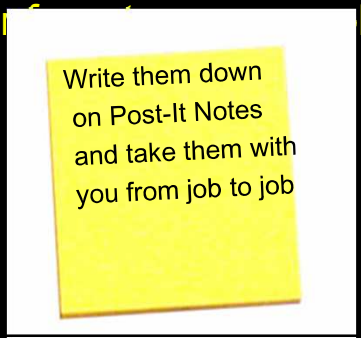


You won't necessarily know that you have made a great discovery

- The meaning of discoveries are often hidden, and may take years to appreciate
- Don't ever forget your unexplained results

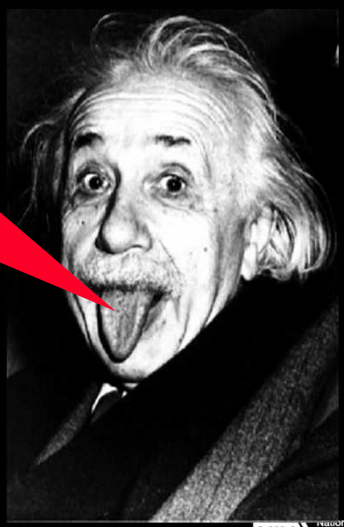
You won't necessarily know that you have made a great discovery

- The meaning of discoveries are often hidden, and may take years to appreciate
- Don't ever [illegible] explained results



Never use the "P" word

"No amount of experimentation can ever prove me right; a single experiment can prove me wrong"



Never use the “P” word

- The best we can do is to “prove” that observations are statistically likely to be accurate
- Nature is essentially unknowable in any definite way
- Interpretations are *always* subject to modification and will eventually be modified

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Scientists *must* be professional skeptics

- Always question your assumptions
- It is *your* job to disprove your most cherished models and ideas

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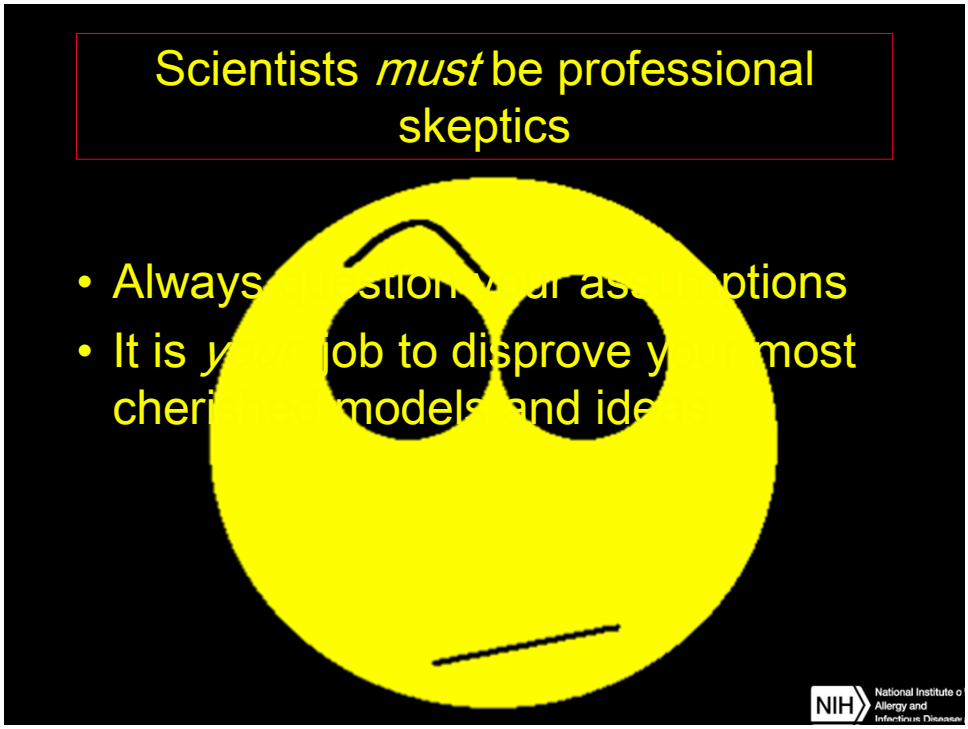
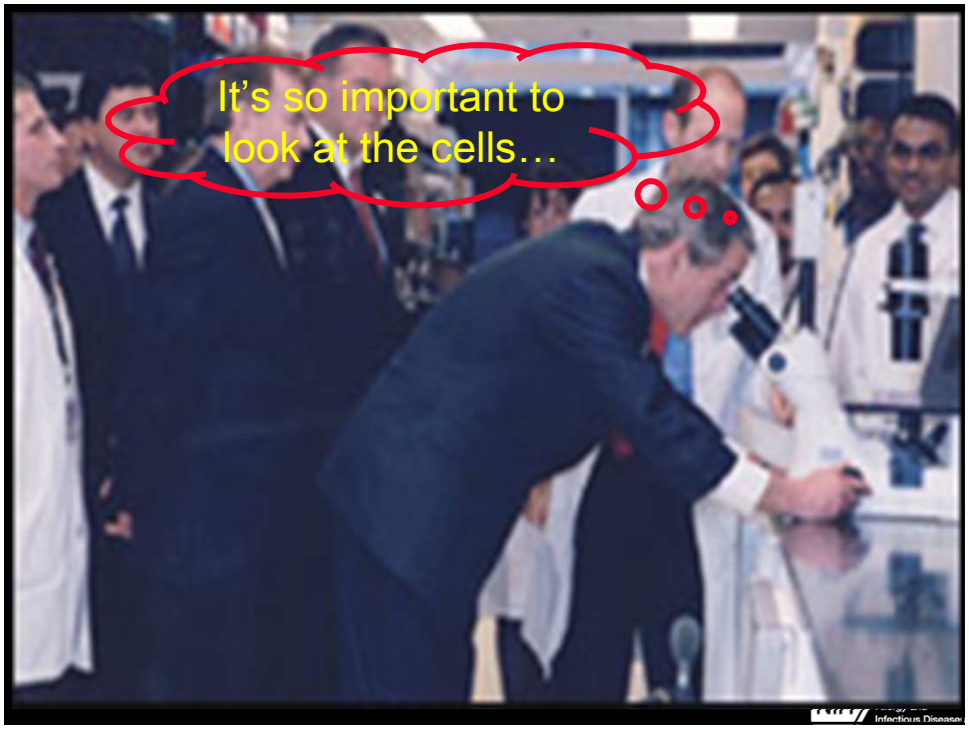


Select a project where you can do lots of experiments

- Avoid single technique based projects
- You need to learn to design and interpret experiments
- You need to be obsessed with controls and to develop "control-creativity"
- Even so, the "essential" control will typically occur to you only after you see the data

Sweat the details

- Know every step of the assay
  - Have an idea of how machines work
- Know your reagents
  - Just because the tube says X, as the Gershwin boys wrote:
    It ain't necessarily so….
  - Use kits wisely
- Every step of every experiment you should be thinking how you can improve the method



Don’t put all your eggs in one basket

Start with a pilot experiment and *gradually* increase the scope of the experiment

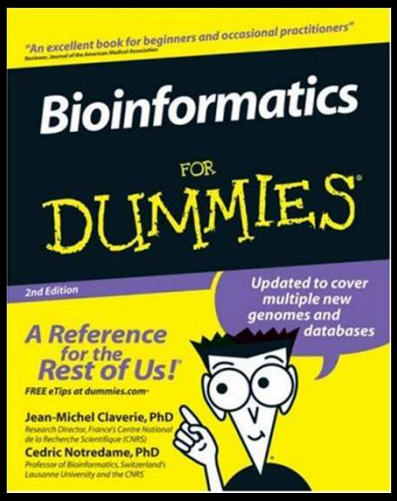
Statistics are important, but don’t be blinded by them

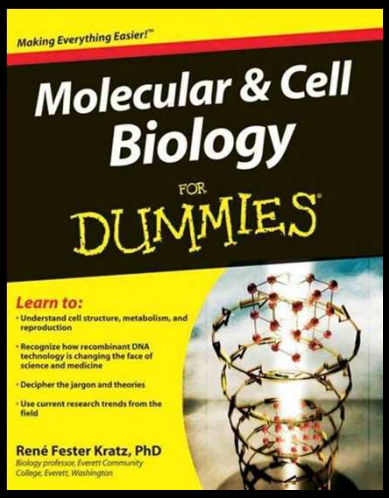
Keep a good notebook

- What is the point of the experiment?
- All info needed to repeat
- Weird observations
- What did you find?

Learn how to finish projects

Learn Some Bioinformatics





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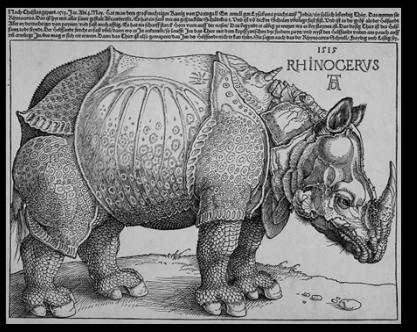
Develop a Thick Skin

- Embrace criticism
- It's not personal
- Anything that leads to better science is good
- Anything that hinders better science is bad
- Our mission is to find the truth, not to be nice, or to honor our elders…



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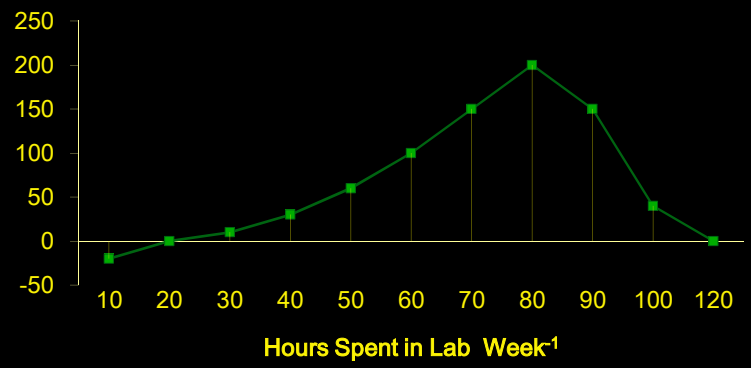
If you have a complaint, offer a solution

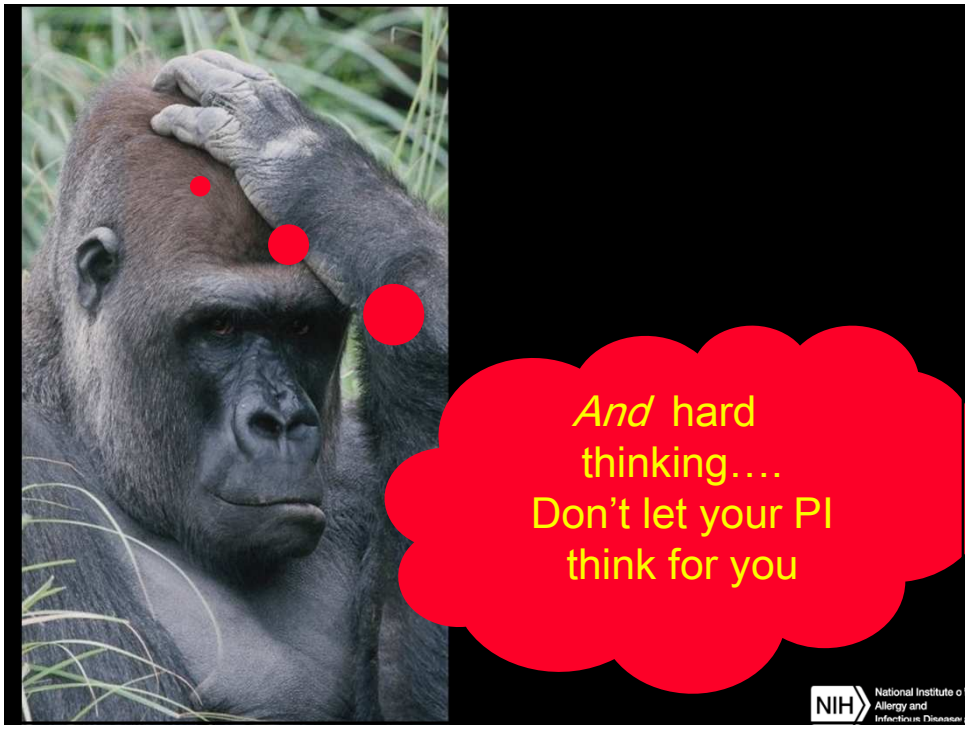
Work hard

- 50+ hours per week is what it usually takes
  - What else do you have to do?
- Do lots of experiments
  - Have more than one thing going

There is simply no substitute for hard work

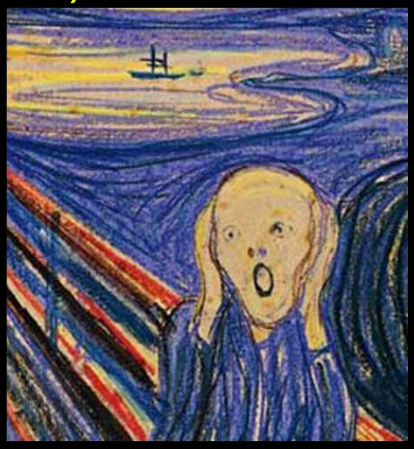
Effort vs. Productivity Curve





All work and no play, makes Jack a dull boy (and maybe also insane)

- Daily exercise is an excellent way to maintain sanity
- Take your vacations



Concentrate on your work

Don’t expect your PI to treat everyone in the lab identically…

Why????

- Your PI may not be a perfect person
- Lab members are all different
- Cut people a lot of slack….

Take the High Road with People
Working Assumption: Everyone is OK

Make yourself slow down when you are in an emotional state

- Wait until you are calm before even starting to make a decision
- Wait, wait, wait
- NEVER WRITE AN EMOTIONAL E-MAIL!!

You

Your e-mail

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Unless absolutely necessary, avoid lab romances !!

Take Ben's Advice


"HOW TO SUCCEED IN
MDPhD
WITHOUT REALLY TRYING""
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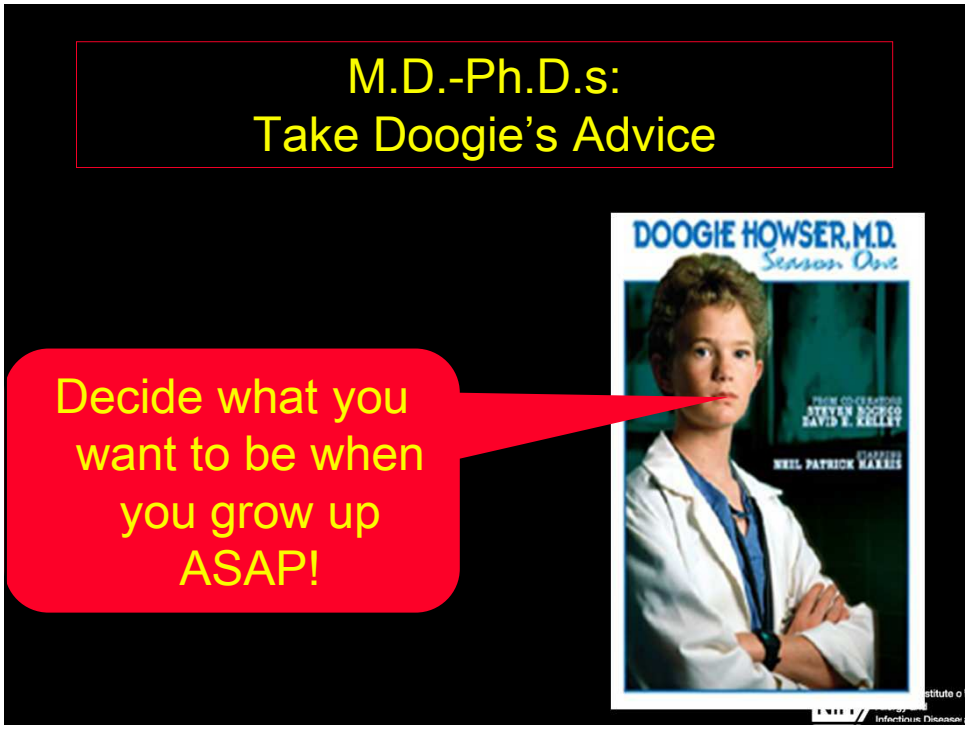

M.D.-Ph.D.s:
Take Doogie's Advice
Decide what you want to be when you grow up ASAP!
DOOGIE HOWSER, M.D.
Season One
NEIL PATRICK HARRIS

M.D.-Ph.D.

- Few people have the energy to do both medicine and science at a high level for extended periods in their careers
- In any event, *you* don't have to!
- Try to graduate as quickly as possible
- What do they call the last person in the medical school class?

Useful things I learned in medical school

- Hospitals are depressing places
- Some people are simply not cut out for medicine
- “Facts” trump logic
- Don’t seek medical assistance unless you are really sick
- Then, find the best doctors
- How to find the best doctors
  - Tap your med school network

More things I learned in Med School

- Physiology, pathology, histology, pharmacology, a.k.a systems biology

Problems with MD PhDs in the lab

- Impatience
- Badditude
  - Arrogance
    - MD-in-lab phenotype
  - Be a team player
    - No job is beneath you
    - Very important attitude when you are a PI

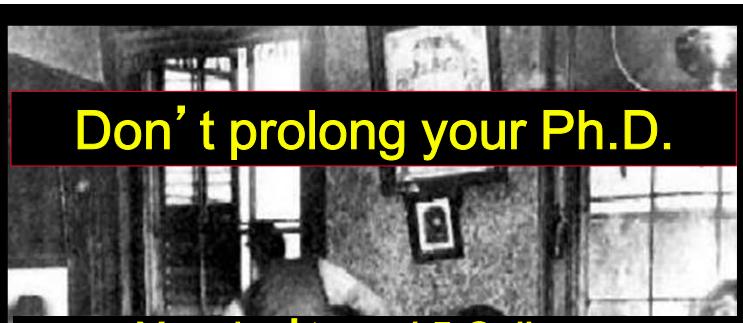
Take responsibility for your own future and happiness

- Develop a career plan
- Life is not about tests-its about contributing to society
  - Tests do not measure creativity
  - Life does
- Achieving to please others ultimately leads to dissatisfaction
- Seek advice, but decide for yourself

Speak up!!
Don’t be afraid to ask questions at seminars and meetings

Attend Conferences

- The talks are the least important part of the meeting
- Meeting people and forming relationships/friendships/collaborations should be your goal….



Don't prolong your Ph.D.

- You don't need 5 Cell papers.
  - 3 will do (rim shot)
- You need to learn:
  - Not to fear the unknown
  - How to design, perform and interpret experiments
  - How to write coherently and succinctly
- Prolongation can be for the sole benefit of your advisor

For future PIs, your post-doc is probably the most important step

- Be careful in choosing a lab
- Go to a wealthy, well connected lab
- This is the time to find the major research topic for your career
- Think about it!!

Visit labs you are interested in

- The lab should pay for your visit
- Most important thing: talk to the post-docs and students
  - May have to talk to people who have left the lab
- What happened to previous post-docs

Info you need to find out…

- Does the p.i. help her/his people?
- Let post-docs take projects and reagents with them?
- Caveat empteur!

Try to get an outside fellowship

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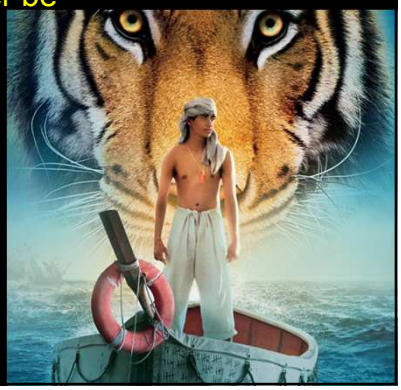
You don't have to be a PI to be a successful scientist

- No longer the Dirty Little Secret of biomedical research:
  - Most graduate students will never be a PI
- Alternative career = PI
- Many potential careers



Alternative Careers

- Taxi Driver
- Staff scientist
- Team scientist
- Teaching
- Scientific administration
  - Public/private
- Public policy
- Journalism
- Science writing
- Patent law
- Pharma/biotech business
- Wall Street
- Politics

Scientists have an important role to play in society and the political process

- Its is incumbent on us to preach the gospel of the scientific method
- Education begins in the local schools
- We need to make science a more attractive career

We need to completely rethink the current system of laboratory research

- We are exploiting young scientists
- It is ridiculous that “training” lasts until age 38
- This is simply a convenient excuse for underpaying the most productive members of the lab
- We’d be much better off with half the number of scientists and treating them twice as well

Scientists dictate how science is performed
Things we need to consider….

- What is the optimal lab set up?
- What is the optimal method of funding research?
  - The contract grant system needs to be rethought

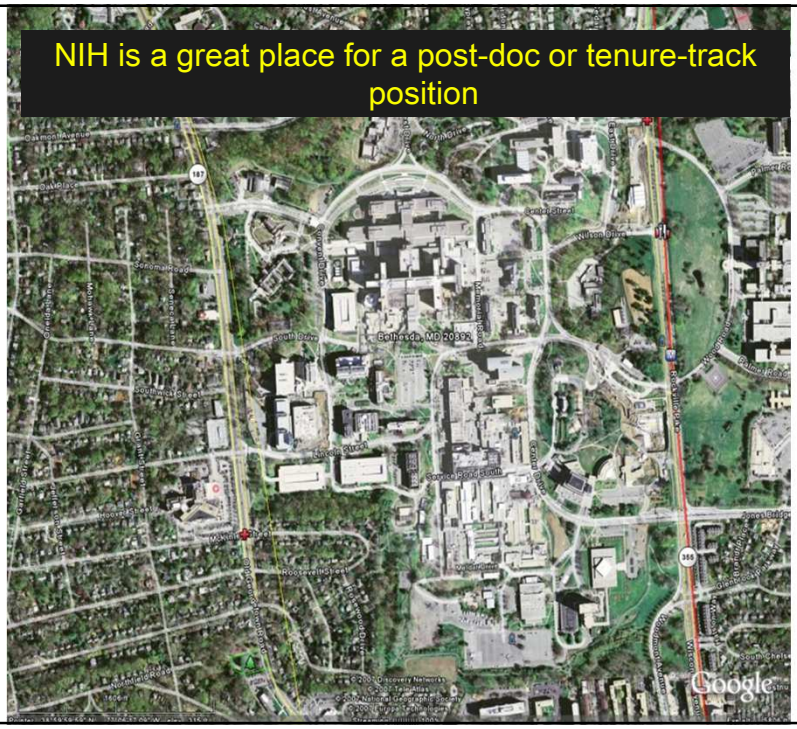
Advantages of Becoming a Life Scientist

- Saving the world
- Freedom
- You can show the world just how smart you are
- Never ending challenge
- Learning never stops
- Free PhD or MD/PhD
- See the world
- Friendship

Oh....One More Thing

NIH National Institute o Allergy and Infectious Disease

NIH is a great place for a post-doc or tenure-track position




That's all Folks
A WARNER BROS. CARTOON