The Research Business:
how to get inspired,
ask good questions,
and find out new stuff

Research is different than coursework.

Coursework:

- established, current scientific knowledge
- problems with known answers
- answering questions
- learning from books and lectures

Research:

- cutting-edge science, often under debate
- unknown answers, open-ended problems
- asking questions
- learning from current journal articles and scientific talks

Why choose a career in research?

- Job freedom
- Esteemed and well-paid
- Creativity
- Constant pool of new things to work on
- Cutting edge science! Solve the world's problems!

How does the research biz work?

- Funds are available
  - from public (NIH, NSF, DOE, etc) and private organizations, often in specific areas
  - from corporations sponsoring research relevant to their products
- Proposal writing and grant awarding
  - Principal Investigators include university professors, research associates at national labs
  - Highly competitive and time-consuming
  - Often collaborative
- Funds support graduate students, postdocs, researchers, equipment, supplies, administrative, travel, **overhead**

The seven warning signs of bogus science

- The discoverer pitches the claim directly to the media.
- The discoverer says that a powerful establishment is trying to suppress his or her work.
- The scientific effect involved is always at the very limit of detection.
- Evidence for a discovery is anecdotal.
- The discoverer says a belief is credible because it has endured for centuries.
- The discoverer has worked in isolation.
- The discoverer must propose new laws of nature to explain an observation.

Robert L. Park
The Chronicle Review
Volume 49, Issue 21, Page B20

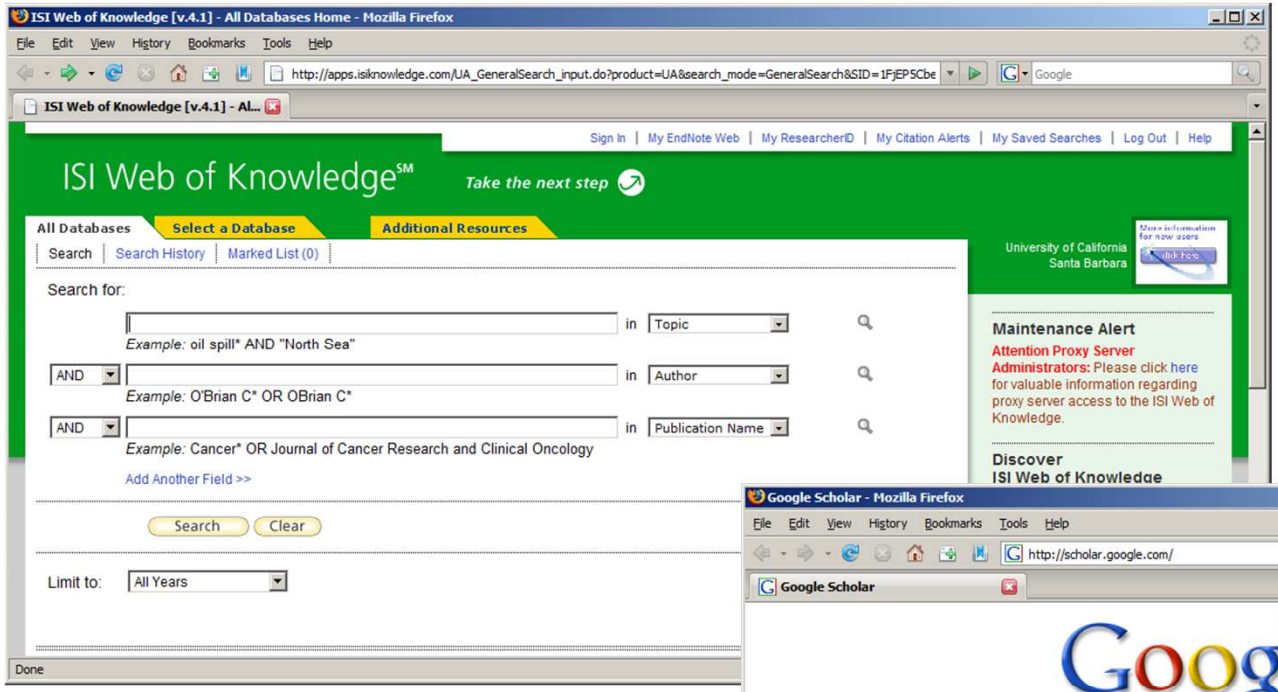
The basic ingredients to real research

- Knowing what's been done, the state-of-the art
- Asking good questions
- Refining good tests to answer them
- Communicating the results

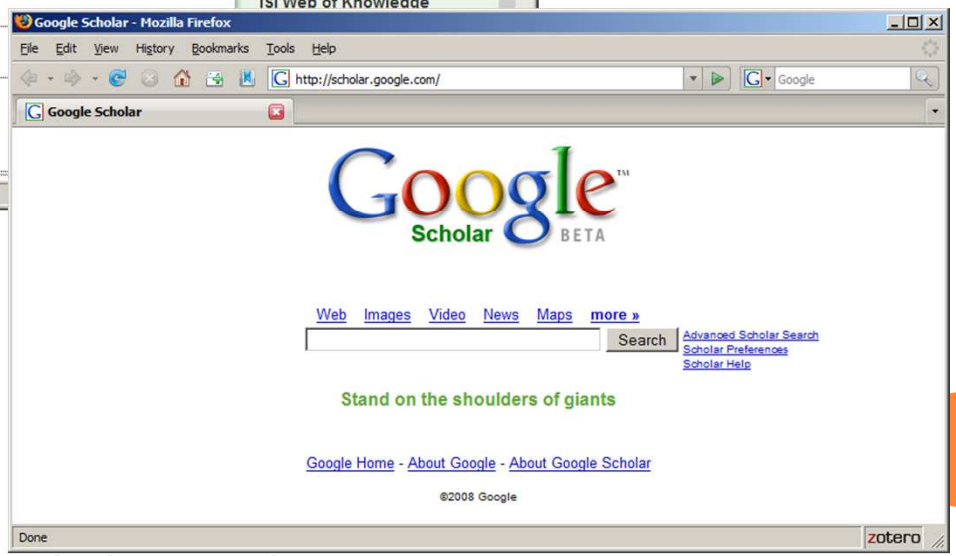
How to learn more about a research area

- General resources: books, websites (get recommendations!)
- Journal articles
  - Blind topical search
  - Follow an author
  - Follow references in introductions
- Chat with others
  - Advisors – “Can I stop by to talk about this?”
  - Experts – “Can I treat you to coffee?”
  - Colleagues / other students – “Can I buy you a beer?”
  - Lab mates – “Can you throw away those Dr. Pepper bottles, and by the way, can I pick your brain about something?”

How to find journal articles



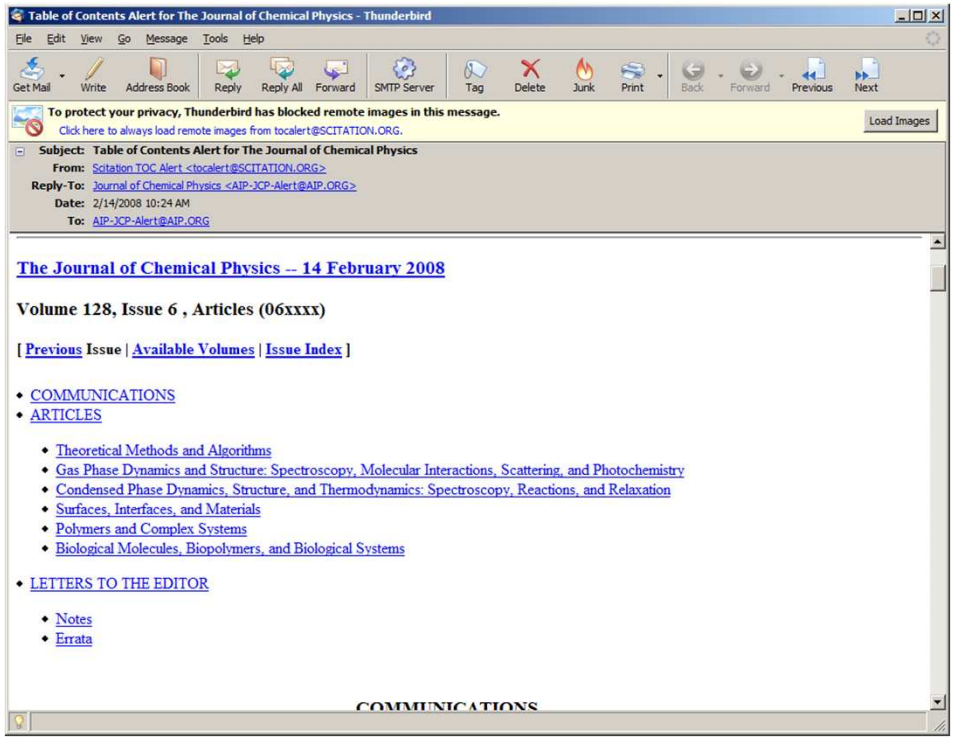
www.isiknowledge.com



scholar.google.com

Keeping up to date with the cutting edge

- Journals publish regularly (most are weekly)
- Journals have “impact factors”
- Electronic table of contents through email:



Reading papers

- Pick a focused time to read each day
- If confused, read more papers, especially review articles, then go back
- Highlight important parts. Summarize on the front with bullet points.
- Write down questions raised
- Work through derivations in important papers

How to dissect the by-line

- Usually, but not always, for non-review research articles:

Biophysical Journal Volume 90 March 2006 1949–1960

Coarse-Grained Strategy for Modeling Protein Stability in Concentrated Solutions. II: Phase Behavior

Vincent K. Shen,* Jason K. Cheung,† Jeffrey R. Errington,† and Thomas M. Truskett§

*Physical and Chemical Properties Division, National Institute of Standards and Technology, Gaithersburg, Maryland; †Department of Chemical Engineering, and §Department of Chemical Engineering and Institute for Theoretical Chemistry, The University of Texas at Austin, Austin, Texas; and ‡Department of Chemical and Biological Engineering, The State University of New York at Buffalo, Buffalo, New York

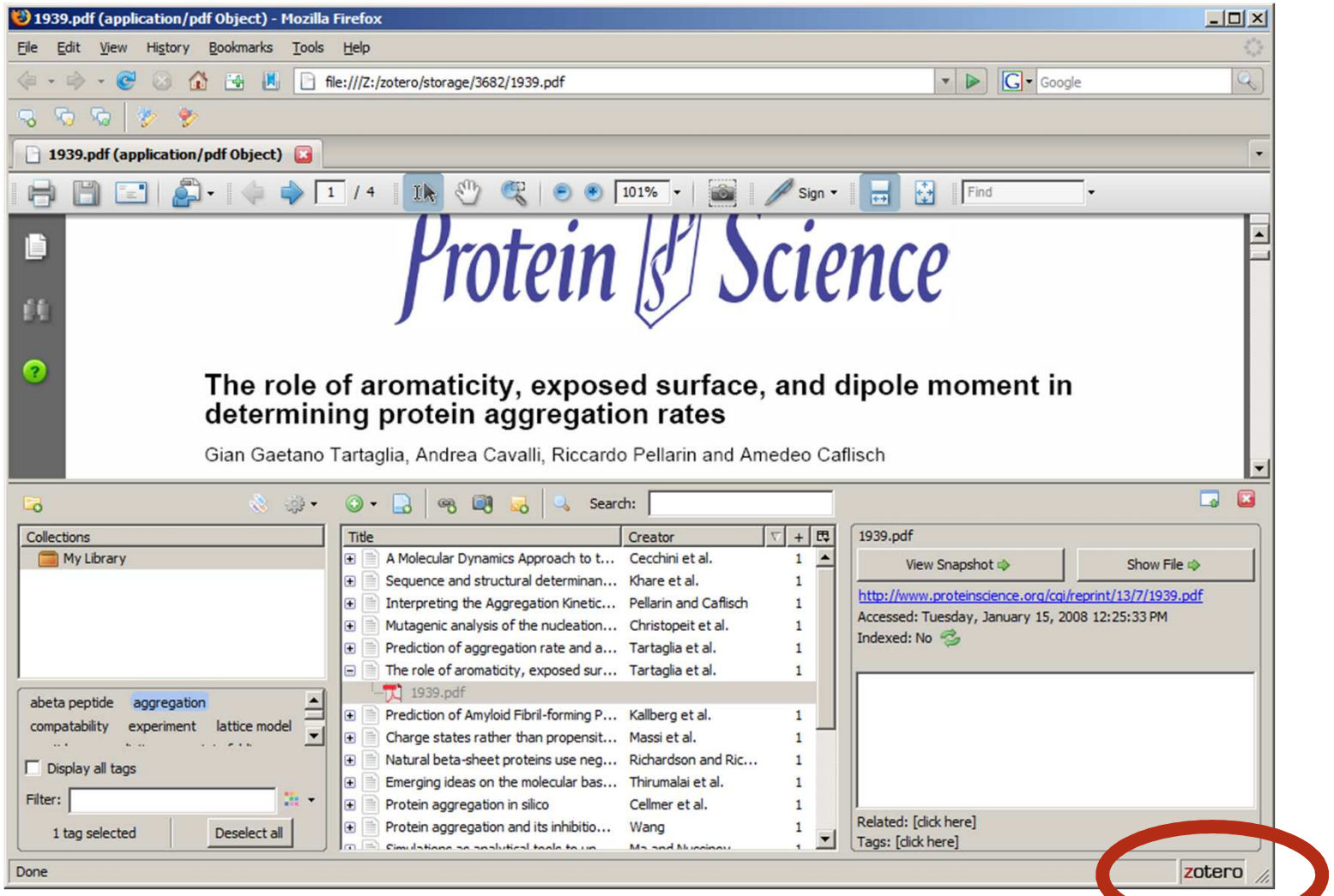
did most of the work and writing

did the second most

advised on the project

initiated and/or paid for the project (lead PI)

Keep tabs on read papers



Research is about asking good questions.

- **Too broad:**
  Why do proteins fold?
- **OK:**
  What is the role of the hydrophobic effect in driving proteins to fold?
- **Better:**
  Do mutations of hydrophobic residues in the protein core drastically destabilize its structure?
- **Best:**
  To what extent are the changes in the free energy of folding upon mutation of a single residue correlated to the change in hydrophobicity of the mutated amino acid?

Typical questions in the literature…

VOLUME 84, NUMBER 10 PHYSICAL REVIEW LETTERS 6 MARCH 2000

Is Random Close Packing of Spheres Well Defined?

S. Torquato,[1,*] T. M. Truskett,[2] and P. G. Debenedetti[2]
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(Received 1 November 1999)

Despite its long history, there are many fundamental issues concerning random packings of spheres that remain elusive, including a precise definition of random close packing (RCP). We argue that the current picture of RCP cannot be made mathematically precise and support this conclusion via a molecular dynamics study of hard spheres using the Lubachevsky-Stillinger compression algorithm. We suggest that this impasse can be broken by introducing the new concept of a *maximally random jammed* state

Protein Science (1998), 7:1201–1207. Cambridge University Press. Printed in the USA.

What should the Z-score of native protein structures be?

LI ZHANG AND JEFFREY SKOLNICK
Department of Molecular Biology, TPC-5, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, California 92037

(RECEIVED November 17, 1997; ACCEPTED January 23, 1998)

Abstract

The Z-score of a protein is defined as the energy separation between the native fold and the average of an ensemble of misfolds in the units of the standard deviation of the ensemble. The Z-score is often used as a way of testing the knowledge-based potentials for their ability to recognize the native fold from other alternatives. However, it is not

Questions are not always explicit

- "In contrast to crystalline solids, quantifying structural order in liquids and glasses has proved difficult because even though such systems possess short-range order, they lack long-range crystalline order."

- "The debate between these two viewpoints has continued, with numerous experimentalists and theoreticians investigating whether proteins reach their global energy minimum in a pathway-independent manner under thermodynamic control, or whether they follow a specific pathway to a possibly local minimum under kinetic control."

- *Common features*: specific, points to previous work done

Good questions lead to great science!

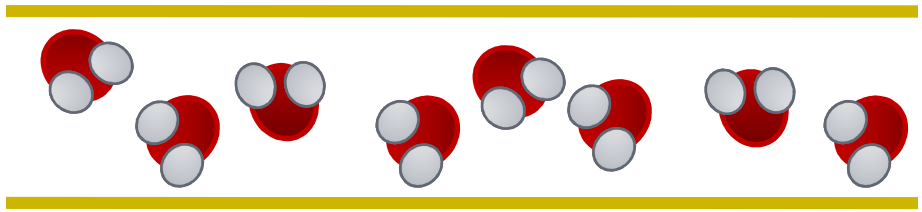
EARTH SHATTERING SCIENCE = IMPACT
X DECISIVENESS
X SURPRISE
X DEPTH
X UNDERSTANDABILITY

How to develop a research project.

- Research occurs in incrementally planned, specific projects $\rightarrow$ not necessarily incremental results.
- Projects need to be well-defined, have concrete planning.
- A recipe for developing a project:
  - Ask a question.
  - Develop a model (simplest that can answer the question).
  - Use the best techniques and analysis available.
  - What other questions arise?
  - Enough new interesting results have been gathered $\rightarrow$ publish

A research project case study

- Ask a question
  - How does the phase behavior of water change when it's confined in nanoporous materials (e.g., boiling temperature changes)?
- Develop a model:



- Use the best techniques and analysis available:
  - Grand Canonical Monte Carlo plus histogram reweighting
- What other questions arise?
  - Does the roughness of the surface matter?

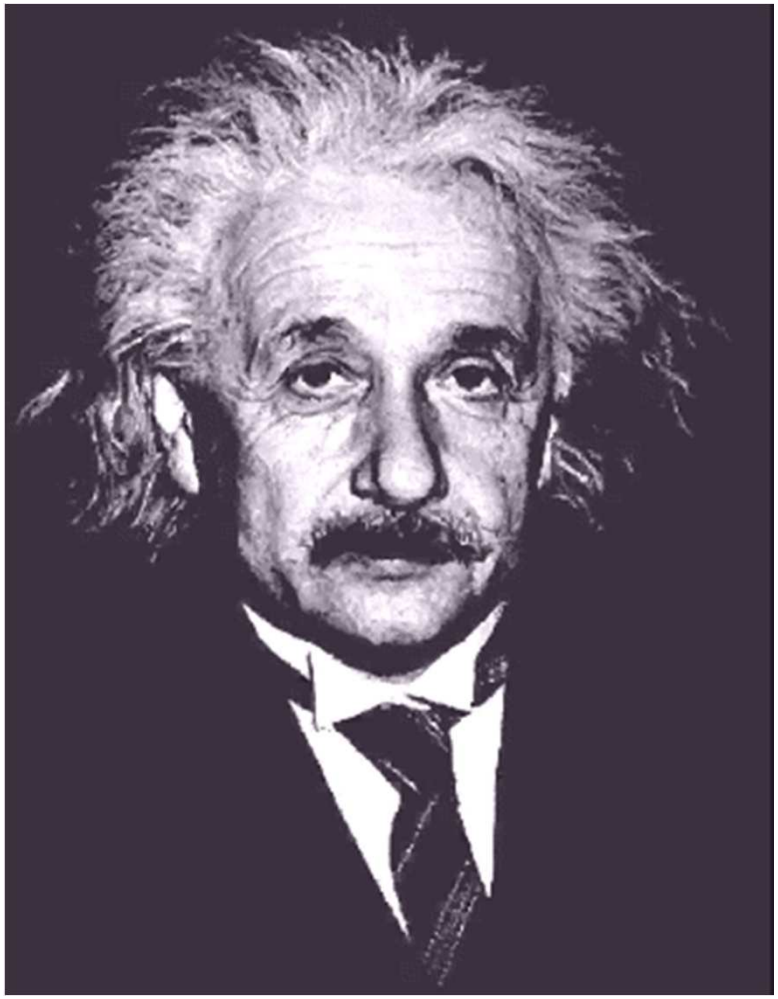
Some kinds of research projects

- Experimental *versus* computational *versus* theoretical
- Improving techniques *versus* new physical understanding
- Verifying previous conclusions with new methods
- Does an alternate viewpoint give the right answer?
- What minimum model is needed to capture the observed behavior? What are the right physical ingredients?

What a good research project knows…

- Why is this project important? What relevance does it have to science and society?
- What has been resolved? What remains unknown?
- What has been done before? What were the limitations?
- What new issue are you trying to resolve?
- How will you resolve it?

How to get inspired, be creative



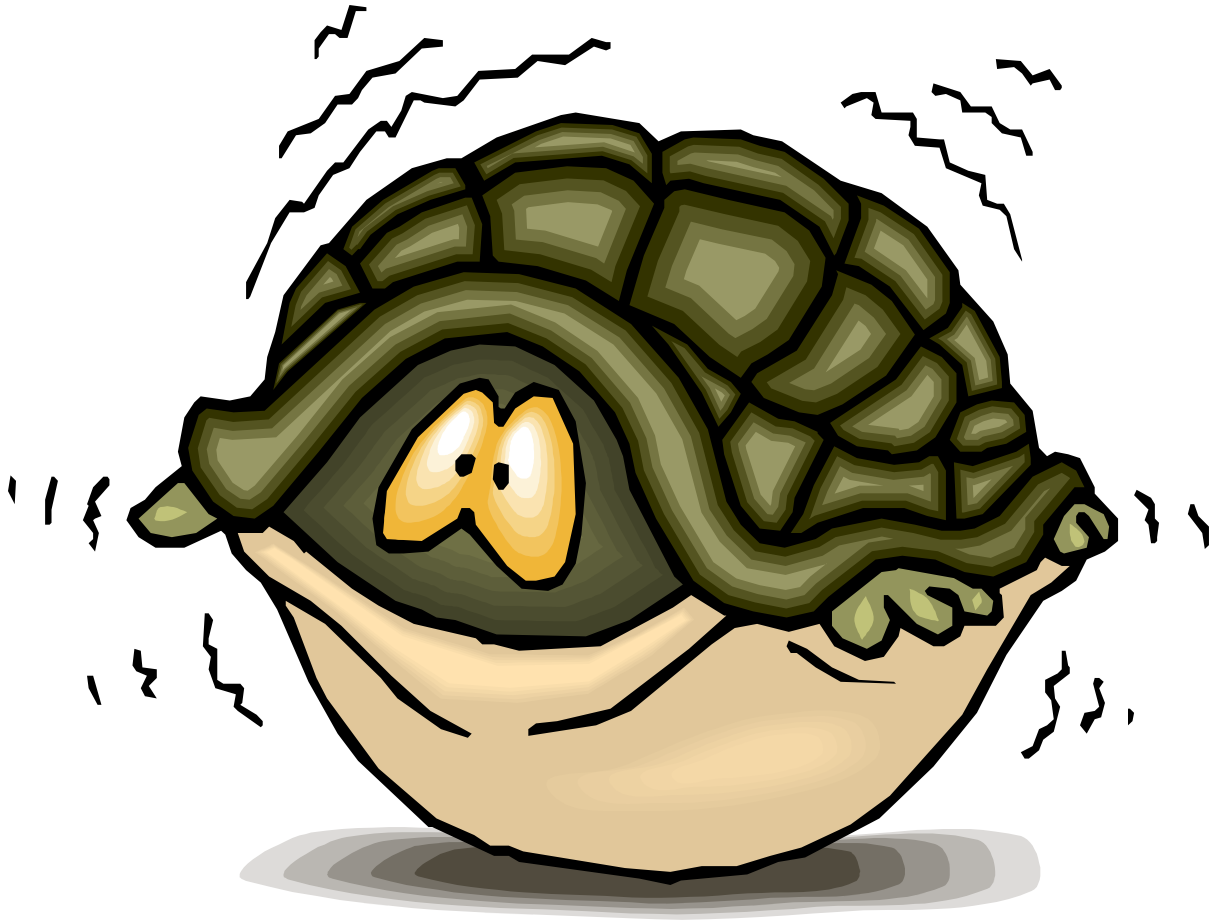
How to get inspired, be creative

- Know your stuff: read, read, read
- Be curious: constantly try out ideas in research (25% of time)
- Attend research talks and conferences: look for topics that bridge your field with others
- Talk to others
- Follow major “general interest” journals like Science and Nature, and read commentaries
- Know that creativity and inspiration take time!

Every good researcher has a notebook!

- Write *everything* down
  - ideas, questions, paper summaries, derivations, meetings and discussions, presentations, computer instructions, code, equations, appointments, horoscope, doodles, *everything*
- Rewrite important things cleanly
- Revisit old questions (may provide research ideas)
- Follow up: check papers of interesting speakers or email them, summarize meetings

Don’t be afraid to ask questions!



Watch out for these pitfalls

- Impatience, not having tolerance for thorough work
- Not deeply studying the details of past work / literature
- Not moving on from an unproductive project idea
- Not having multiple approaches / ideas / a backup plan
- Not taking ownership
- Working in a vacuum
- Taking things personally

Communicating and defending your research

Communicating and defending your research

- Seek opportunities to speak in front of others – become comfortable!
- The KISS principle – Keep It Simple, Stupid
- Don’t tell people what you did, tell them why they care
- Have a point, tell a story
- Respect your audience

What should keep you motivated

- Never boring… exciting new discoveries all the time
- Great personal reward in developing new knowledge and in teaching it to others
- Interaction with people and places all over the world
- Enormous amounts of caffeine

Research skills improve your everyday life

Materials and Methods [edit]

An assortment of donuts (*cf. doughnut*) are brought into the laboratory area at approximately 10.00 hours. The assortment typically consists of, but is not limited to, the following:


Raised glazed.


Glazed old-fashioned.


Apple fritter.


Twists (assorted).


Bear claw (common variety).

Donuts are rated on the "NIH" scale of 1-5, (1 being the best and 5 being the worst), in four main categories:

- Overall Experience
- Raised Glazed
- Old-Fashioned
- Apple Fritter

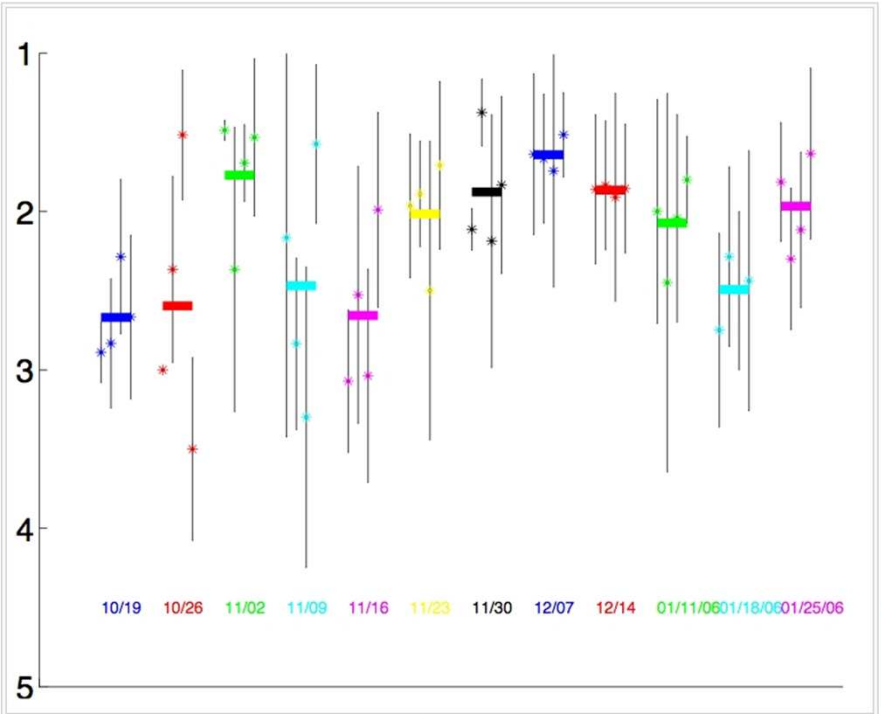


Figure 1: Each group of four category scores (in order: overall, raised glazed, old fashioned, apple fritter) are plotted for consecutive Donut Days (asterisks). The vertical bar for each score is the standard deviation, and the thick horizontal bar is the average over the four categories.