

# “Secrets of Success” or “The yin & yang of career success”

Thomas E. Nichols

Oxford Big Data Institute

Li Ka Shing Centre for Health Information and Discovery

Nuffield Department of Population Health

University of Oxford

Well, how did I get (t)here?



# Pittsburgh

- Carnegie Mellon: BS Computer Science

A map of the United States with a red dot in Pittsburgh, Pennsylvania. The text "Carnegie Mellon U." is next to the dot.

● Carnegie Mellon U.

# Pittsburgh

- Carnegie Mellon: BS ~~Computer Science~~

A map of the United States with a red dot in Pittsburgh, Pennsylvania. The text "Carnegie Mellon U." is next to the dot.

● Carnegie Mellon U.

# Pittsburgh

- Carnegie Mellon: BS Statistics

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# Pittsburgh

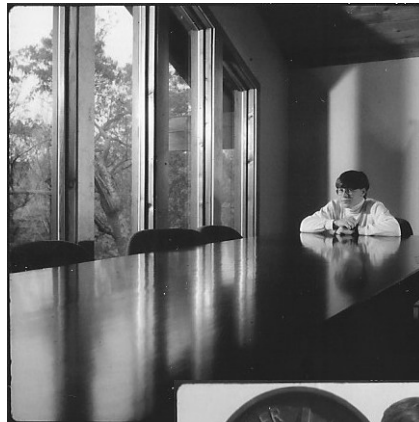
- Carnegie Mellon: BS Statistics
- Photography

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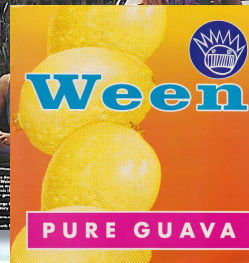
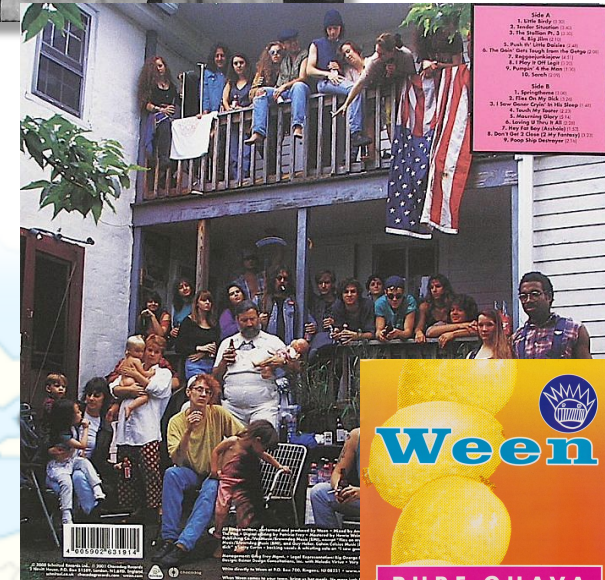
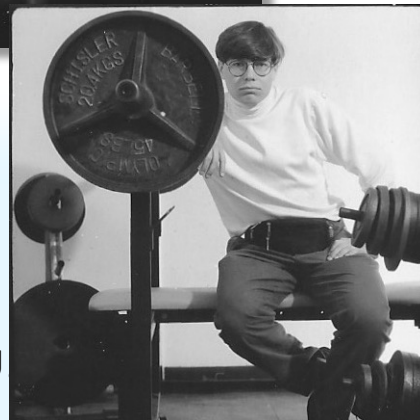
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# Pittsburgh

- Carnegie Mellon: BS Statistics
- Photography



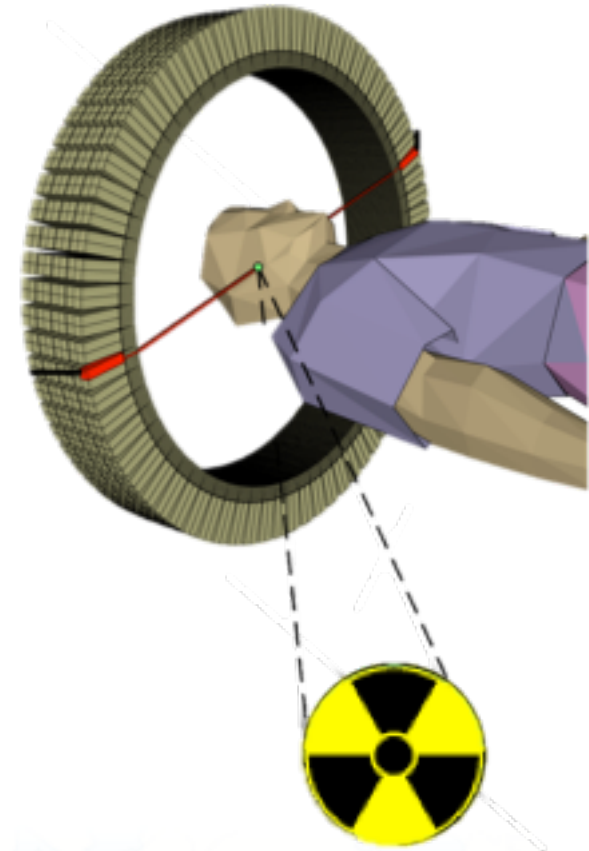
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# Pittsburgh

- Carnegie Mellon: BS Statistics
- Photography
- University of Pittsburgh PET Facility

Positron Emission  
Tomography



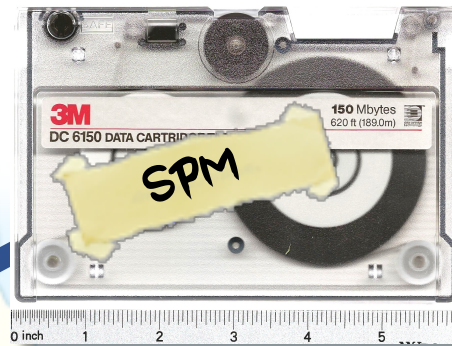
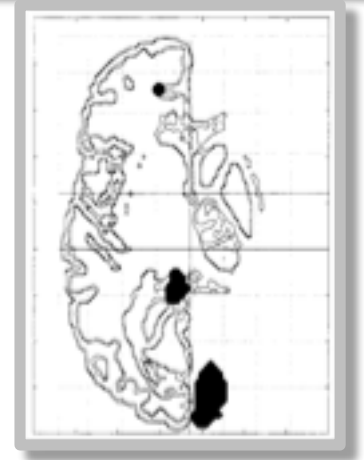
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/_)(/_\(_/_/)	Statistical
\_ \ )_/_/ ) (	Parametric
(_/_/(_ )(_/_/_/)	Mapping

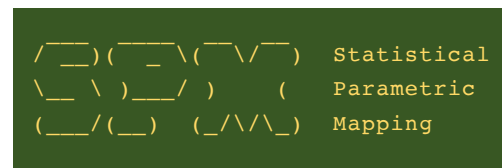
- Carnegie Mellon: BS Statistics
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- University of Pittsburgh PET Facility
  - SPM – PET Analysis software by Karl Friston



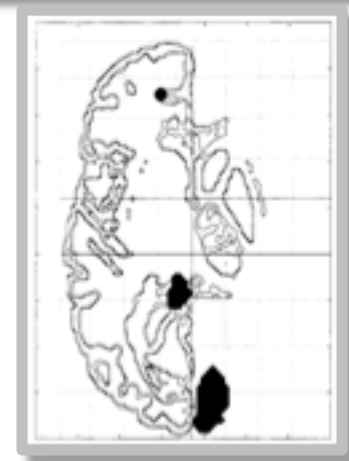
Early distribution method for SPM

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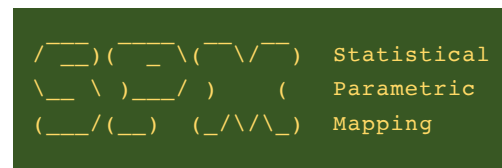


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  - SPM – PET Analysis software by Karl Friston
  - MRC Cyclotron Unit visit: Andrew Holmes

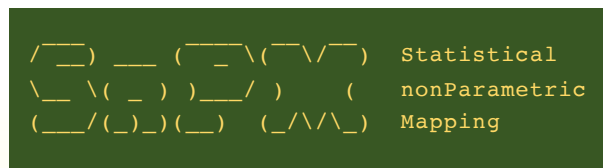
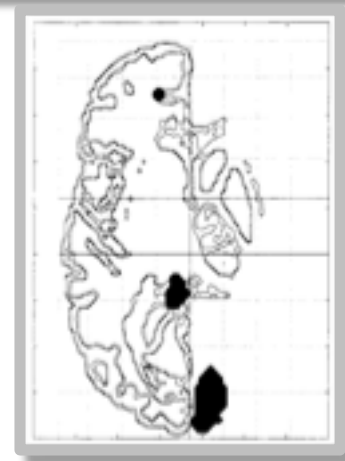


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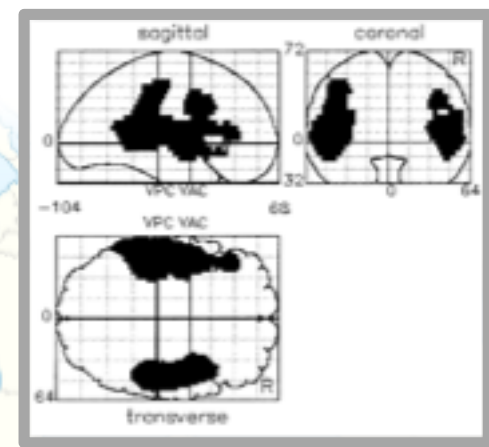


- Carnegie Mellon: BS Statistics
- Photography
- University of Pittsburgh PET Facility
  - SPM – PET Analysis software by Karl Friston
  - MRC Cyclotron Unit visit: Andrew Holmes
    - SnPM – Nonparametric version of SPM



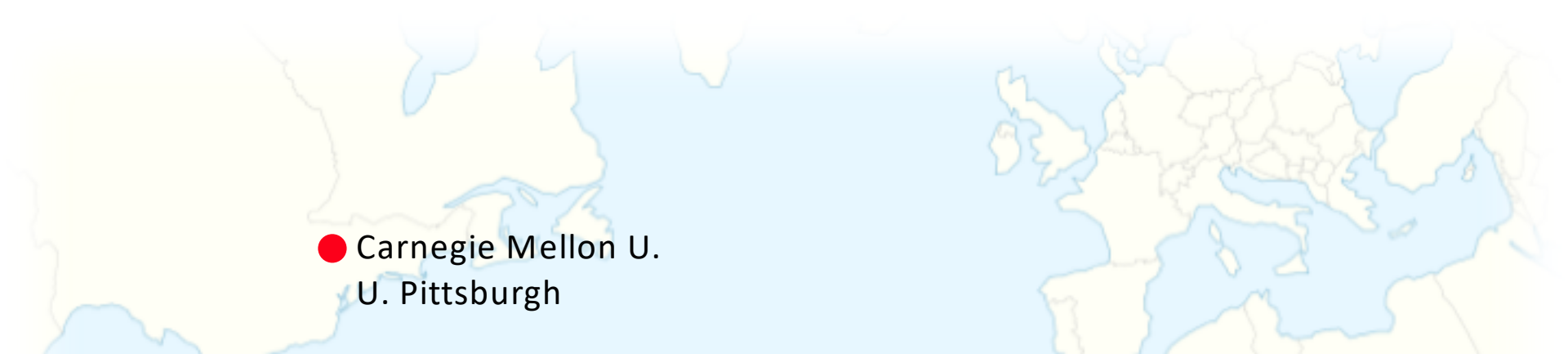
SnPM released 1997

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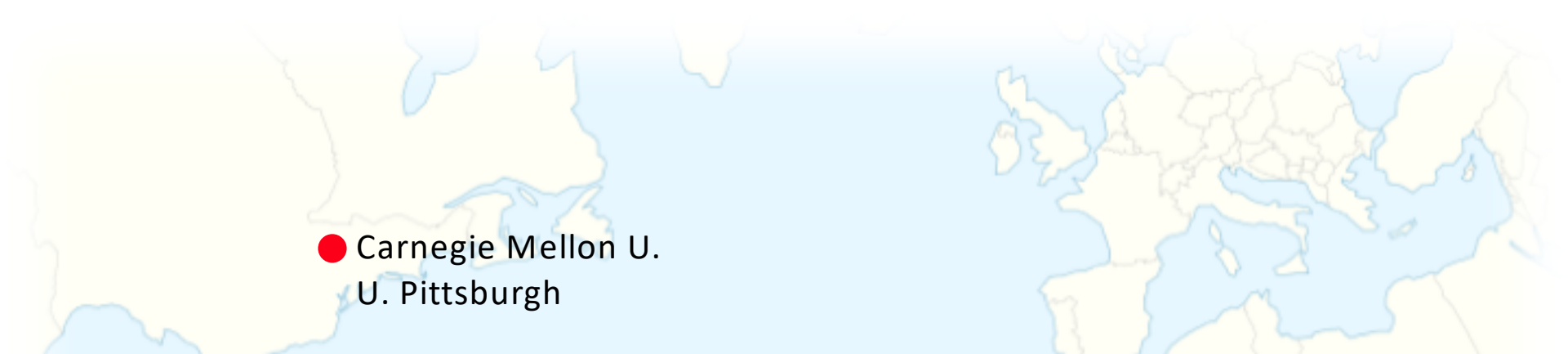
- Carnegie Mellon: BS Statistics
- Photography
- University of Pittsburgh PET Facility
- Carnegie Mellon: PhD Statistics

A map of the Pittsburgh area, showing the city and surrounding regions. The map is light blue and yellow, with a red dot indicating the location of Carnegie Mellon University and the University of Pittsburgh.

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# Pittsburgh

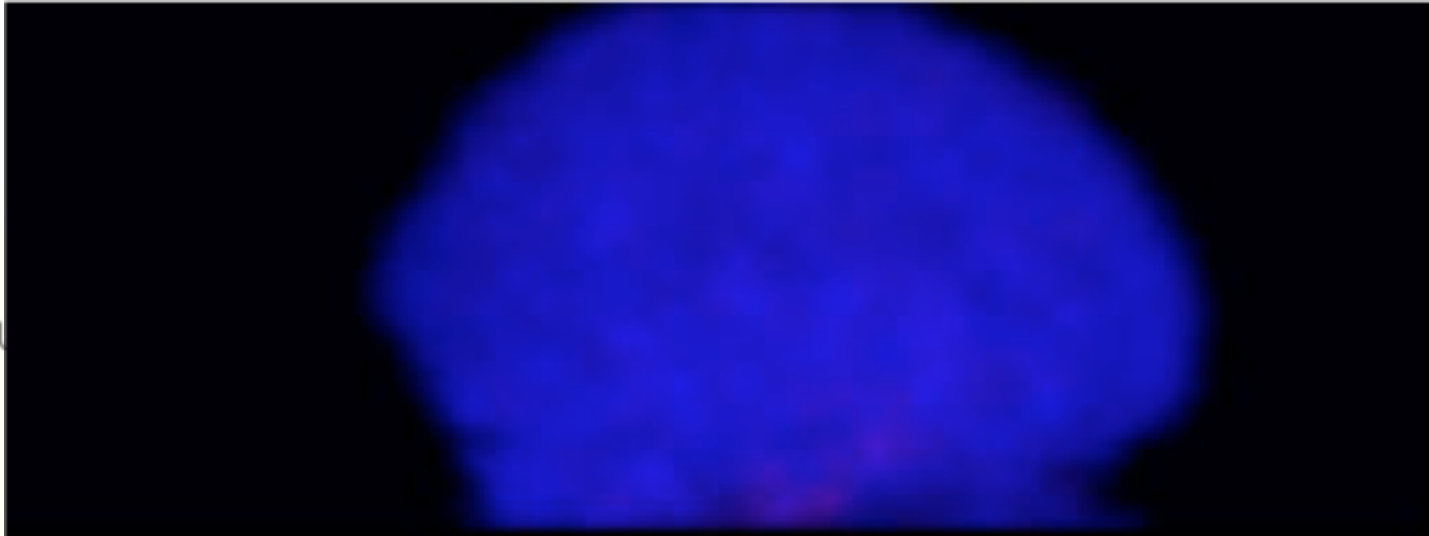
- Carnegie Mellon: BS Statistics
- Photography
- University of Pittsburgh PET Facility
- Carnegie Mellon: PhD Statistics
  - University Southern California visit: PET Movies

A map of the United States with a red dot in Pittsburgh. The text "Carnegie Mellon U." and "U. Pittsburgh" is written next to the dot.

● Carnegie Mellon U.  
U. Pittsburgh

# Pittsburgh

- Carnegie Mellon: BS Statistics
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- University of Pittsburgh PET Facility
- Carnegie Mellon: PhD Statistics
  - University Southern California visit: PET Movies



# Pittsburgh Lessons

- Profound impact of open software...
  - When shared *and* supported
- Collaboration
  - See the world *and* do science

A stylized map of the world with yellow landmasses and light blue oceans. A red dot is placed on the eastern coast of North America, specifically in the region of the United States.

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# Michigan

- University of Michigan Department of Biostatistics
- Continued software development
  - SnPM, but also FSL's randomise
- Focus on inference for MRI
  - False Discovery Rate
  - Continued FWE permutation evaluations
  - Conjunction Inference

U. Michigan





# Conjunction Inference in SPM

- Example, 3 variants of N-Back

Letter memory:	D	J	D	F	P	R	A	R	.	.	.
Number memory:	4	2	4	8	4	2	3	2	.	.	.
Shape memory:	♣	⊂	♣	♥	∩	♠	×	♠	.	.	.

- Only want voxels that activate all three
- Friston & Worsley (2000) Conjunction
  - Found null distribution of  $\min_k T_k$  random field
    - FWE thresholds on min image<sup>k</sup>

Worsley, Friston (2000). A test for a conjunction. *Statistics and Probability Letters*, **47**, 135-140.

“No effects present”  $H_0 : \bigcap_k \{H^k = 0\}$

“Some effects present”  $H_A : \bigcup_k \{H^k = 1\}$

## 2. Integral geometry and stereology

In this section we shall state some results from integral geometry and stereology that will be used to prove our main result (see, for example, Santaló, 1979).

Let  $\mu(A)$  be the (0) Minkowski functional of a set  $A \subset \mathbb{R}^D$ , scaled so that it is invariant under embedding of  $A$  into any higher-dimensional Euclidean space. If  $A$  has a twice differentiable boundary  $\partial A$ , then it can be defined as follows. Let  $\omega_{j-1} = 2\pi^{j/2}/\Gamma(j/2)$  be the surface area of a unit  $(j-1)$ -sphere in  $\mathbb{R}^j$ . For  $M$  an  $n \times n$  matrix let  $\det(M)$  denote the sum of the determinant of all  $j \times j$  principal minors of  $M$ , so that  $\det_n(M) = \det(M)$ ,  $\det_1(M) = \text{tr}(M)$  and we define  $\det_0(M) = 1$ . Let  $Q$  be the  $(D-1) \times (D-1)$  curvature matrix of  $\partial A$ . Then for  $0 < i < D$ ,

$$\mu(A) = \frac{1}{\omega_{D-1}} \int_{\partial A} \det_{D-1-i} Q \, d\mathcal{H}^i$$

and define  $\mu_0(A) = |A|$ . Note that  $\mu(A)$  is the EC of  $A$  by the Gauss-Bonnet Theorem, and  $\mu_{D-1}(A)$  is half the surface area of  $A$ . For example, the Minkowski functionals of a ball  $A$  of radius  $r$  in  $\mathbb{R}^D$  are

$$\mu_0(A) = 1, \quad \mu_1(A) = 4\pi, \quad \mu_2(A) = 2\pi^2, \quad \mu_3(A) = (4/3)\pi r^3. \quad (3)$$

We shall use the result that any set functional  $\phi(A)$  that obeys the additivity rule

$$\phi(A \cup B) = \phi(A) + \phi(B) - \phi(A \cap B) \quad (4)$$

is a linear combination of the Minkowski functionals. Let  $A, B \subset \mathbb{R}^D$ , then the Kinematic Fundamental Formula

# Conjunction Inference – Right null

- Rather, want:

$$H_0 : \bigcup_k \{H^k = 0\} \quad \text{“Not all effects present”}$$

$$H_A : \bigcap_k \{H^k = 1\} \quad \text{“All effects present”}$$

- Correct conjunction test:
  - Take conjunction of tests, each at usual level
  - E.g. if  $K = 3$  tests are all significant at  $\alpha = 0.05$ 
    - Reject conjunction null  $H_0$  in favour of  $H_A$

# Michigan Lessons

- Just because a result is published & cited, doesn't mean its right
- Great rewards for working closely with the user
- Build generic, tools (keep on) supporting them
- It doesn't need to be published in JASA/JRSS (your own discipline's top journal) to be impactful

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# GlaxoSmithKline

GSK House



# GlaxoSmithKline

GSK House



GSK Clinical Imaging Centre  
Hammersmith Hospital Campus



Wormwood Scrubs Prison

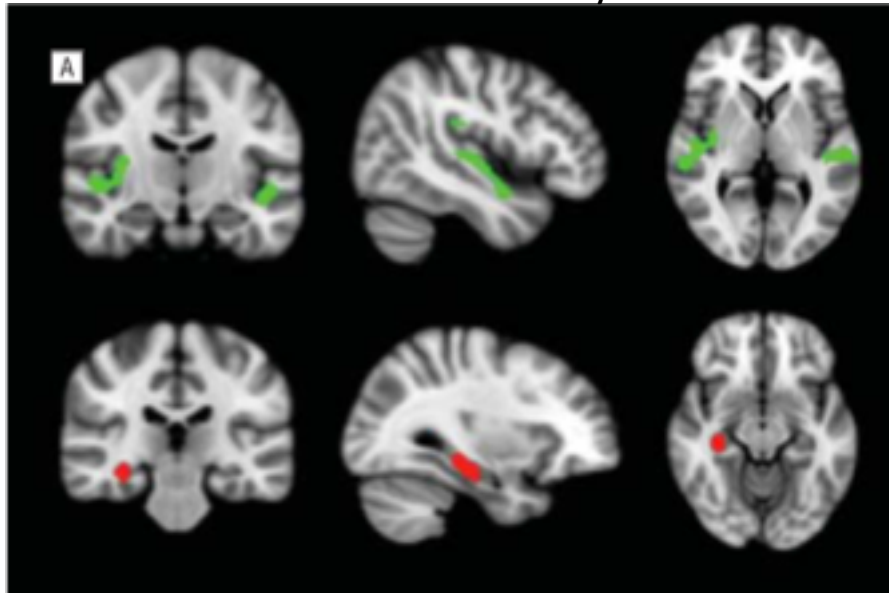




# GSK: Imaging Genetics of Depression & Glycogen Synthase Kinase-3 $\beta$ (GSK3 $\beta$ )

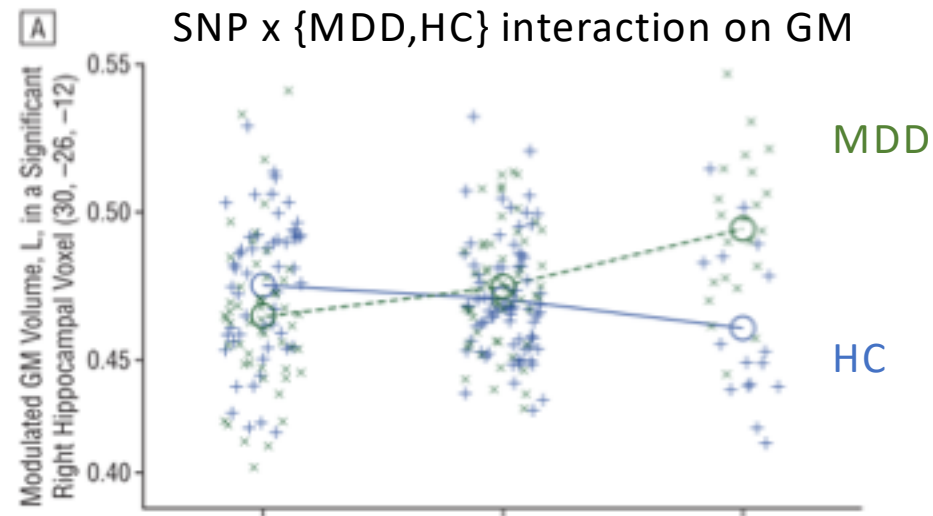
- Main effects of SNP
  - Green: Superior temporal gyrus:  $P < 0.001$  (Space, 15 SNPs)
  - Red: Right Hippocampus:  $P < 0.02$  (Space only)
- SNP x MDD interaction

Main effect SNP on Grey Matter



rs6438552

L Hippocampus:  
SNP x {MDD,HC} interaction on GM



rs6438552

# GlaxoSmithKline Lessons

- Amazing smart, driven scientists
- Pharma priorities change at lightening speed
- Clinical trials are hard

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GlaxoSmithKline



Inter-  
disciplinary  
training

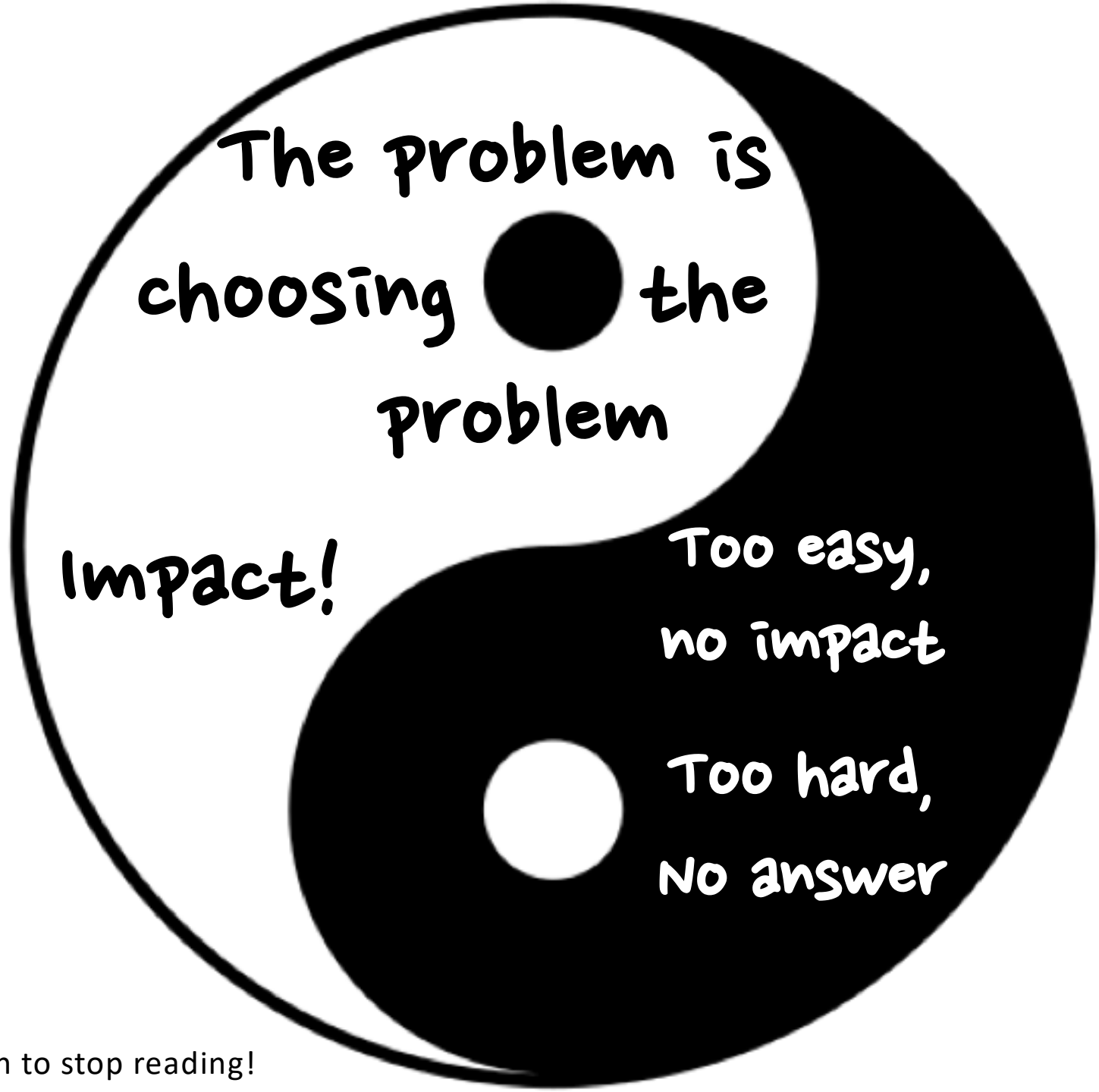
Deep  
disciplinary  
training





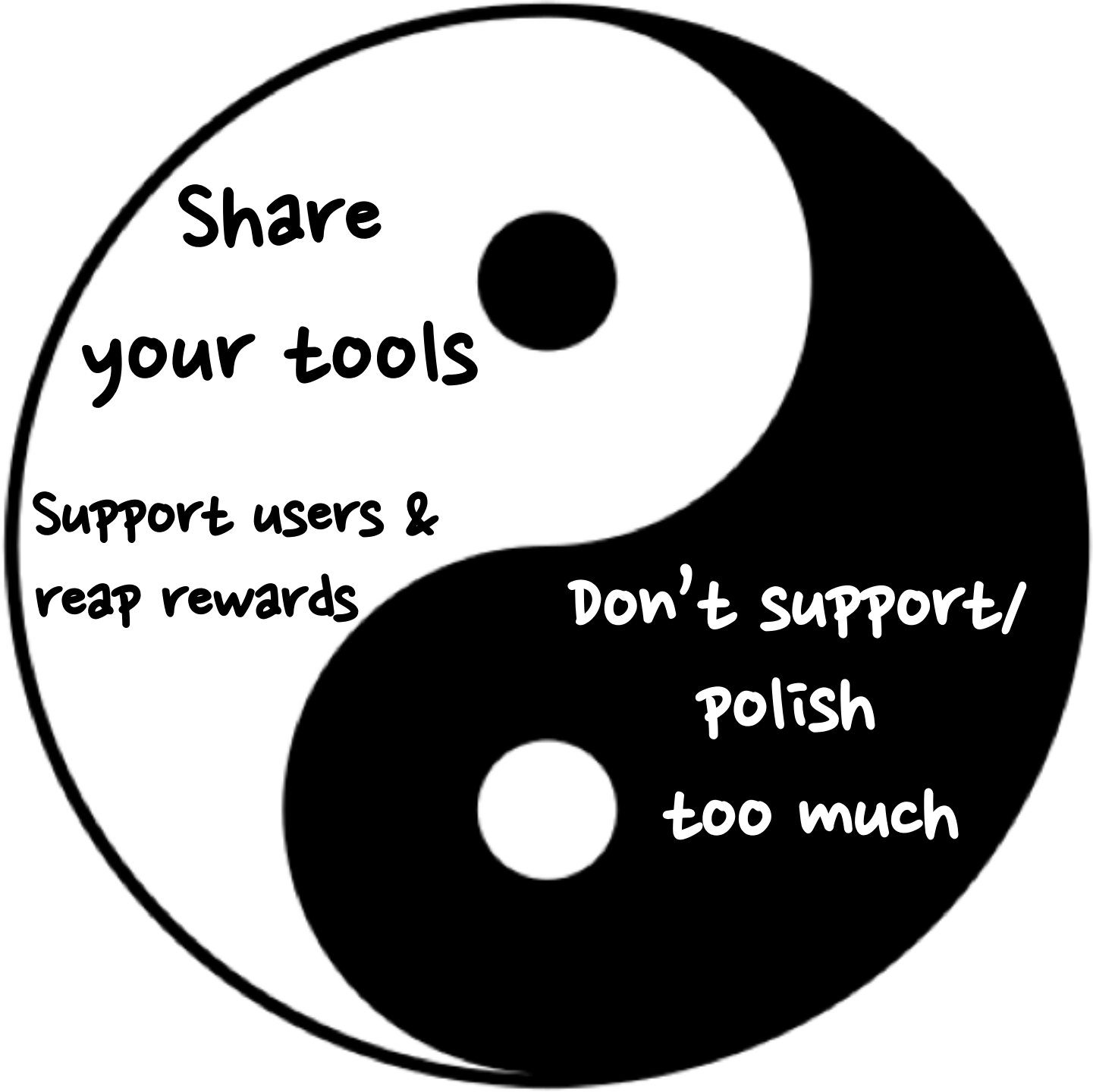
Look  
everywhere  
for mentors

Mentors  
are only  
human



Know when to stop reading!

# Methodologists



# Non-Methodologists

Learn stats, coding early.

Always know:

- What exactly is your question?
- Are you collecting data that can answer that question?
- Are you using stat. methods that answer that question?



Thank you!