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Data Visualisation: Saying it all in a bite-sized chunk

Ed Champness, Matt Segall & Peter Hunt

Overview

- Data visualisation
- Less is more?
- The many dimensions of drug discovery data
- Multi-Parameter Optimisation
- Conclusions

Data Visualisation

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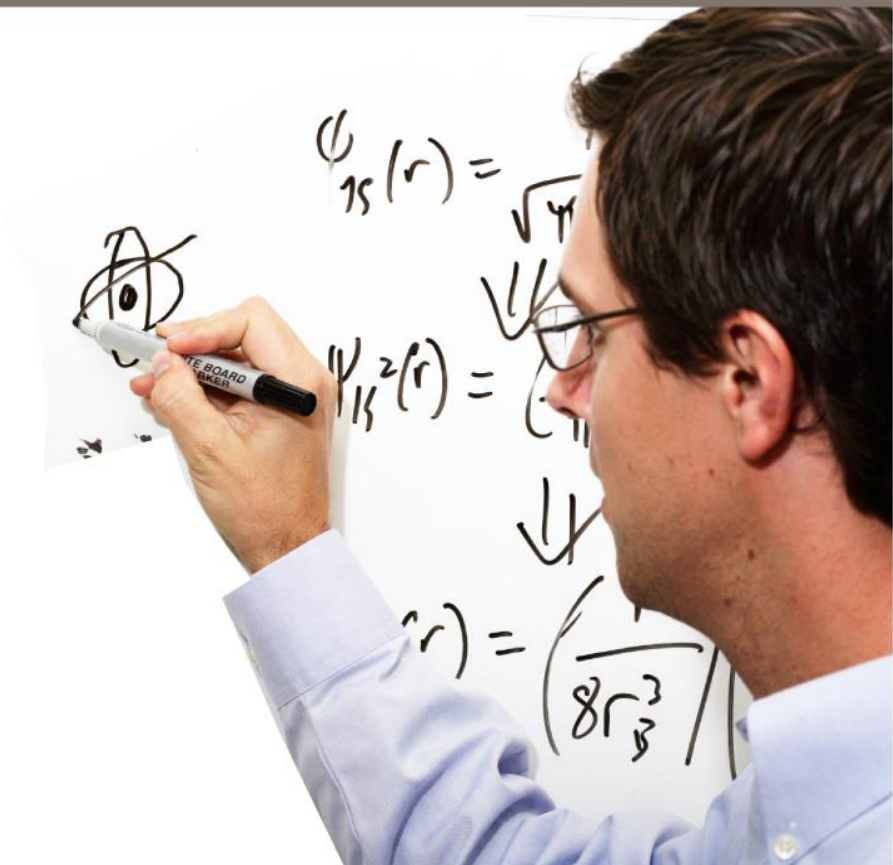


Why use data visualisation?

- Visualisation systems provide visual representations of data sets designed to help people carry out tasks more efficiently
- Visualisation allows people to analyse data when they don't know exactly what they are looking for
- …when there is a need to augment human capabilities rather than replace people with computational decision-making methods

Visualization Analysis and Design – Tamara Munzner (UBC)

Use of data visualisation

When the statistics deceive us… Anscombe's quartet

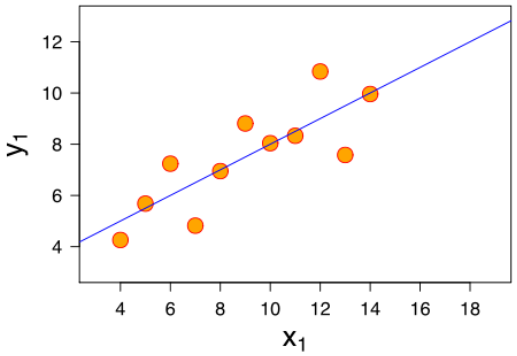
1		2		3		4	
X1	Y1	X2	Y2	X3	Y3	X4	Y4
10.0	8.04	10.0	9.14	10.0	7.46	8.0	6.58
8.0	6.95	8.0	8.14	8.0	6.77	8.0	5.76
13.0	7.58	13.0	8.74	13.0	12.74	8.0	7.71
9.0	8.81	9.0	8.77	9.0	7.11		
11.0	8.33	11.0	9.26	11.0	7.81		
14.0	9.96	14.0	8.10	14.0	8.84		
6.0	7.24	6.0	6.13	6.0	6.08		
4.0	4.26	4.0	3.10	4.0	5.39		
12.0	10.84	12.0	9.13	12.0	8.15		
7.0	4.82	7.0	7.26	7.0	6.42		
5.0	5.68	5.0	4.74	5.0	5.73		

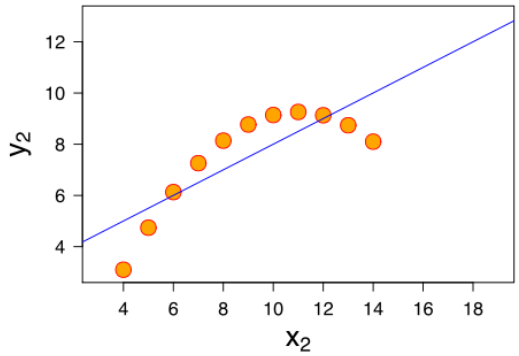
Property	Value
Mean(x)	9
Variance(x)	11
Mean(y)	7.5 (2dp)
Variance(y)	4.122 or 4.127 (3dp)
Pearson r	0.816 (3dp)
Linear regression	y = 3 + 0.5x (2dp)

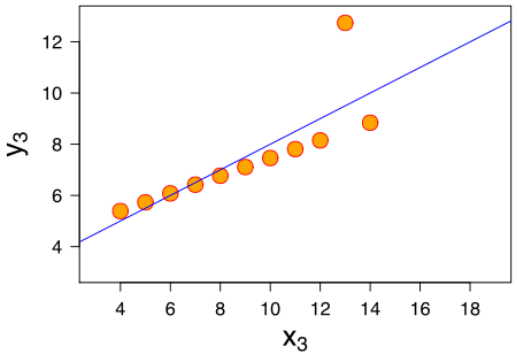
en.wikipedia.org/wiki/Anscombe%27s_quartet

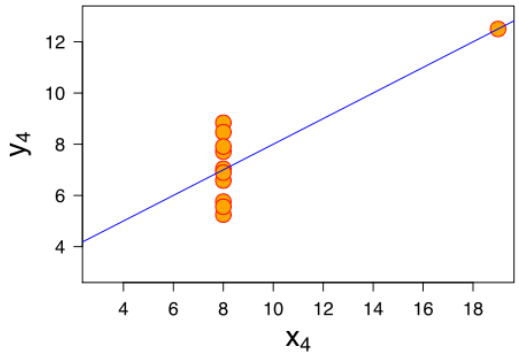
Use of data visualisation

When the statistics deceive us… Anscombe's quartet









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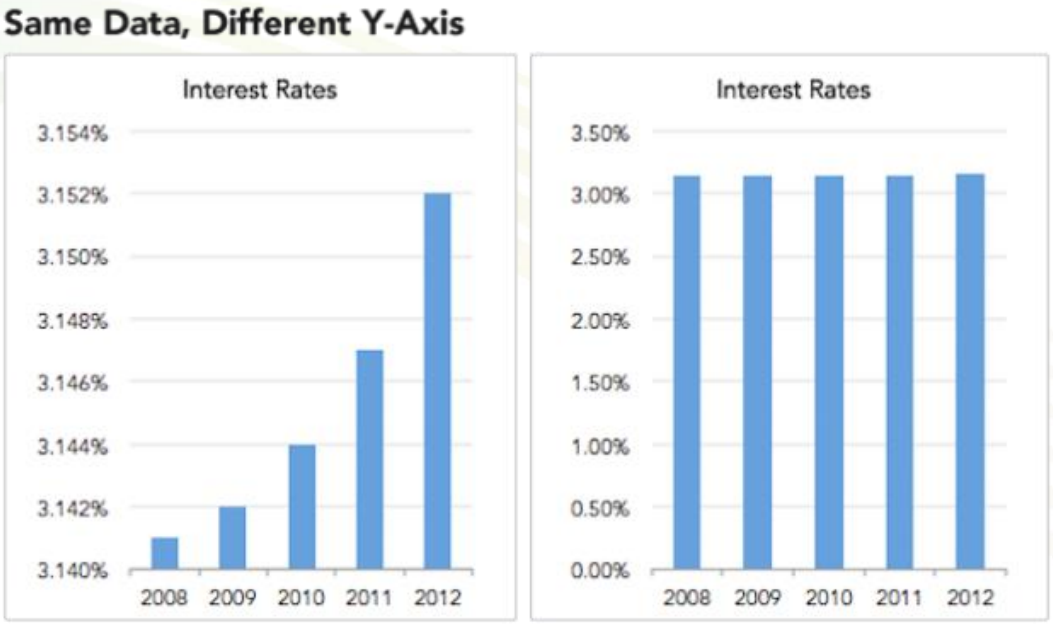
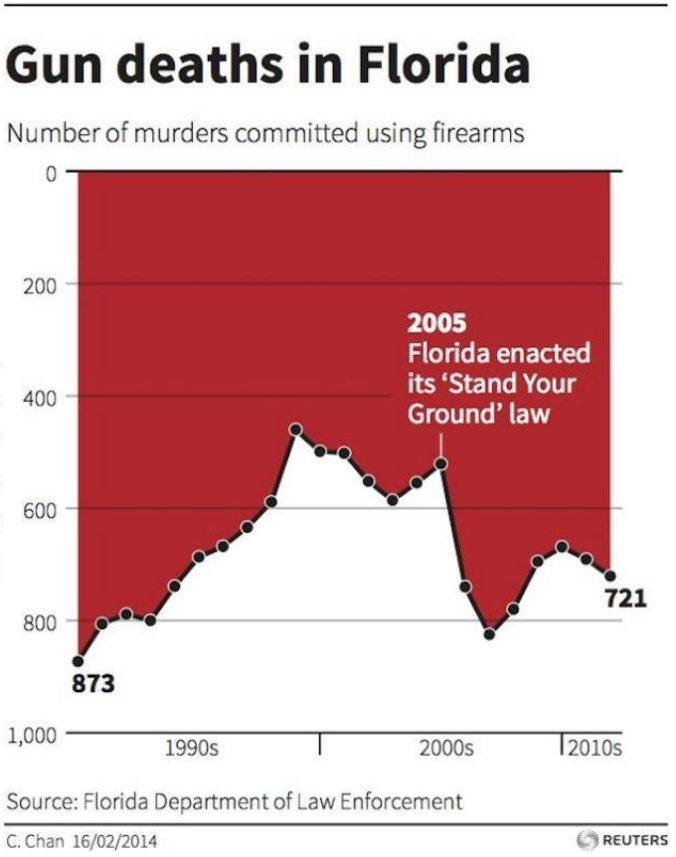
A few (obvious?) do's and don'ts

- Don't distort the data

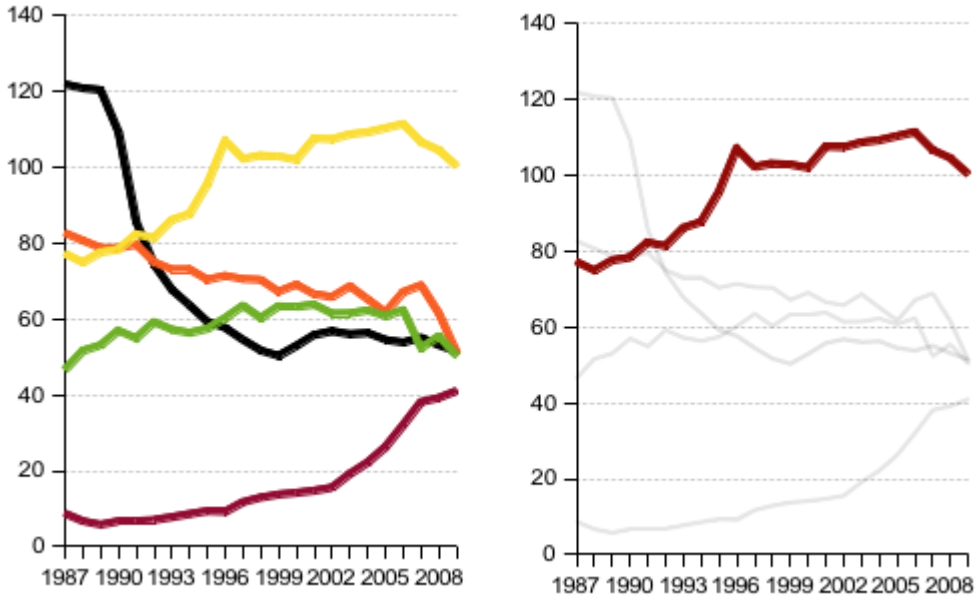




Ravi Parikh - Heap Analytics: gizmodo.com/how-to-lie-with-data-visualization-1563576606

A few (obvious?) do's and don'ts

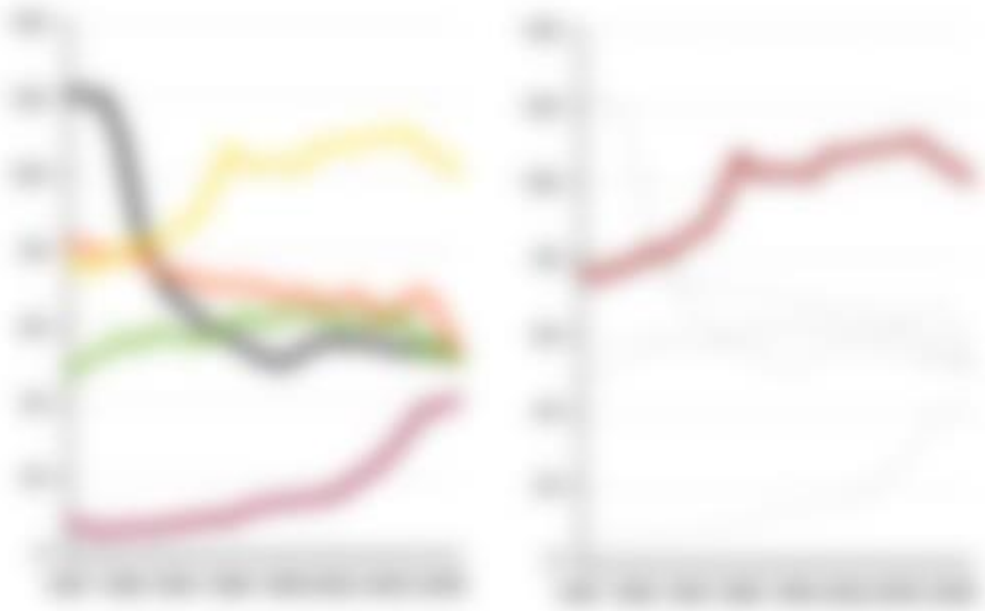
- Don't distort the data
  - But do simplify the less important information



https://www.vis4.net/blog/posts/doing-the-line-charts-right/

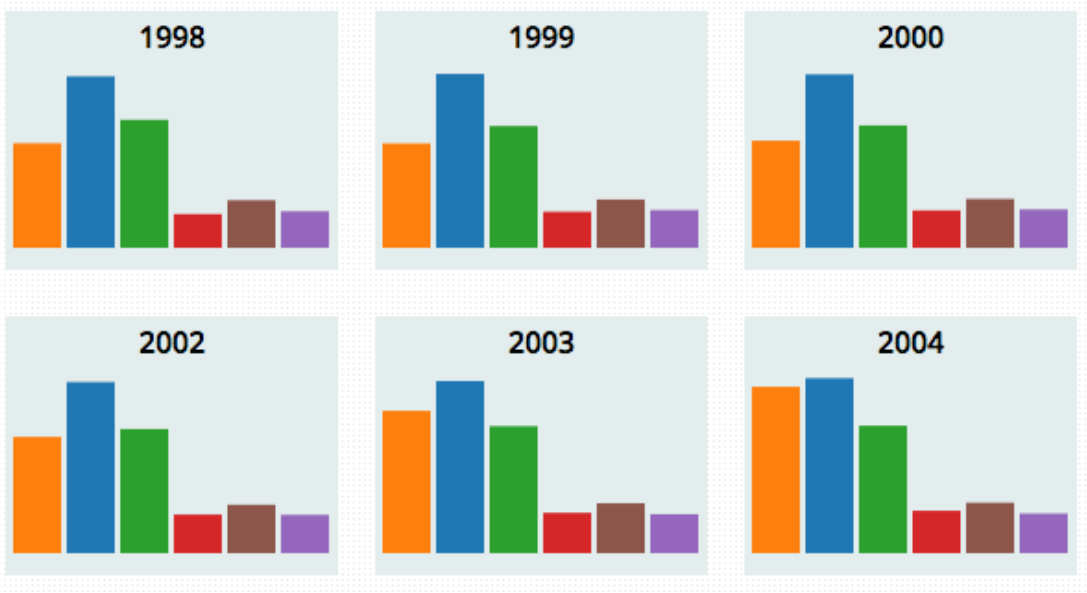
A few (obvious?) do's and don'ts

- Don't distort the data
  - But do simplify the less important information
- Consider the squint test



A few (obvious?) do's and don'ts

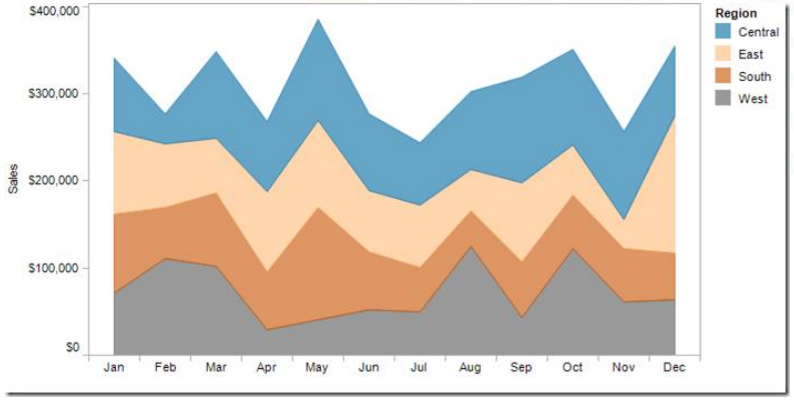
- Don't distort the data
  - But do simplify the less important information
- Consider the squint test
- Use consistent layout



http://vallandingham.me/small_multiples_with_details.html

A few (obvious?) do's and don'ts

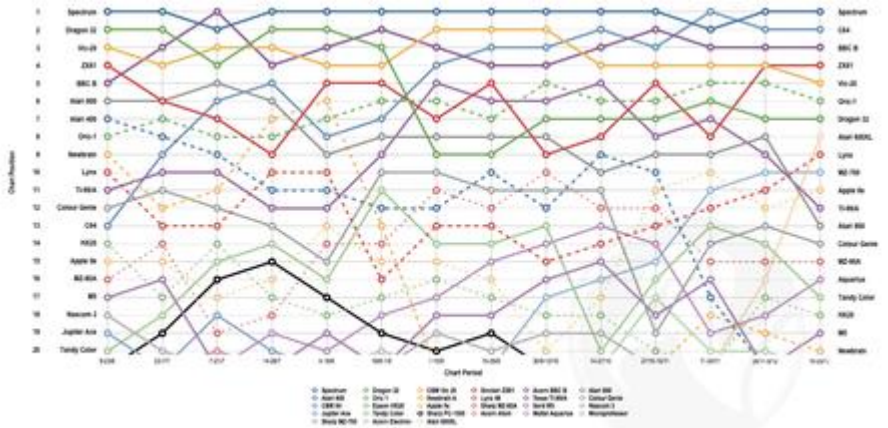
- Don't distort the data
  - But do simplify the less important information
- Consider the squint test
- Use consistent layout
- Don't force the reader to calculate differences



http://www.vizwiz.com/2012/10/stacked-area-chart-vs-line-chart-great.html

A few (obvious?) do's and don'ts

- Don't distort the data
  - But do simplify the less important information
- Consider the squint test
- Use consistent layout
- Don't force the reader to calculate differences
- Don't overload the chart



http://junkcharts.typepad.com – Kaiser Fung

Less is more?

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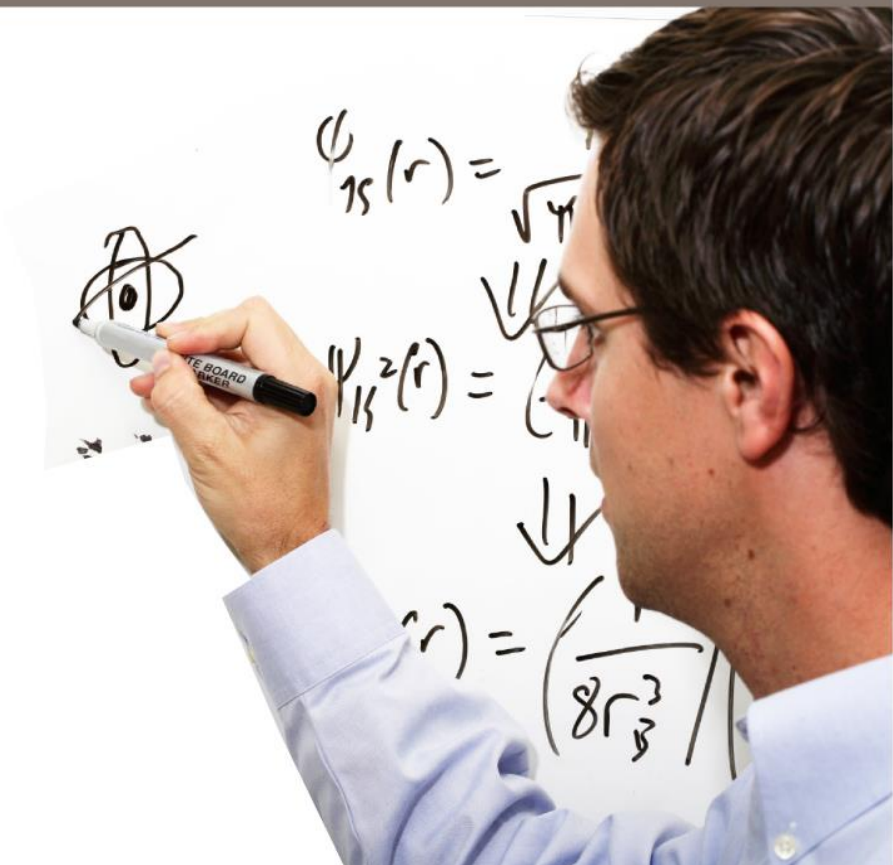
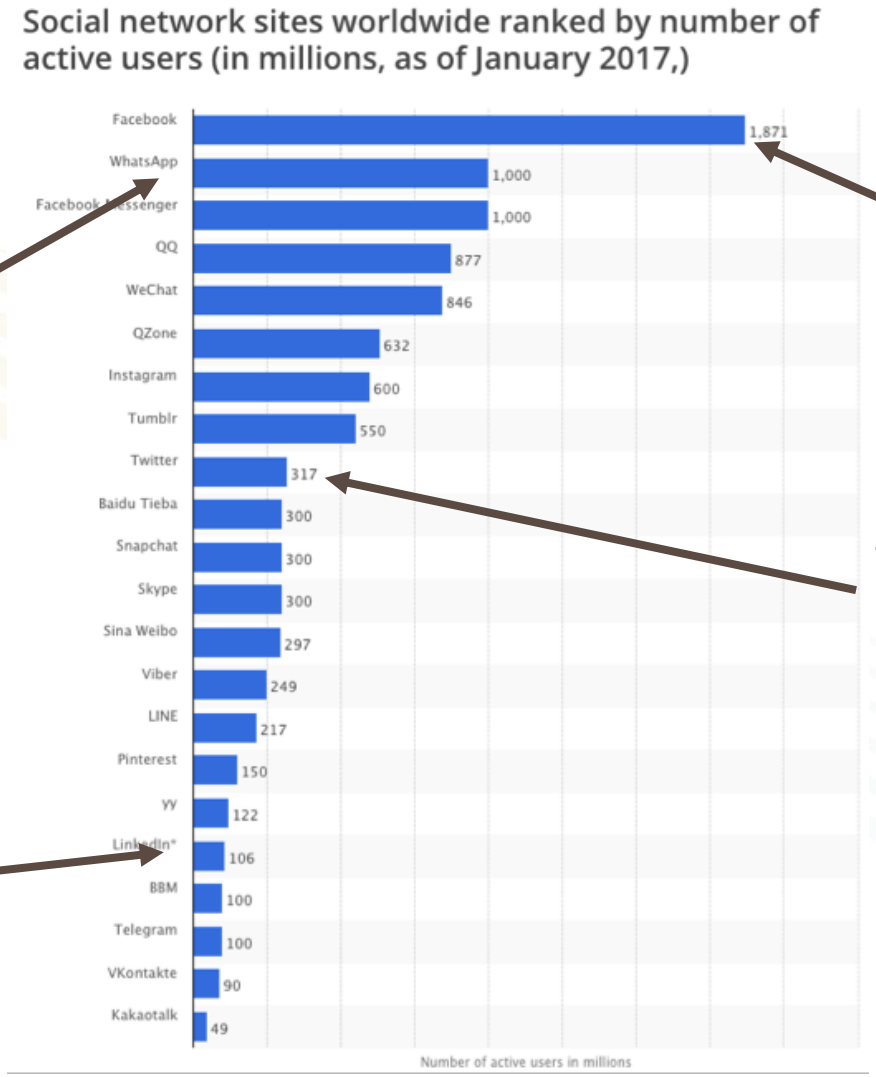


The predominance of social media



WhatsApp
1,000

Facebook
1,871

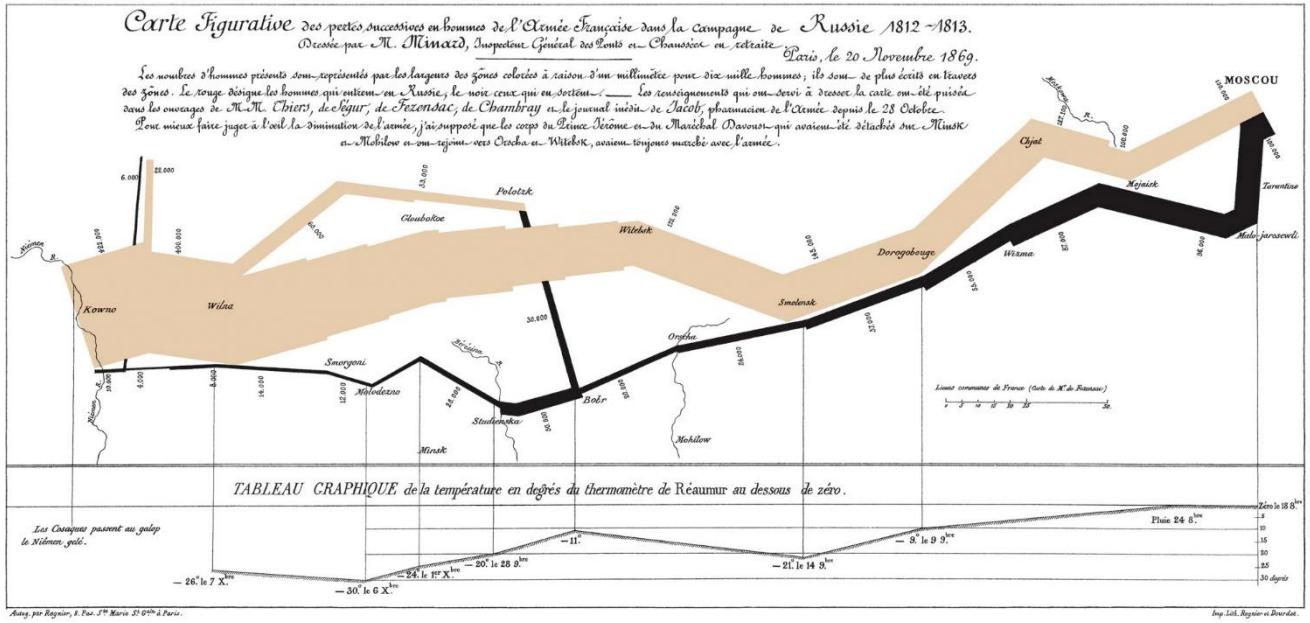
Twitter
317

LinkedIn
106

www.smartinsights.com

Designing a Visualisation

- Tufte: What makes for such graphical elegance? … Good design has two key elements: Graphical elegance is often found in simplicity of design and complexity of data.



- Minard's graphic of Napoleon's Russian march and retreat

The Visual Display of Quantitative Information – Edward Tufte

The many dimensions of drug discovery data

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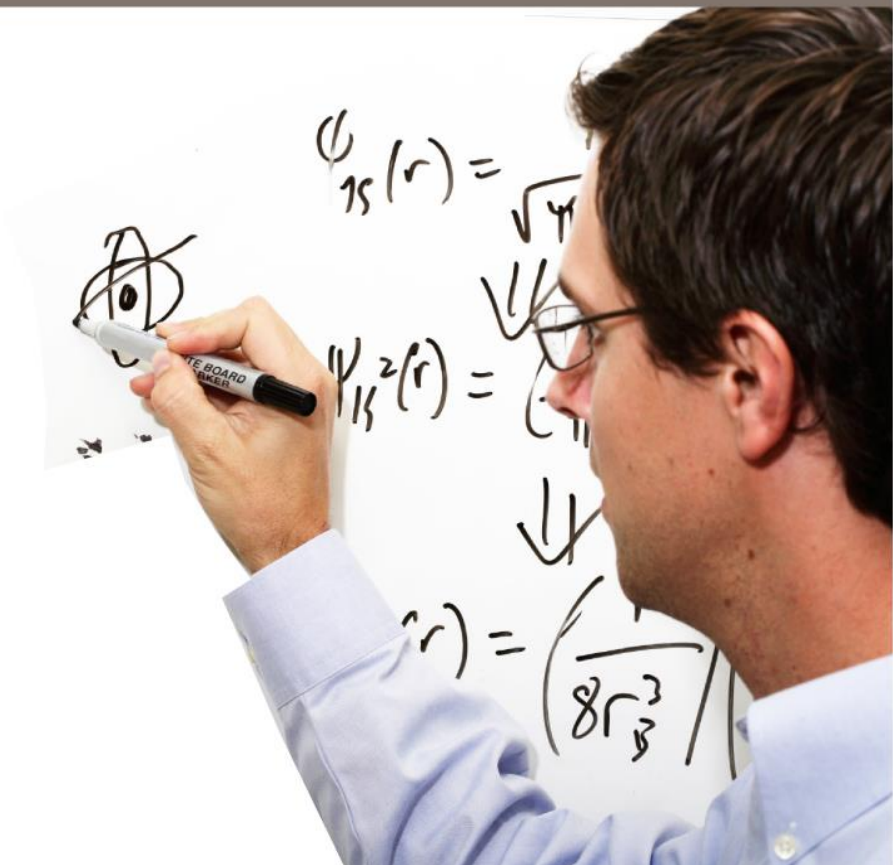
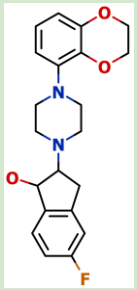
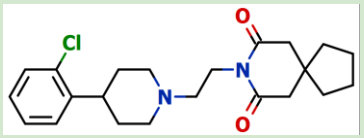
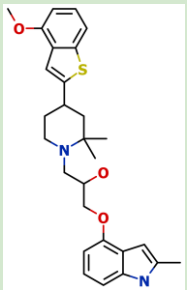
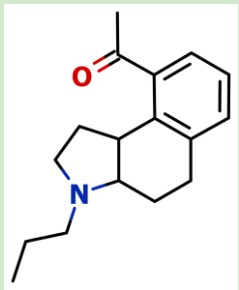
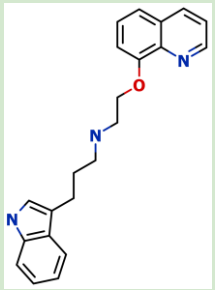
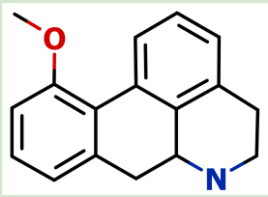


Drug discovery example

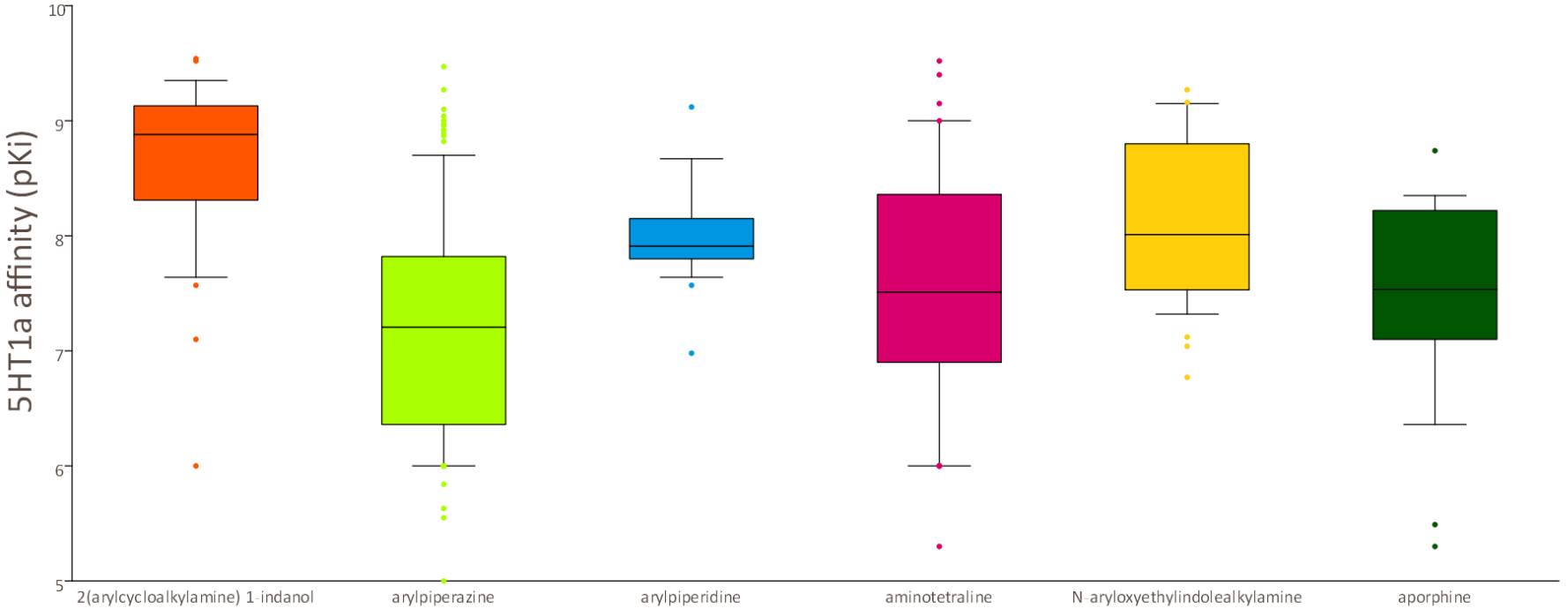
Let's looks at some drug discovery data:

- Library of 264 5HT1a compounds
- Measured potencies and other ADME/physicochemical properties
- Six different chemotypes:

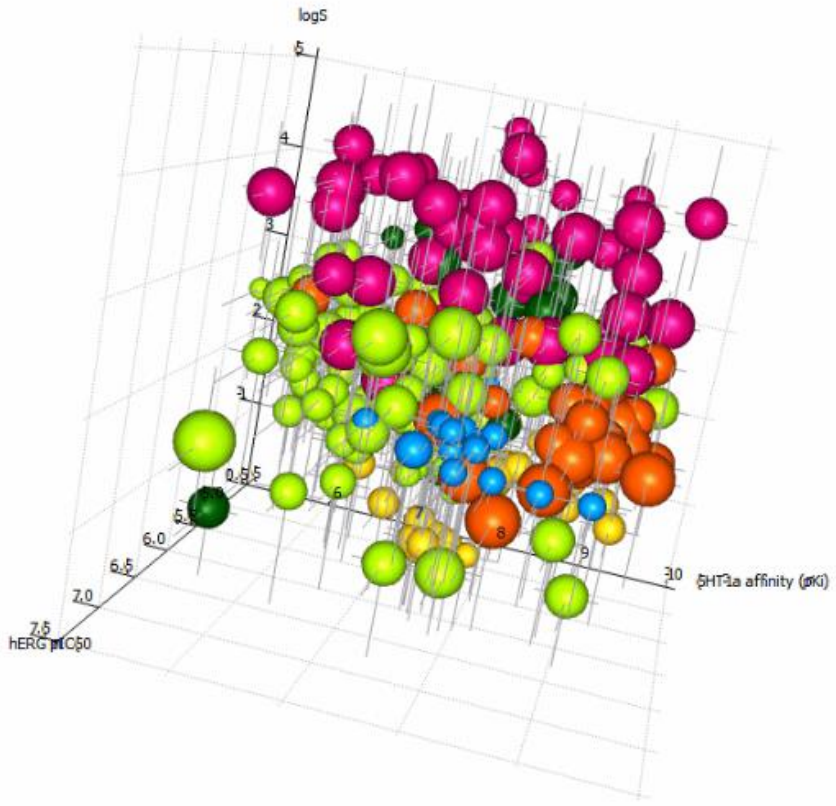
2(arylcycloalkylamine) 1-indanols (27)	Arylpiperazines (120)	Arylpiperidines (17)	Aminotetralines (51)	N-aryloxyethylindolealkylamines (29)	Aporphines (20)
					

Let's think about how we might prioritise these…

Potencies of chemotypes



…but we have many properties



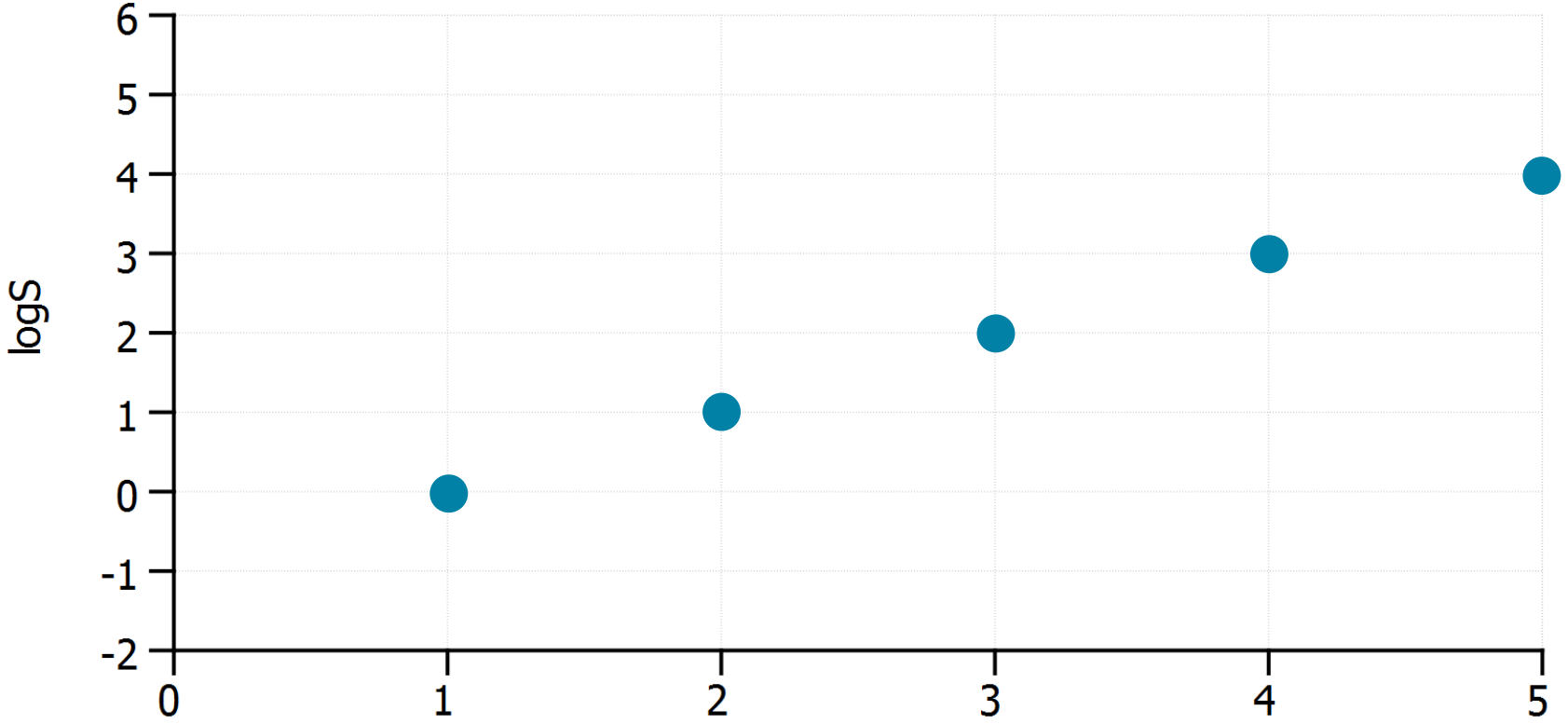
Data in drug discovery

- What's certain?
  - We know some simple properties of our compounds
- What's not so certain?
  - *In vitro*/*In vivo* measurements
    - experimental variability
  - *In silico* predictions
    - statistical error
  - Inference/translation

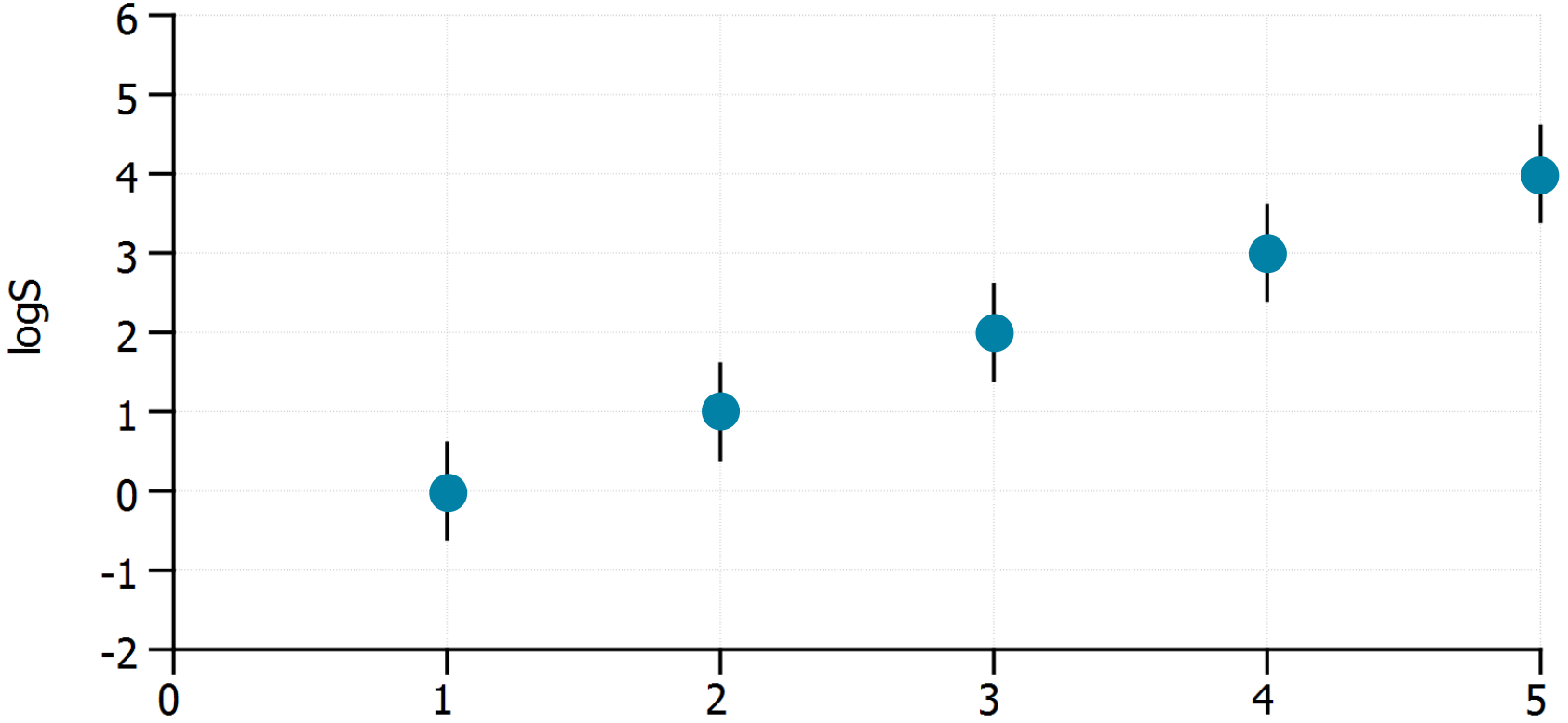
Uncertain data

- A good RMSE for logS (solubility) is 0.6
- Assuming normal distribution a logS value of 2 (that's 100µM) means:
  - 68% of the time this represents an actual value between 1.4 and 2.6 (25µM to 400µM)
  - 95% of the time this represents an actual value between 0.8 and 3.2 (6µM to 1.6mM)
  - 99% of the time this represents an actual value between 0.2 and 3.8 (1.6µM to 6.3mM)

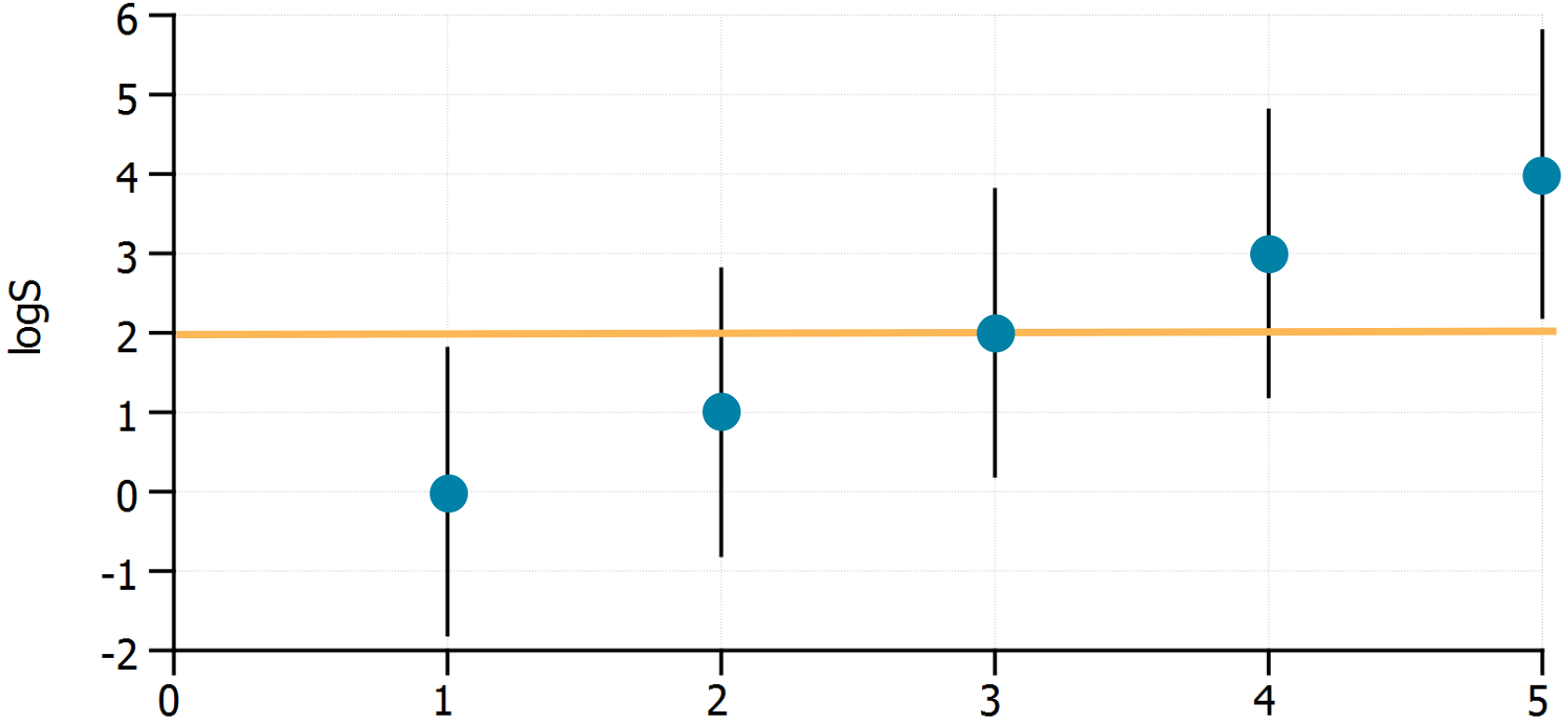
LogS – Without Error Bars



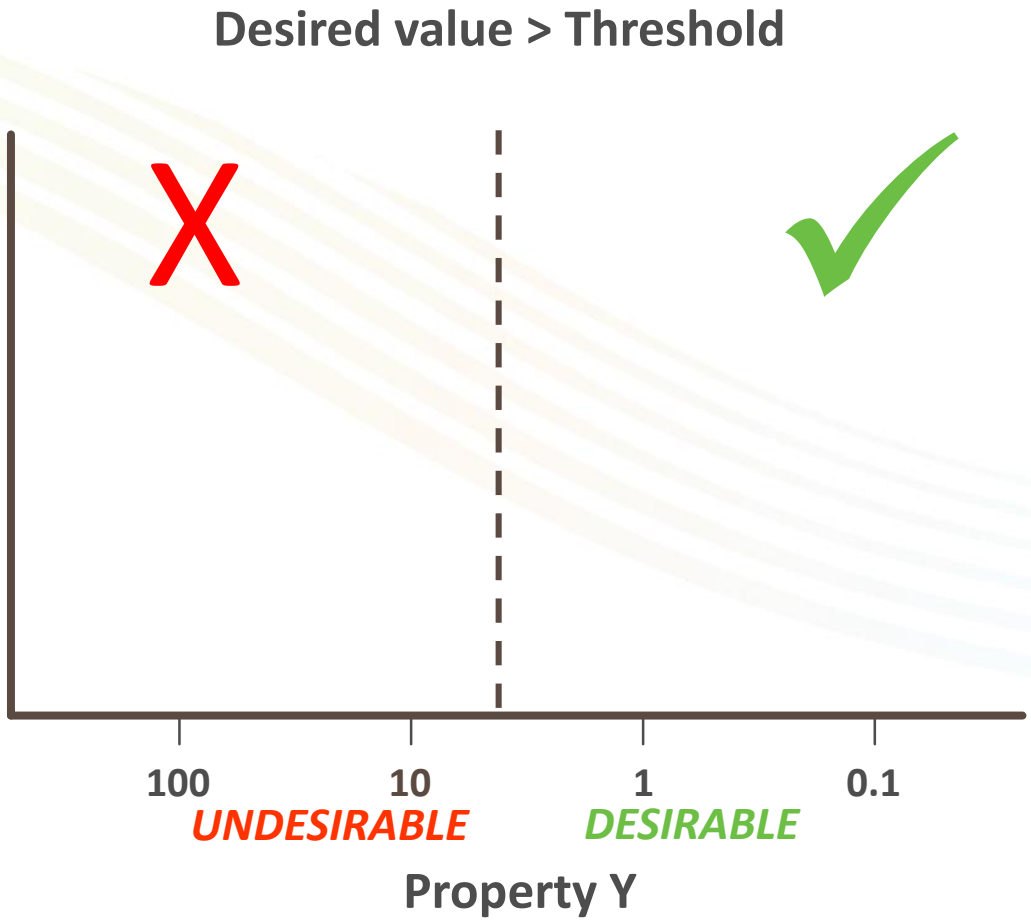
LogS – 1 Standard Deviation



LogS – 3 Standard Deviations



Importance of Uncertainty



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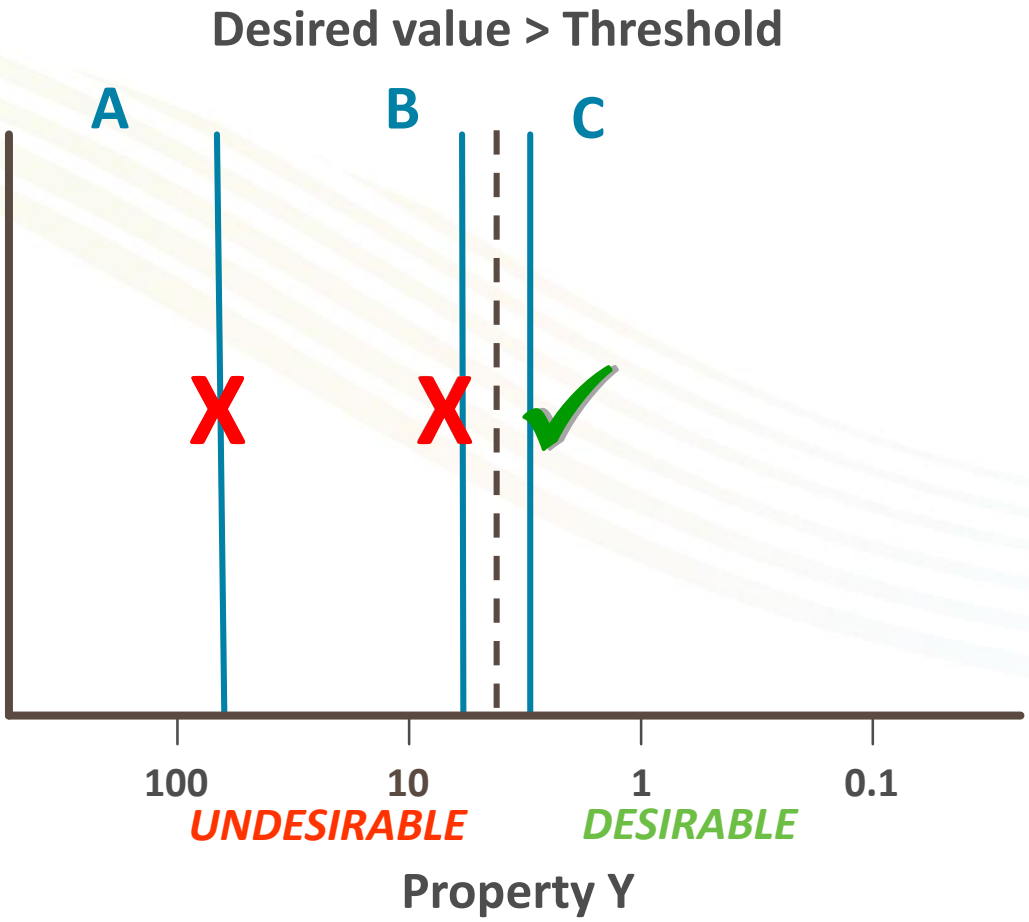

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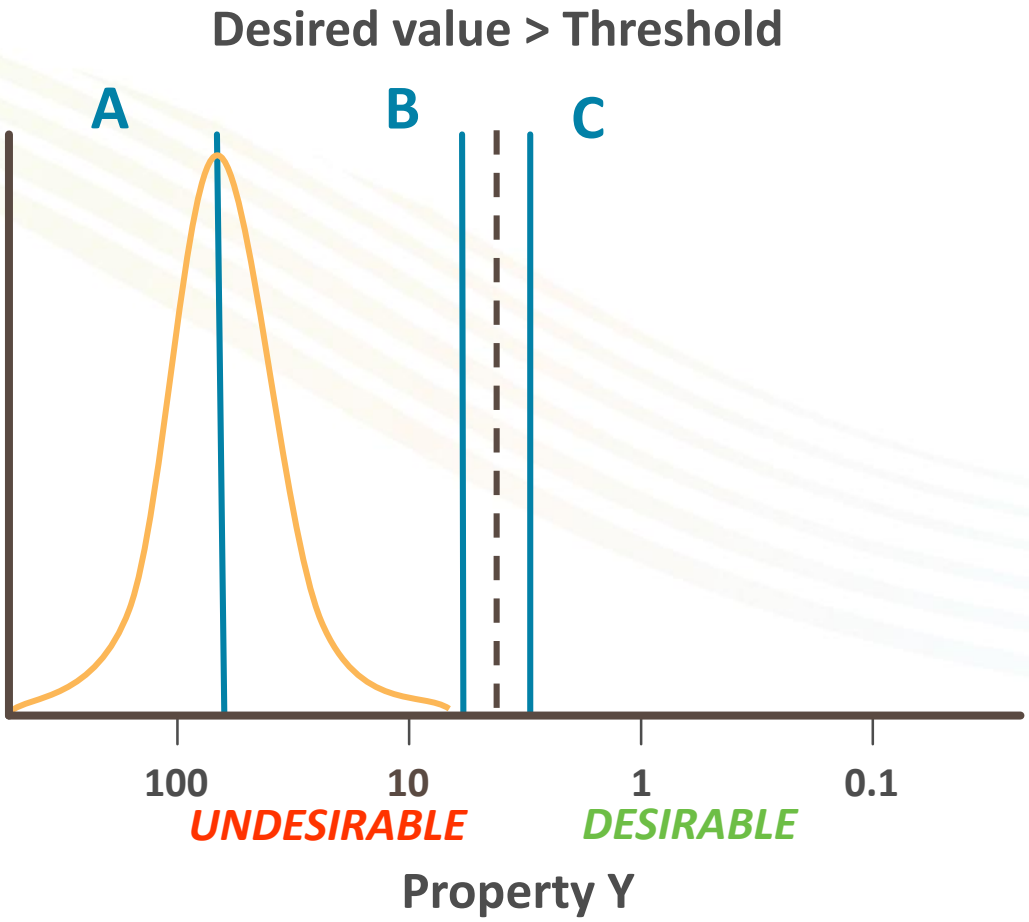

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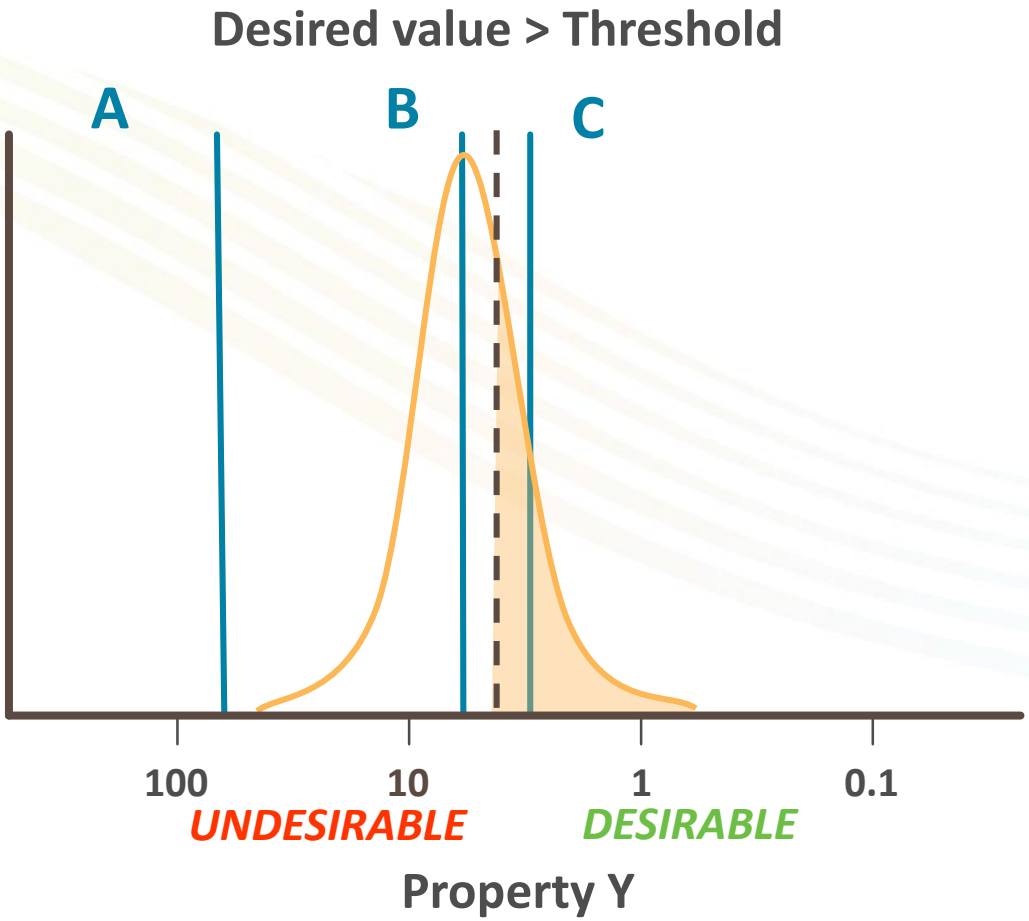

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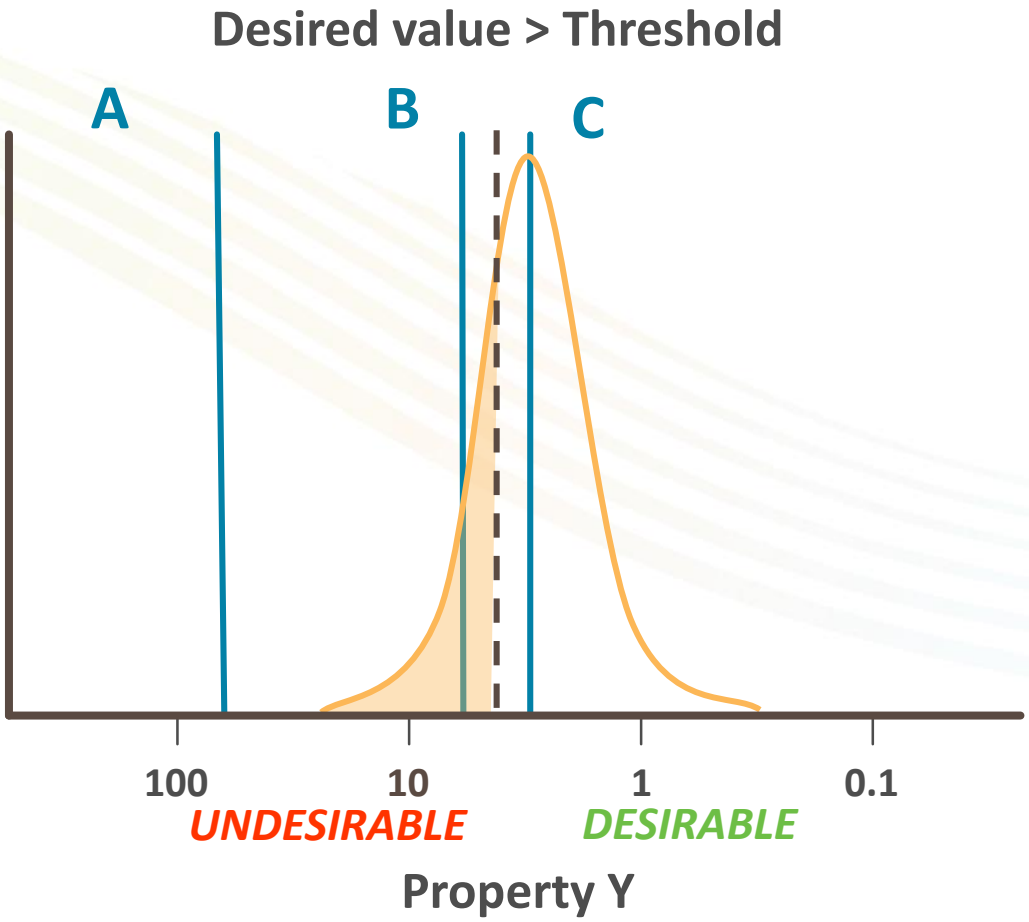

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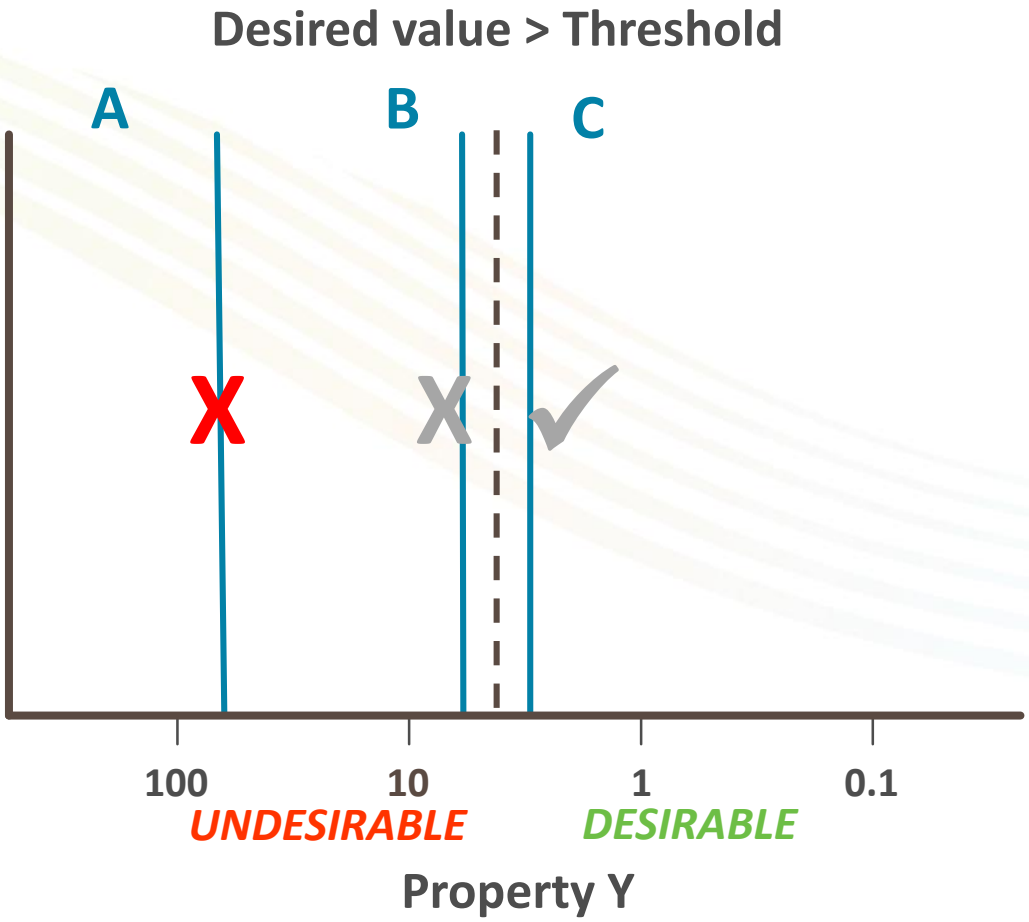

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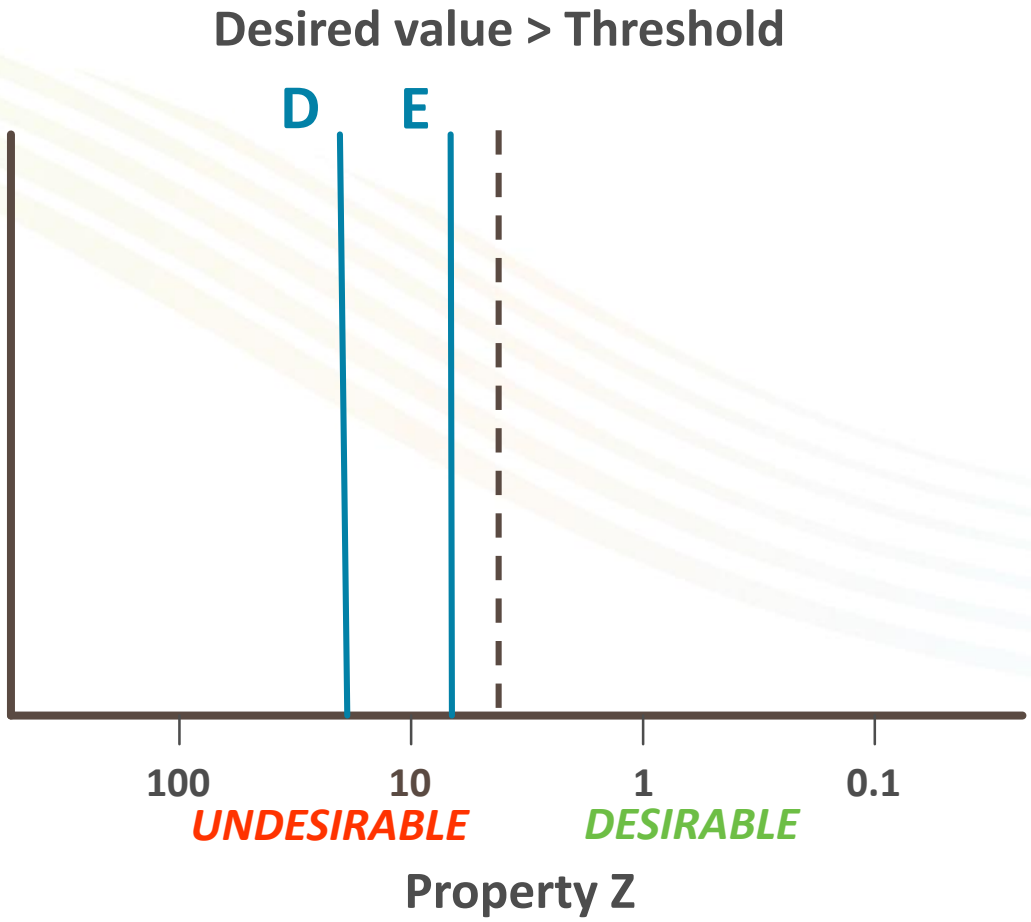

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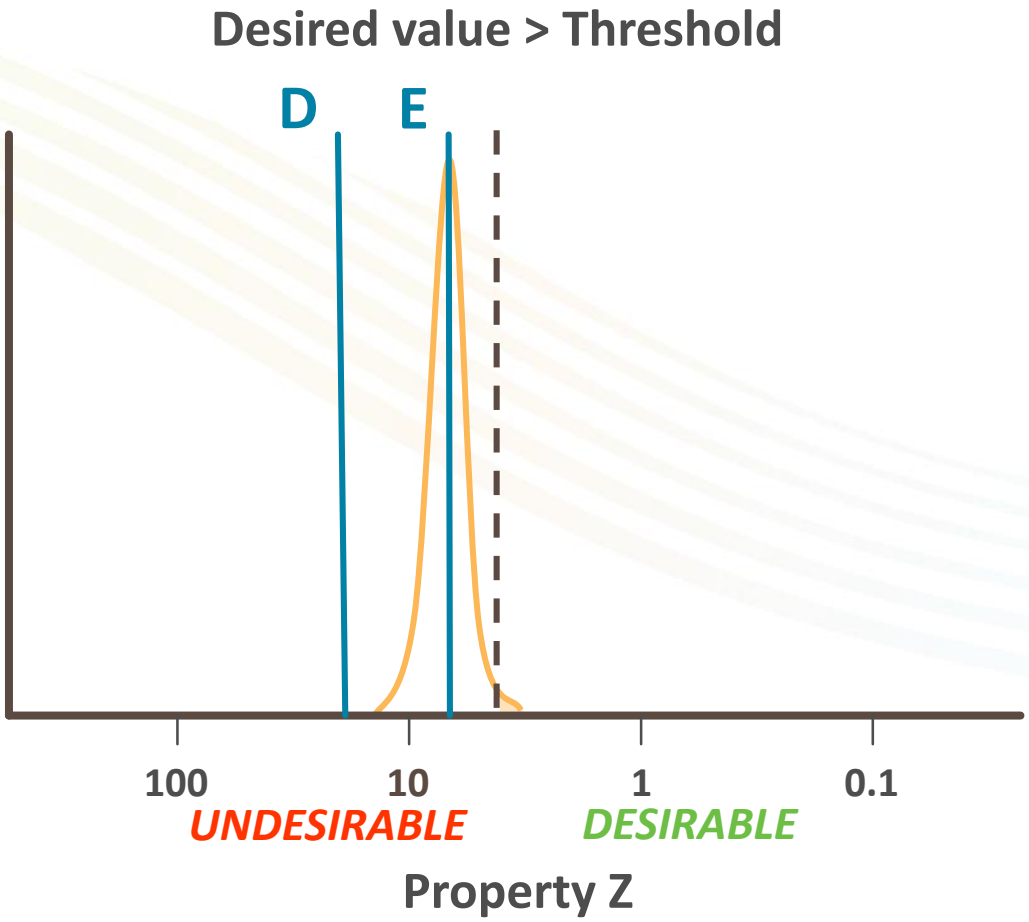

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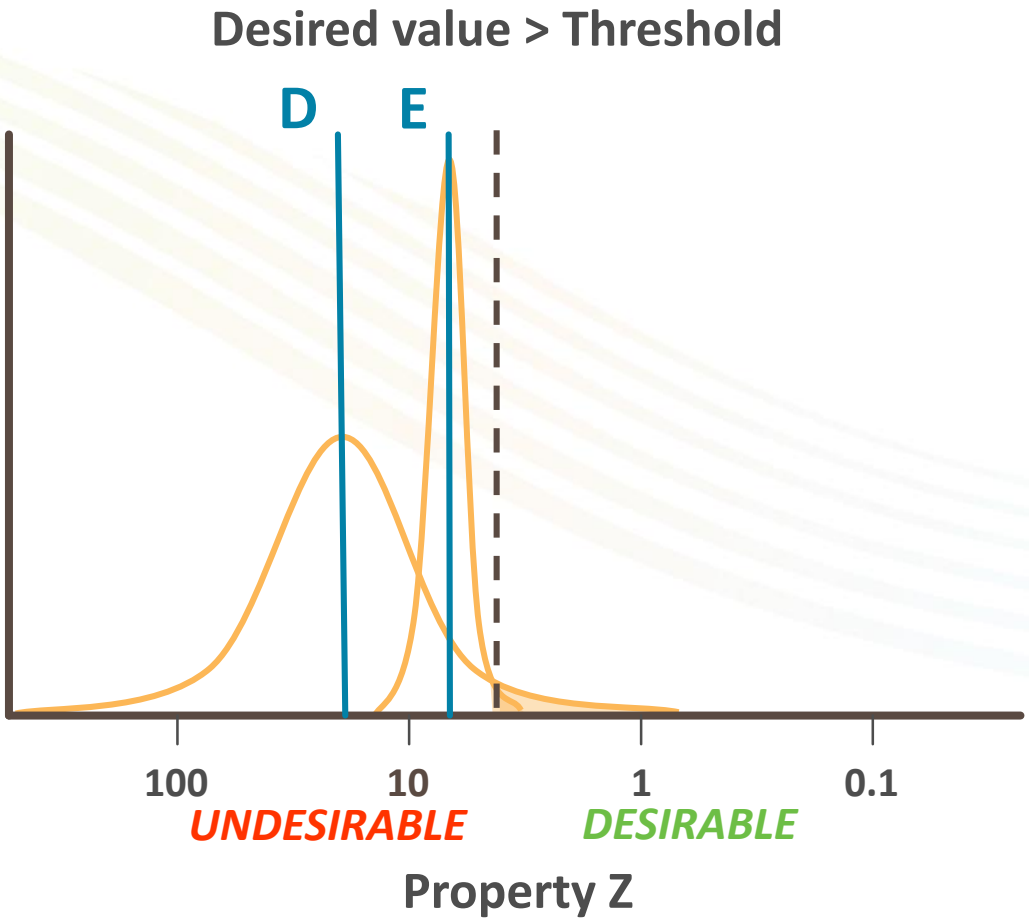

…and don't forget

- We probably have quite a few properties we need to optimise!
  - Each will have their own uncertainty
  - Each will have its own criteria we'd like to achieve
  - Each will have its own level of importance relative to the other properties

Multi-Parameter Optimisation

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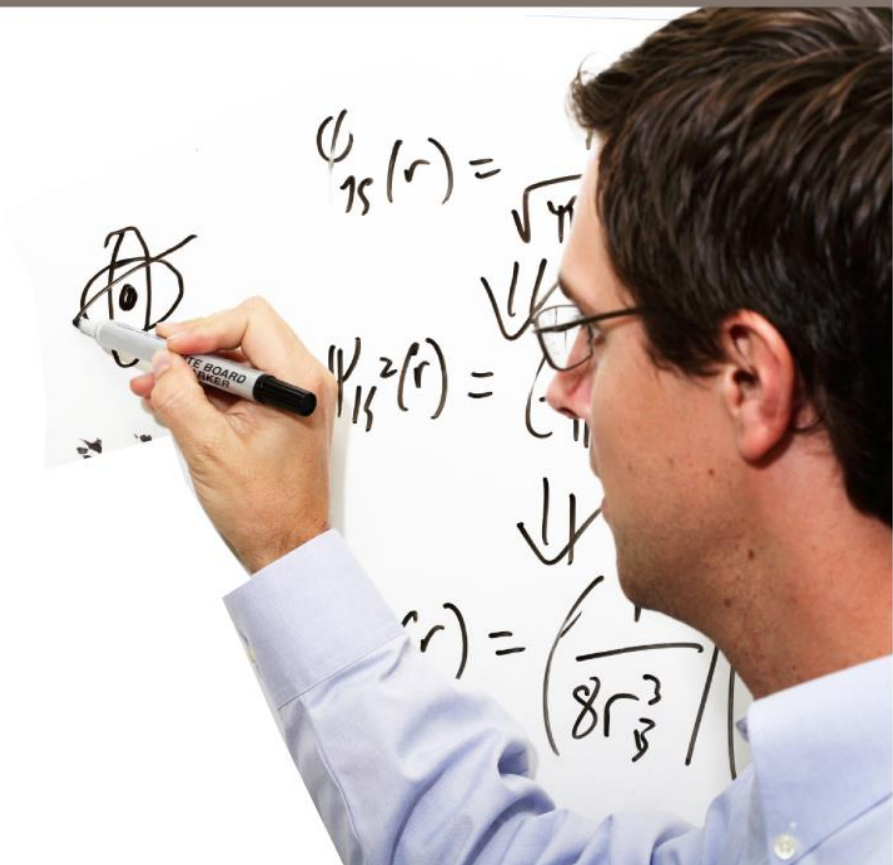
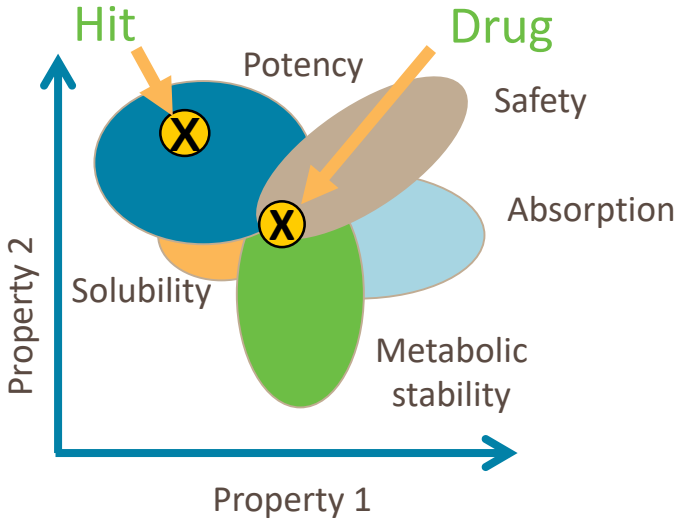


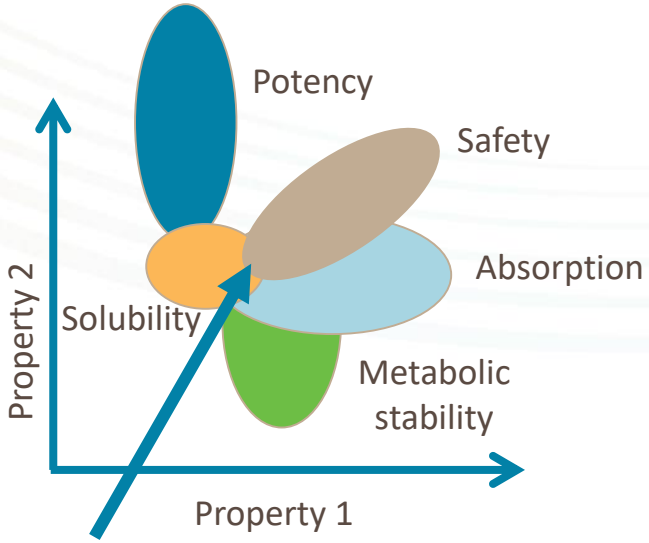
Guiding Decisions in Compound Optimisation

Multi-parameter optimisation

- Identify chemistries with an optimal **balance** of properties



- Quickly identify situations when such a balance is not possible
  - –Fail fast, fail cheap
  - –Only when **confident**
  - –Avoid **missed opportunities**



No good drug

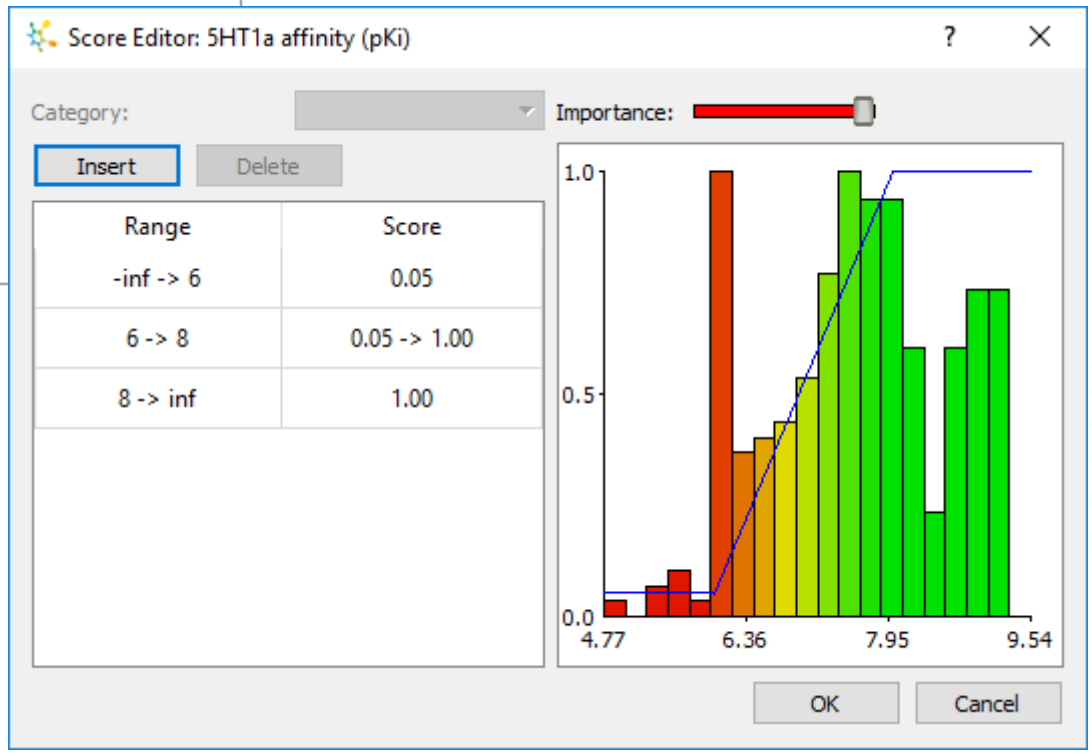
Back to our 5HT1a library

- Example criteria we might like to achieve for an ideal compound

Property	Desired value	Importance
Potency (pK_i)	> 7	High
logS (log µM)	> 1	High
Human Intestinal Absorption (category)	+	High
BBB log([brain]:[blood])	-0.2 -> 1	High
logP	0 -> 3.5	Medium
P-gp (category)	No	Medium
hERG pIC50	≤ 5	Medium
2C9 pK_i	≤ 6	Low
2D6 affinity (category)	Low/Medium	Low
Plasma protein binding (category)	Low	Low

Putting it all together (MPO):
Probabilistic Scoring* – Scoring Profile

Property	Desired Value	Importance
5HT1a affinity (pKi)	> 7	
logS	> 1	
HIA category	+	
logP	0 -> 3.5	
BBB log([brain]:[blood])	-0.2 -> 1	
BBB category	+	
P-gp category	no	
hERG pIC50	⩽ 5	
2C9 pKi	⩽ 6	
2D6 affinity category	low medium	
PPB90 category	low	



* Segall *et al.* (2009) Chem. & Biodiv. **6** p. 2144

Multi-parameter Optimisation
Probabilistic Scoring*

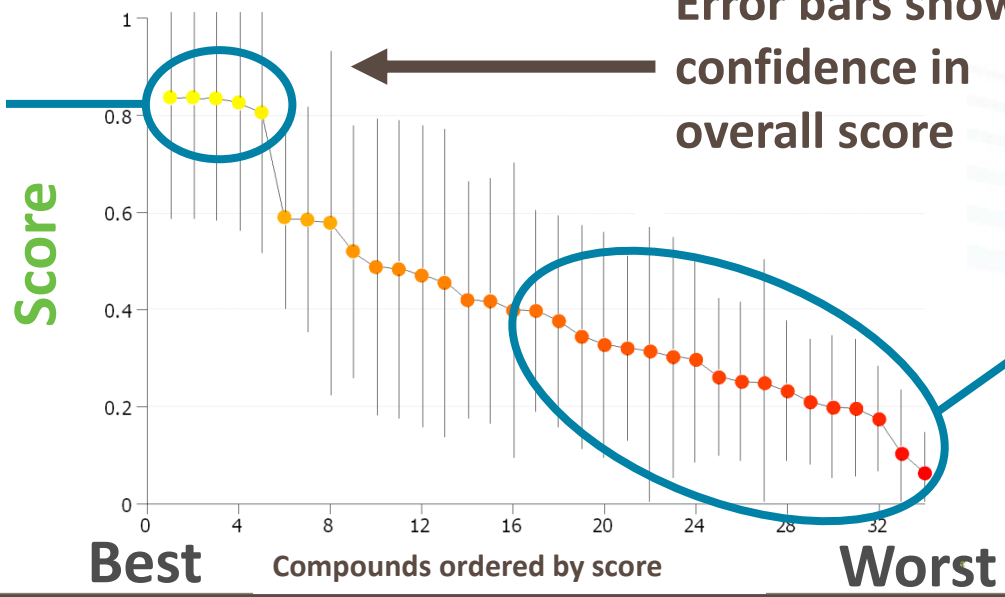
- **Property data**
  - Experimental or predicted
- **Criteria for success**
  - Relative importance
- **Uncertainties in data**
  - Experimental or statistical

- **Score (Likelihood of Success)**
- **Confidence in score**

Data do not separate these as error bars overlap

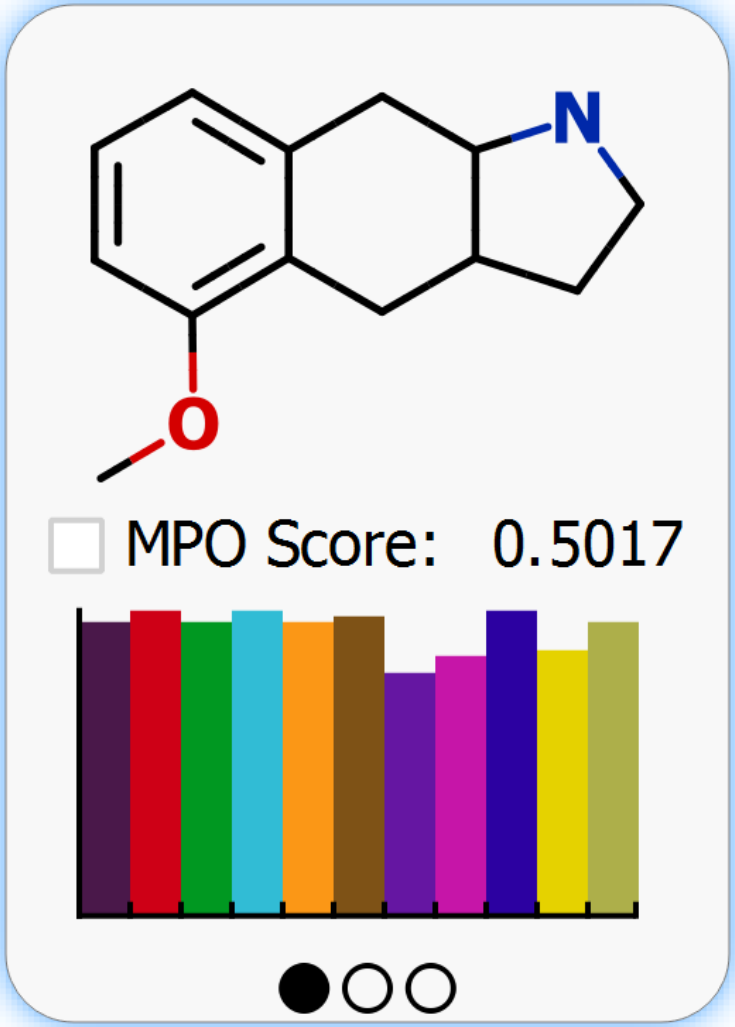
Error bars show confidence in overall score

Bottom 50% may be rejected with confidence



*M.D. Segall (2012) Curr. Pharm. Des. **18**(9) pp. 1292-1310

The best compound



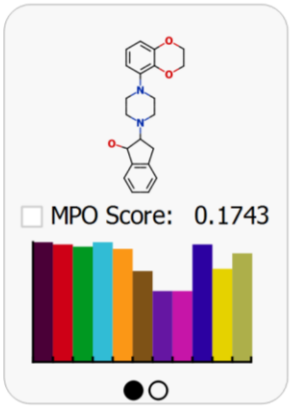
The context:

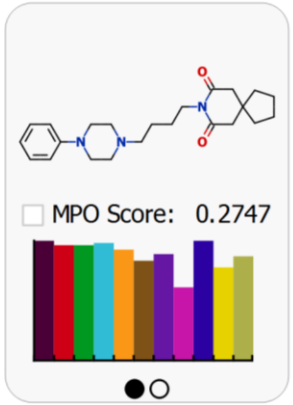
Property	Desired Value	Importance
5HT1a affinity (pKi)	> 7	
logS	> 1	
HIA category	+	
logP	0 -> 3.5	
BBB log([brain]:[blood])	-0.2 -> 1	
BBB category	+	
P-gp category	no	
hERG pIC50	⩽ 5	
2C9 pKi	⩽ 6	
2D6 affinity category	low medium	
PPB90 category	low	

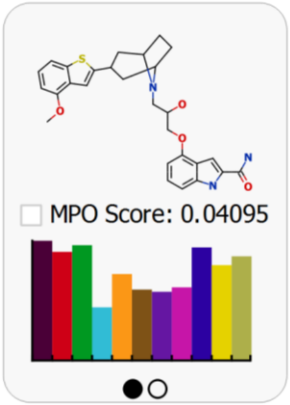
The best of each chemotype

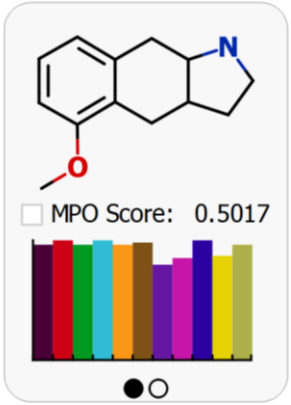
The context:

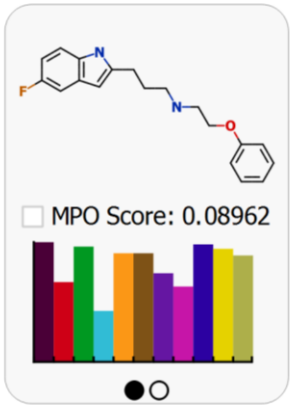
Property	Desired Value	Importance
5HT1a affinity (pKi)	> 7	
logS	> 1	
HIA category	+	
logP	0 -> 3.5	
BBB log([brain]:[blood])	-0.2 -> 1	
BBB category	+	
P-gp category	no	
hERG pIC50	⩽ 5	
2C9 pKi	⩽ 6	
2D6 affinity category	low medium	
PPB90 category	low	

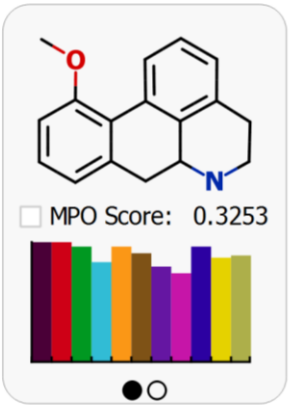




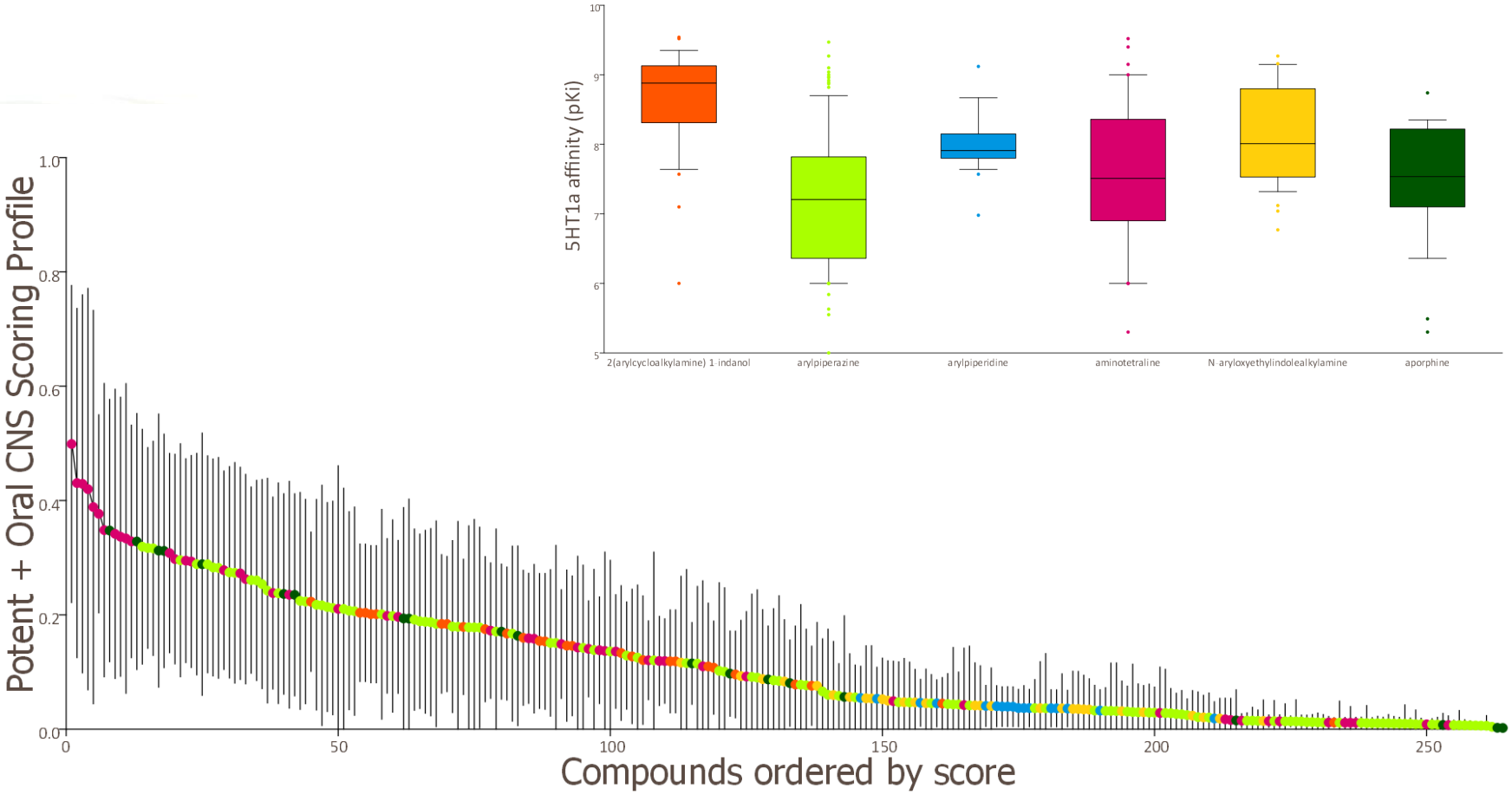




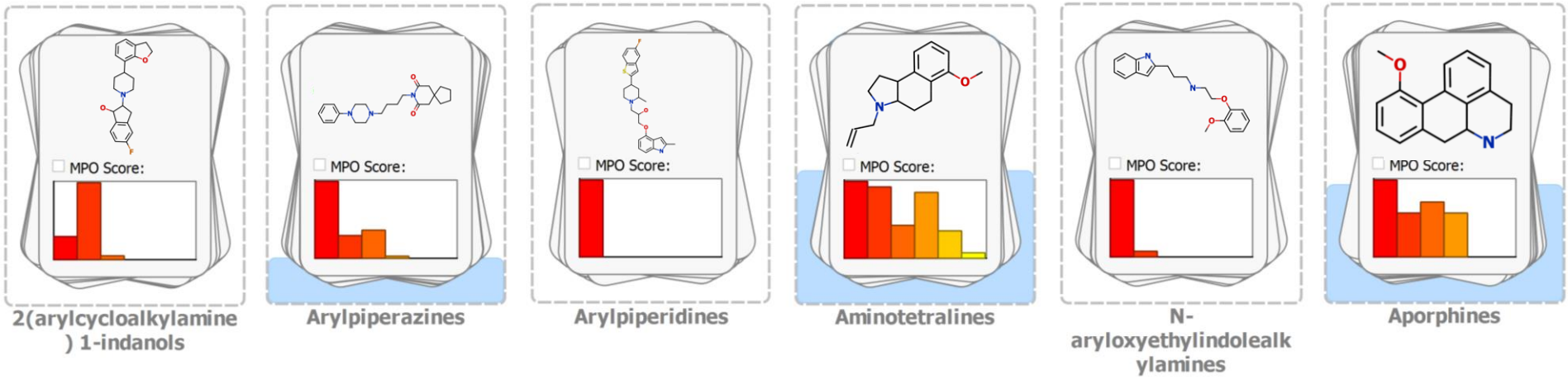




Snake plot for complete library



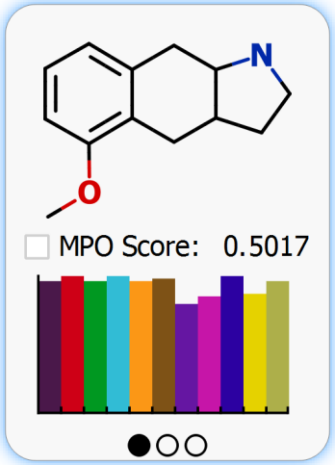
An appropriate selection?



(N.B. There are 2.77×10^{54} possible ways to select 50 compounds)

Conclusions

- We are always dealing with many dimensions of data while making decisions in drug discovery and so our visualisations should reflect this appropriately
- Only a small proportion of the possible visualisations we can create will be relevant/informative to our decision-making
- We tend to be draw towards information in small, easily-digestible chunks so…
- …could we tweet this?



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