Experimental Design

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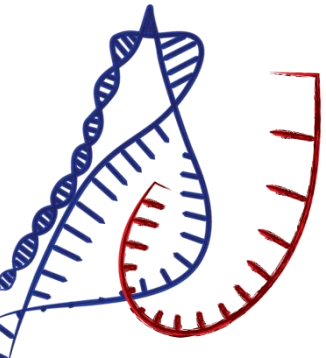
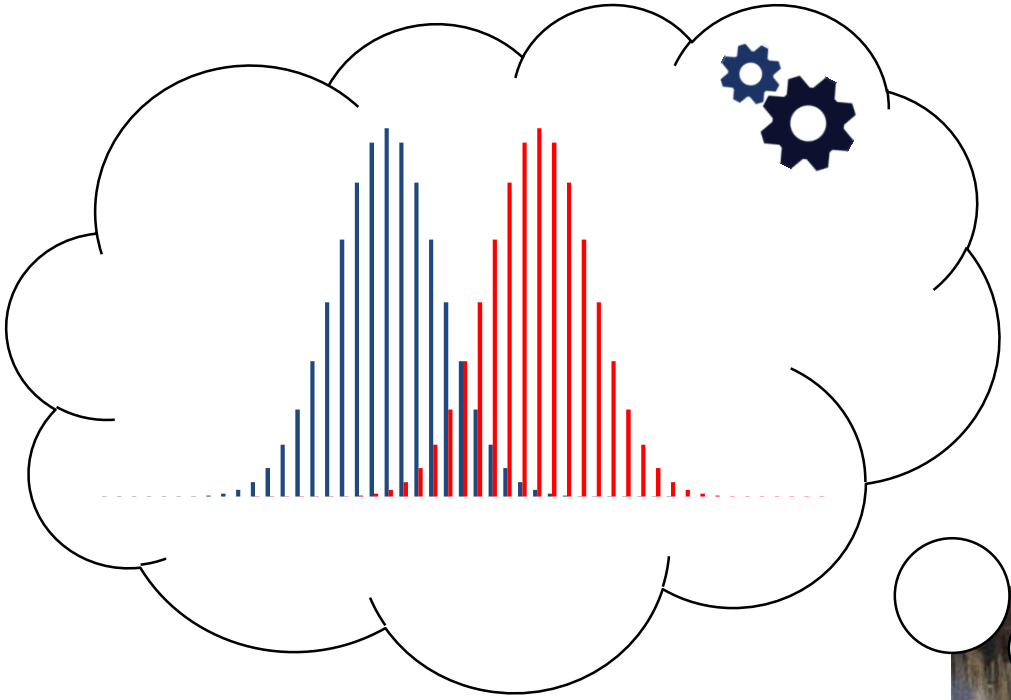


Groups and Categories



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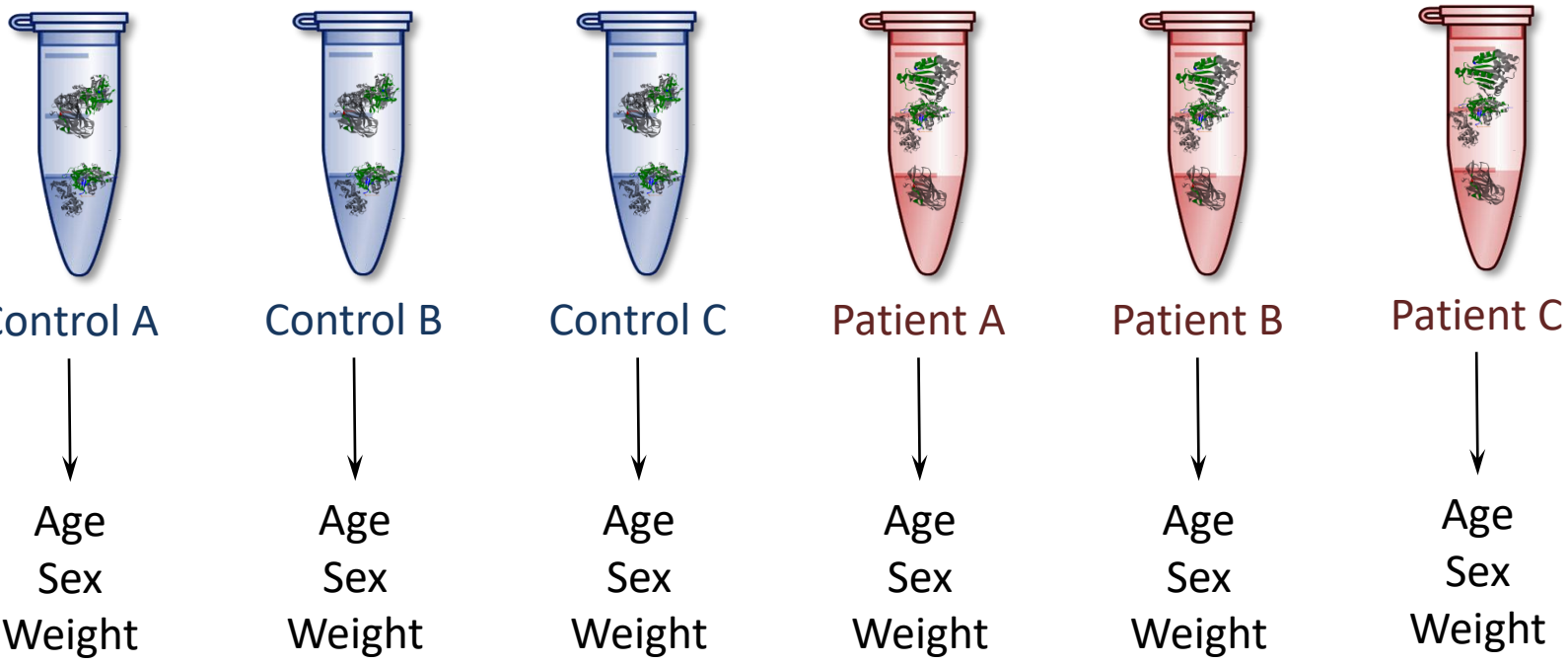
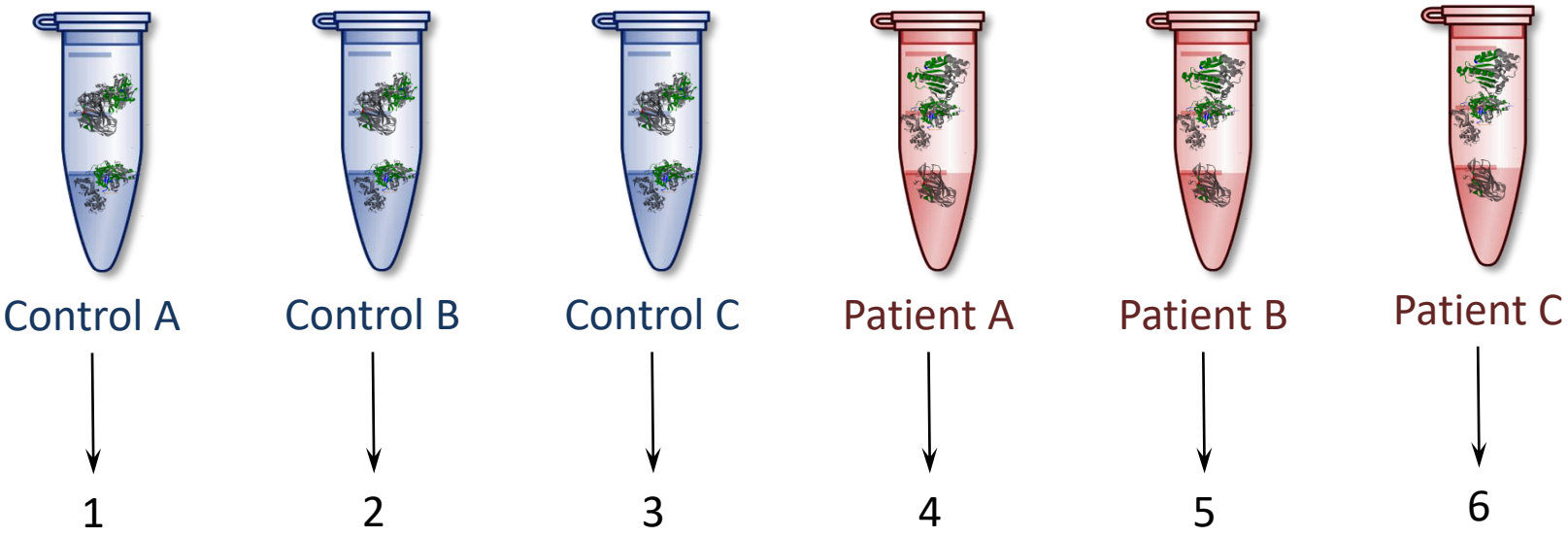


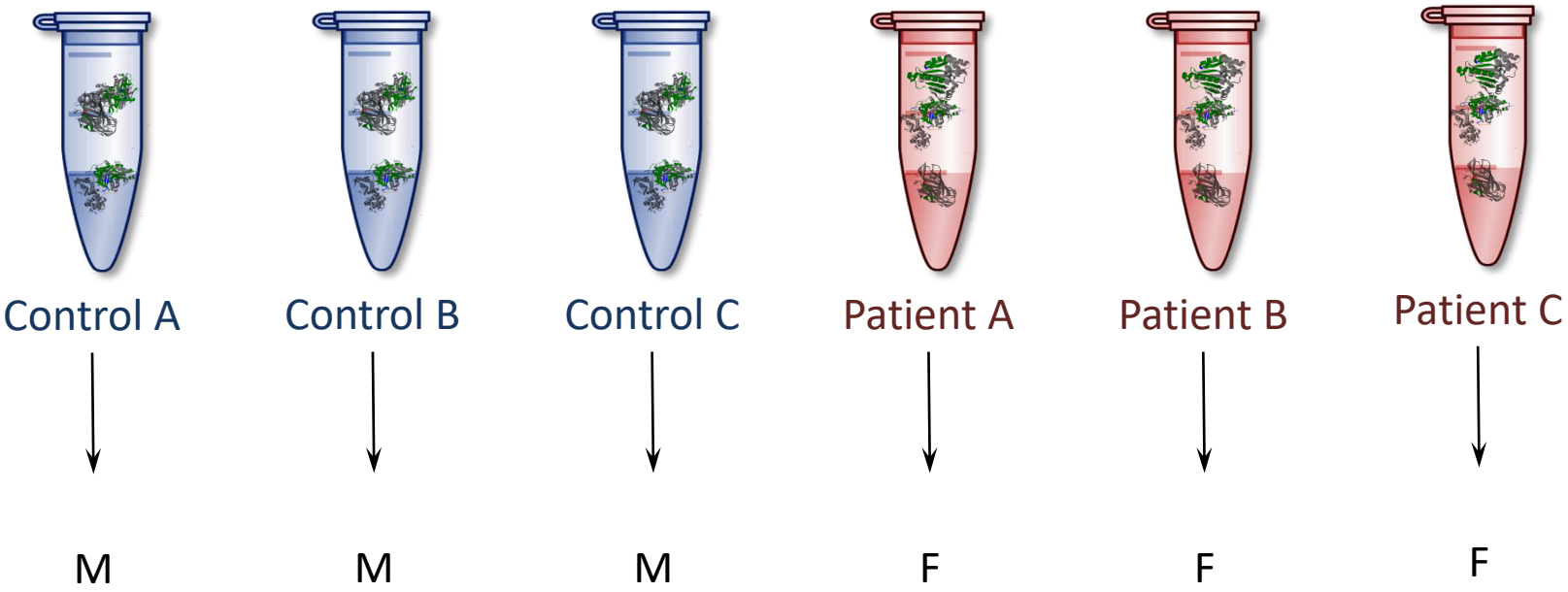
1- Document
2- Uniformize to reduce biases and covariates

Groups and Categories



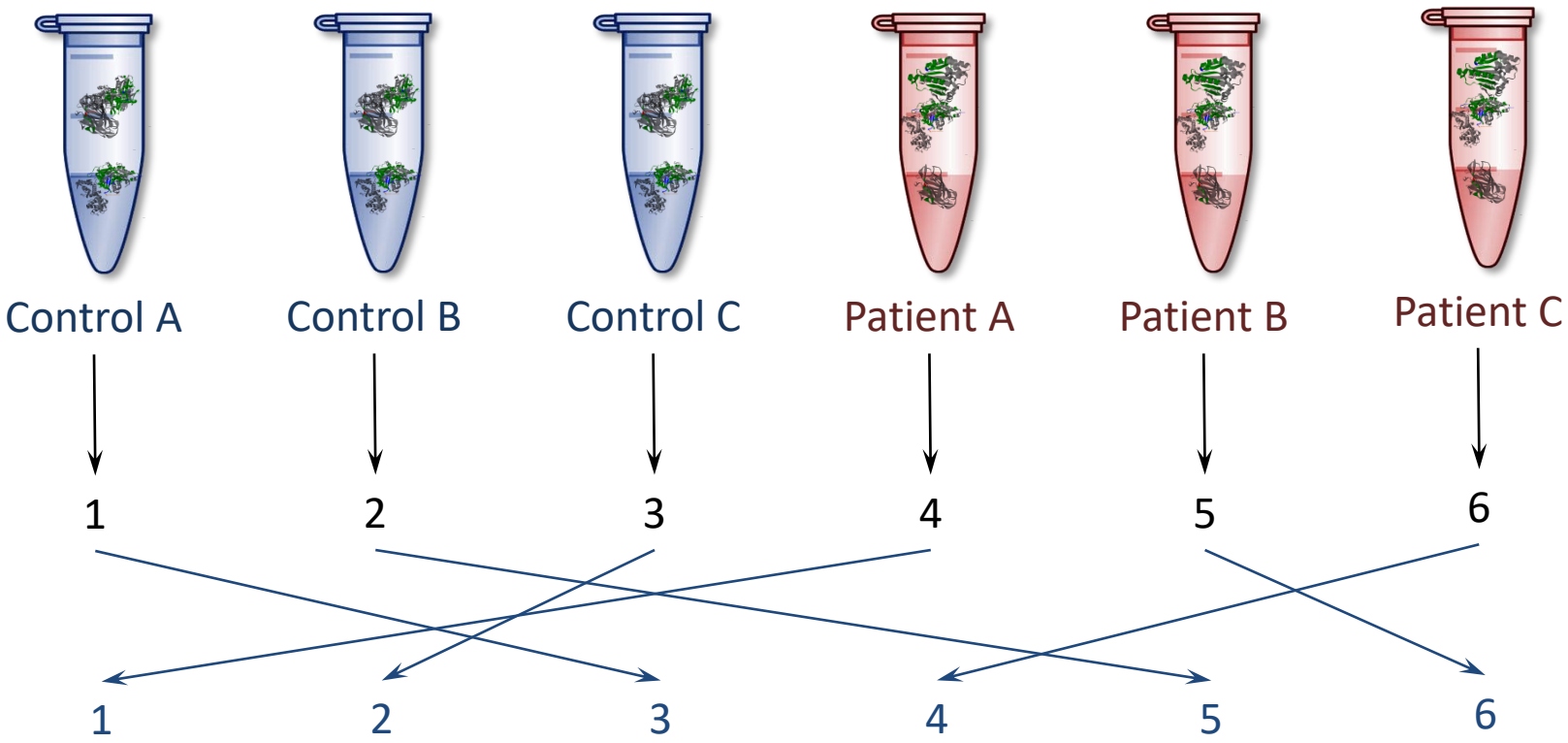
1- Document
2- Uniformize to reduce biases and covariates
3- Anonymize

My best biomarker study



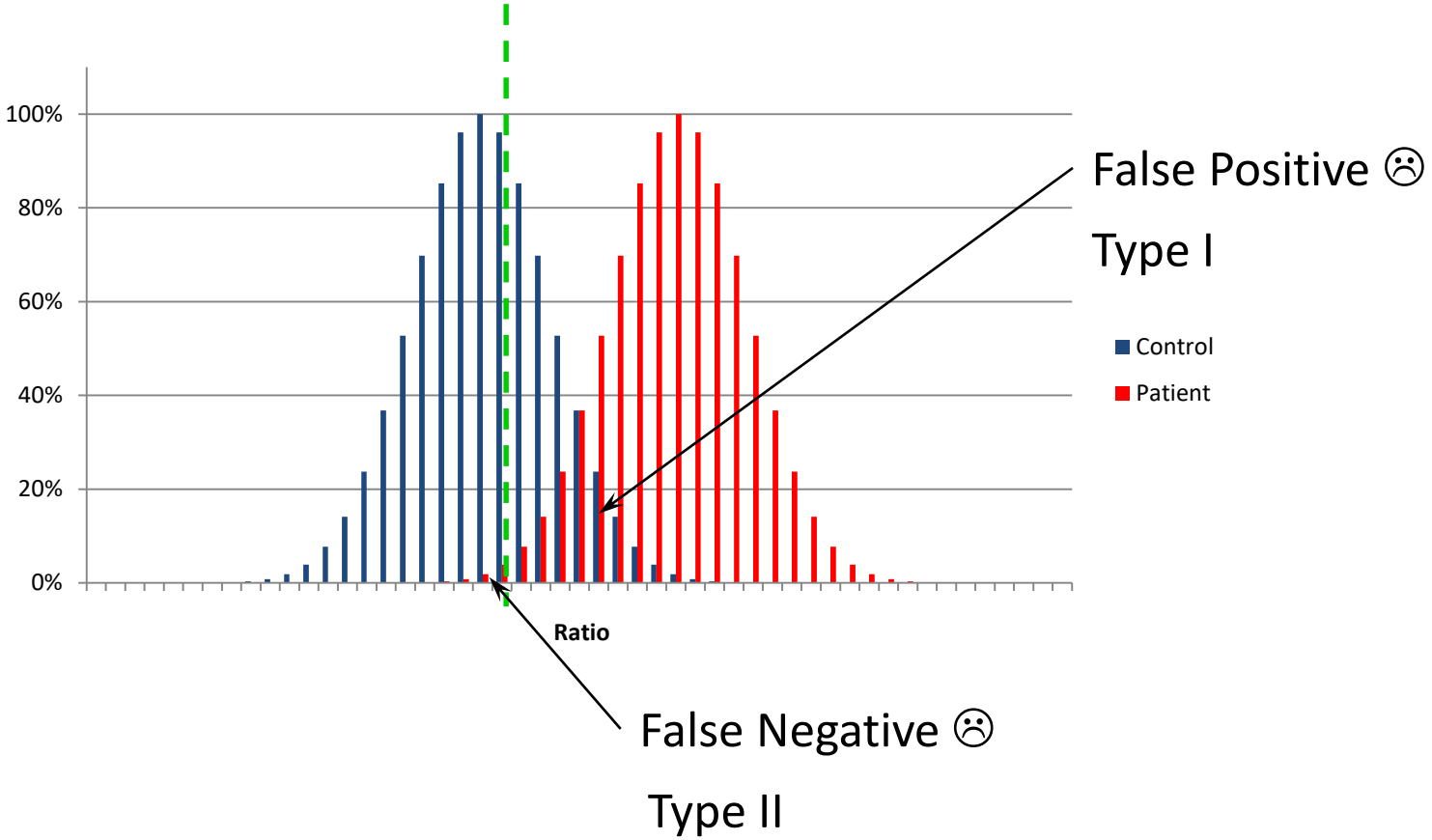
Tip: Think of family controls!

Groups and Categories

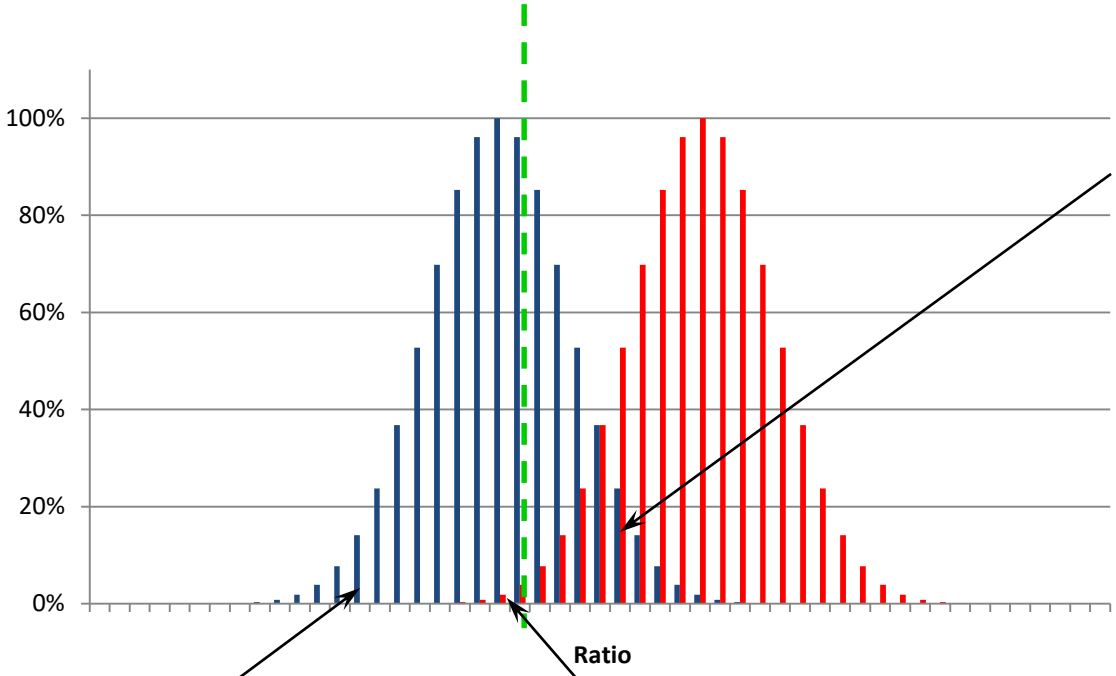


1- Document
2- Uniformize to reduce biases and covariates
3- Anonymize
4- Randomize

Errors and Power



Errors and Power



False Positive ☹

Type I

$\alpha = \Phi_{control}(ratio)$

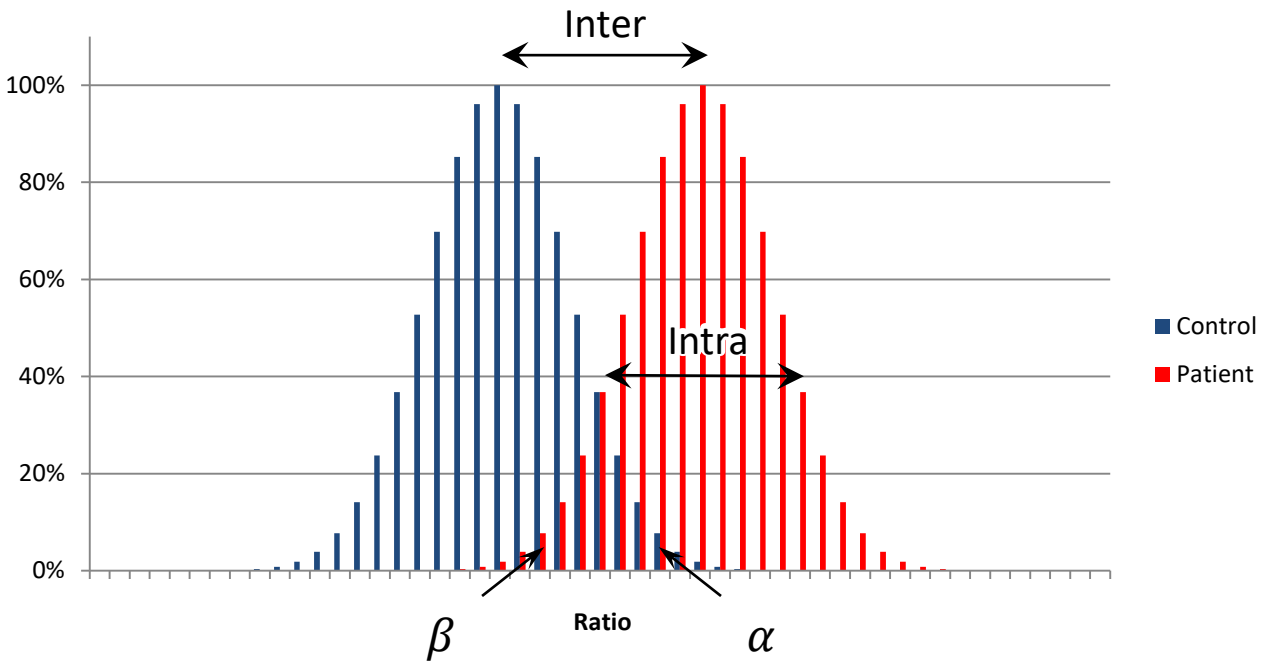
$power = 1 - \beta$

False Negative ☹

Type II

$\beta = \Phi_{patient}(ratio)$

Multiple Variables Optimization

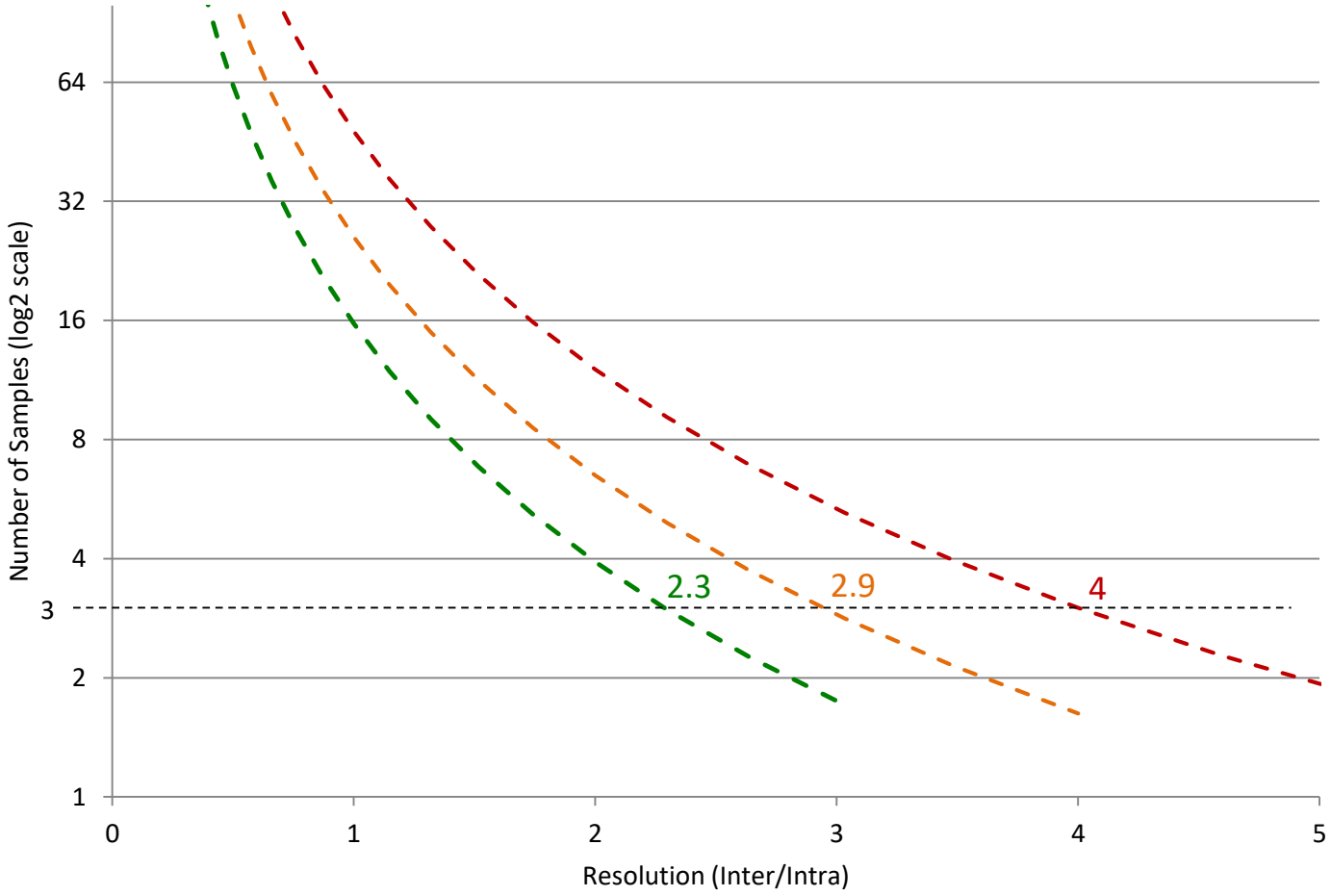


-> On normal distributions, Student's t-test:

$$n \geq \frac{2\left(\Phi^{-1}\left(1-\frac{\alpha}{2}\right)+\Phi^{-1}(1-\beta)\right)^2}{\left(\frac{Inter}{Intra}\right)^2} \xrightarrow[r = Inter/Intra]{} n \geq \frac{A}{r^2}$$

Experimental Design

$\alpha = 5\%$ $\beta = 20\%$ $\alpha = 5\%$ $\beta = 5\%$ $\alpha = 1\%$ $\beta = 1\%$



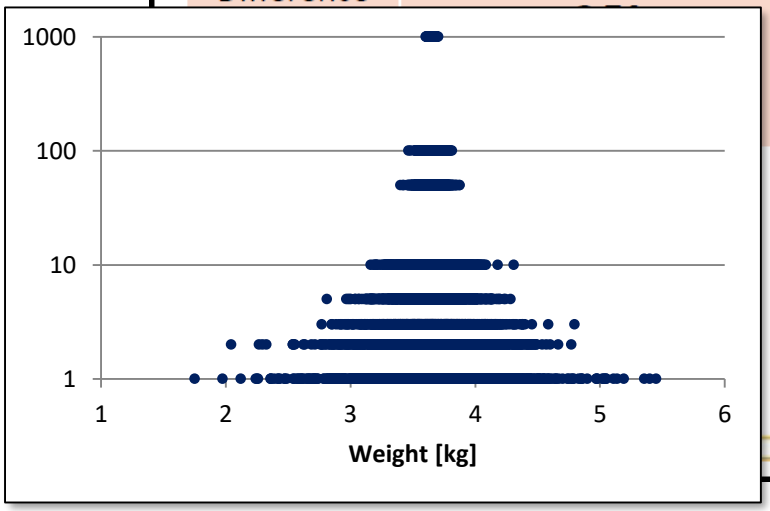
$$n \geq \frac{16}{\left(\frac{Inter}{Intra}\right)^2}$$

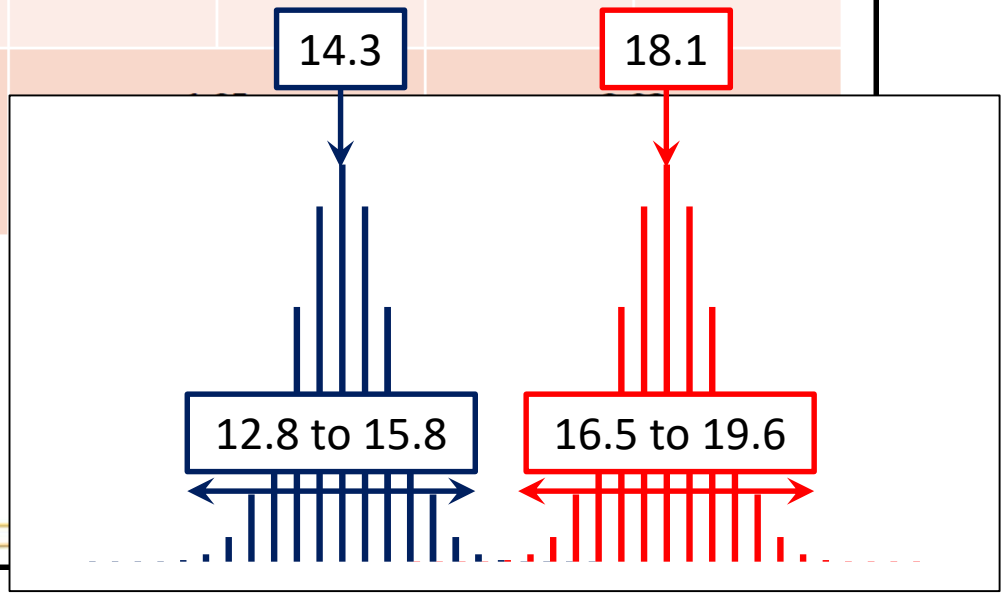
$$n \geq \frac{26}{\left(\frac{Inter}{Intra}\right)^2}$$

$$n \geq \frac{48}{\left(\frac{Inter}{Intra}\right)^2}$$

Phase 2: Growth velocity (g/kg/day)

	Study 020 Formula N=33		Study 021 Past. milk N=27		020 & 021 Combined N=60	
	rhBSSL	Placebo	rhBSSL	Placebo	rhBSSL	Placebo
LS mean (95% CI) [g/kg/day]	18.1 (16.5 to 19.6)	14.3 (12.8 to 15.8)	15.6 (13.8 to 17.3)	13.6 (11.9 to 15.4)	16.9 (15.7 to 17.8)	13.9 (12.8 to 15.1)
Difference						





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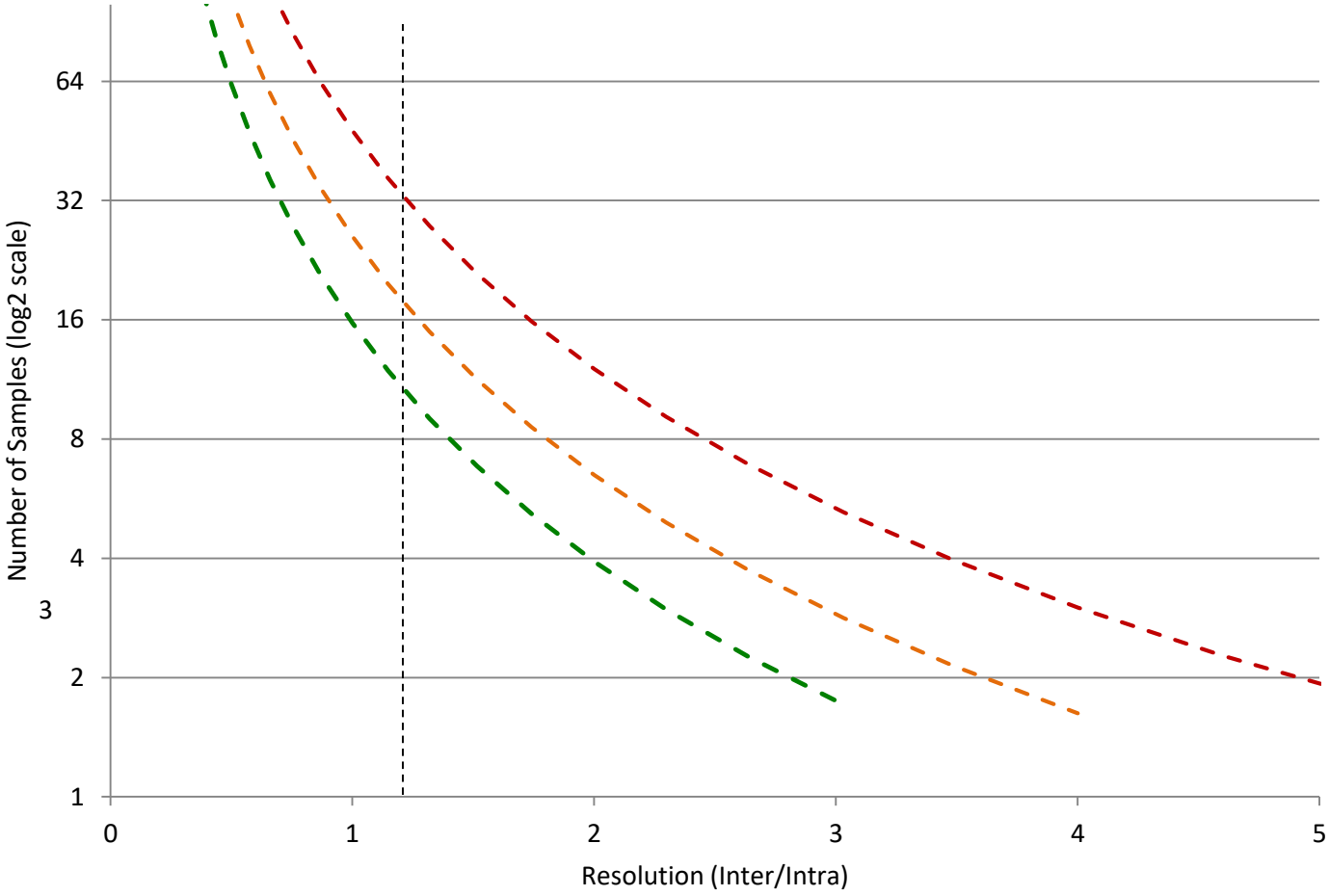
	rhBSSL	Placebo	rhBSSL	Placebo	rhBSSL	Placebo
LS mean (95% CI) [g/kg/day]	18.1 (16.5 to 19.6) 3.8 14.3 (12.8 to 15.8) 3.1 3		15.6 (13.8 to 17.3)	13.6 (11.9 to 15.4)	16.9 (15.7 to 17.8)	13.9 (12.8 to 15.1)
Difference (95% CI) [g/kg/day] p-value	**3.74** (1.58 to 5.90) p=0.001		**1.95** (-0.54 to 4.43) p=0.119		**2.93** (1.35 to 4.51) p<0.001	

Power calculation

$\alpha = 5\%$ $\beta = 20\%$ | $\alpha = 5\%$ $\beta = 5\%$ | $\alpha = 1\%$ $\beta = 1\%$



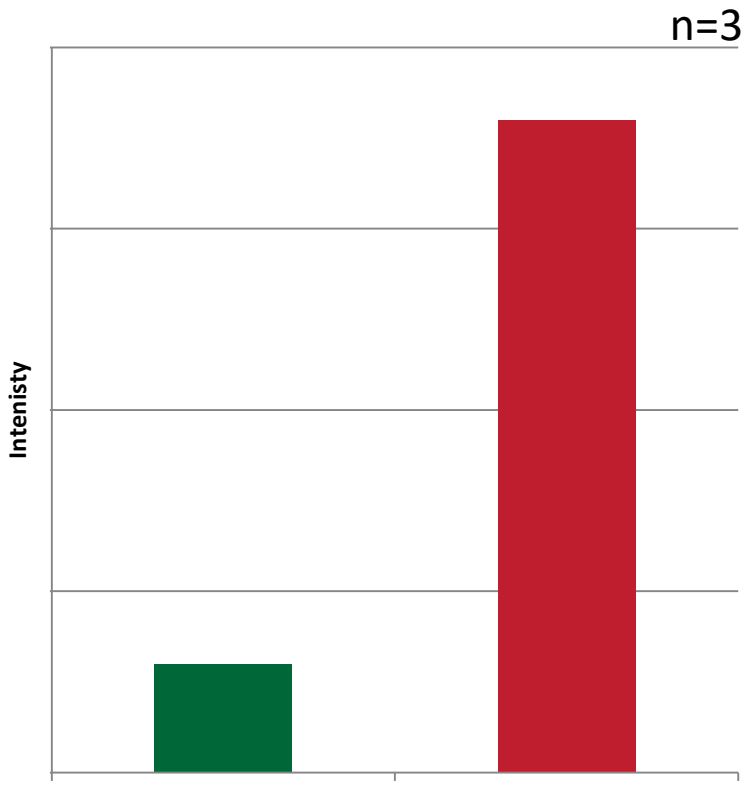
$$n \geq \frac{16}{\left(\frac{Inter}{Intra}\right)^2}$$

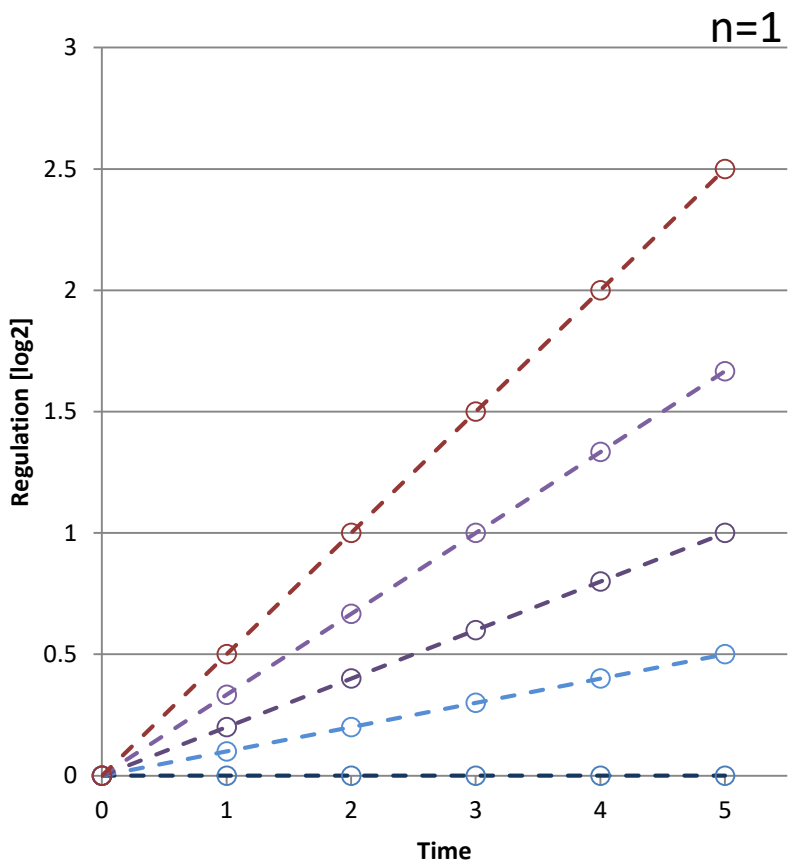
$$n \geq \frac{26}{\left(\frac{Inter}{Intra}\right)^2}$$

$$n \geq \frac{48}{\left(\frac{Inter}{Intra}\right)^2}$$

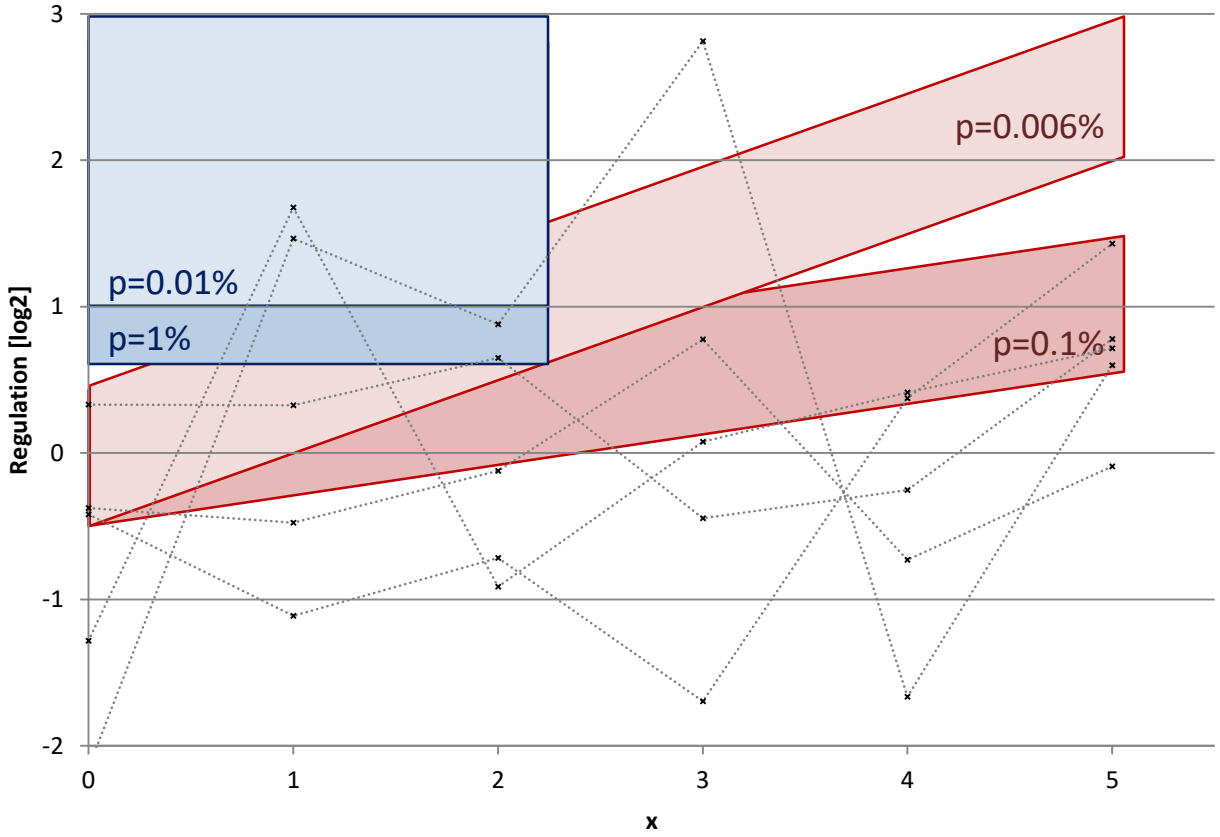
More complex setups?

Time series:

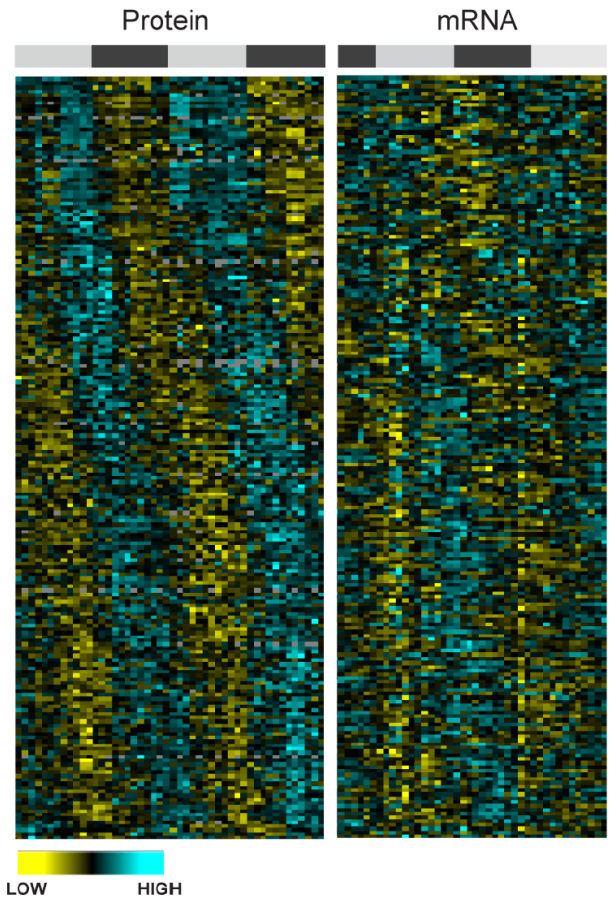


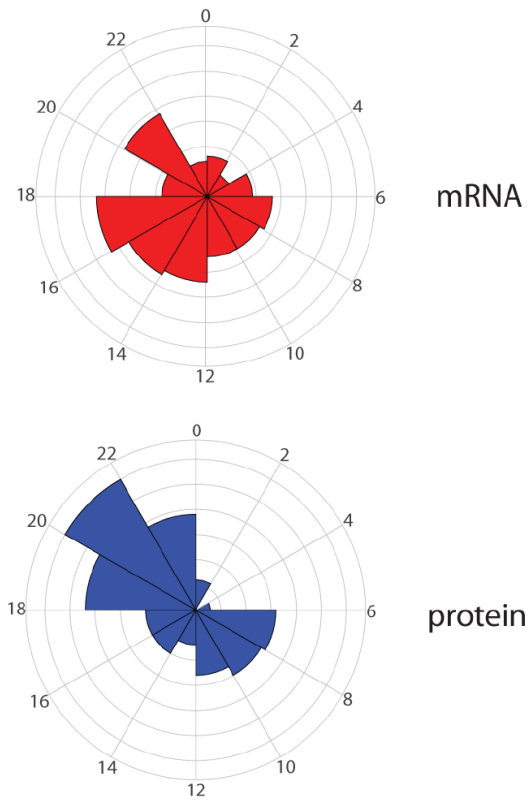


Time series:



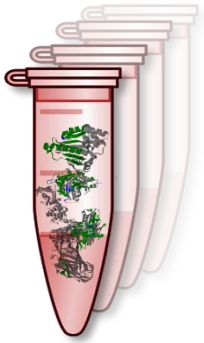
Circadian Cycle



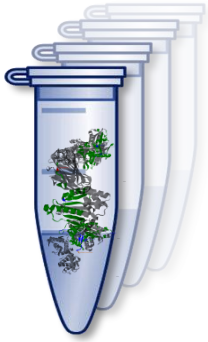


Robles et al., *PLOS Genetics, 2014*

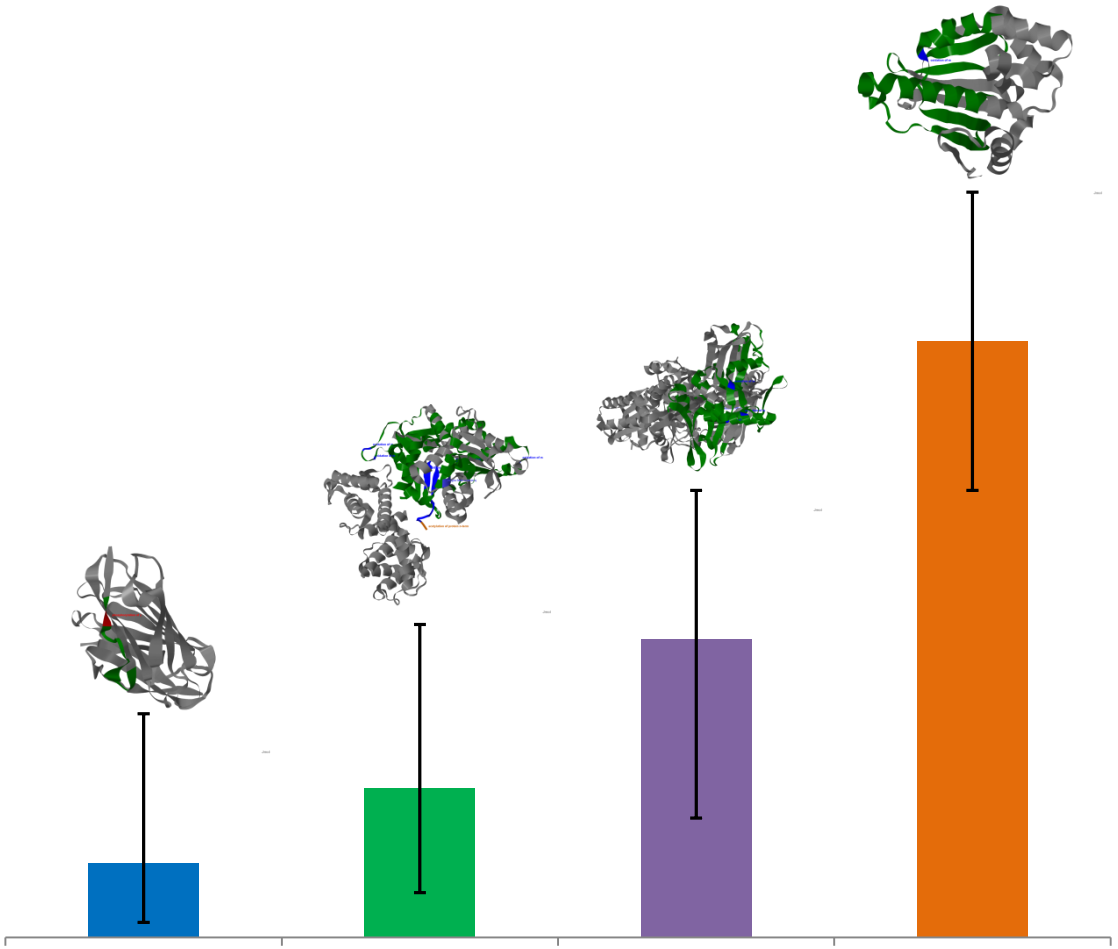
Pooling



Patient



Control



+ Increases sample amount
+ Reduces variability
- Reduces power

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Would you do a better job?