Parametrically modulated regressors

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What question does a parametrically modulated regressor answer?

- Show emotional stimuli in scanner
  - Use post-fMRI behavioral task to estimate valence
  - Q: Does BOLD activation increase with valence?

- Gambling task
  - Can win variable amounts for each gamble
  - Q: Does BOLD activation increase with amount a person could lose on a gamble?

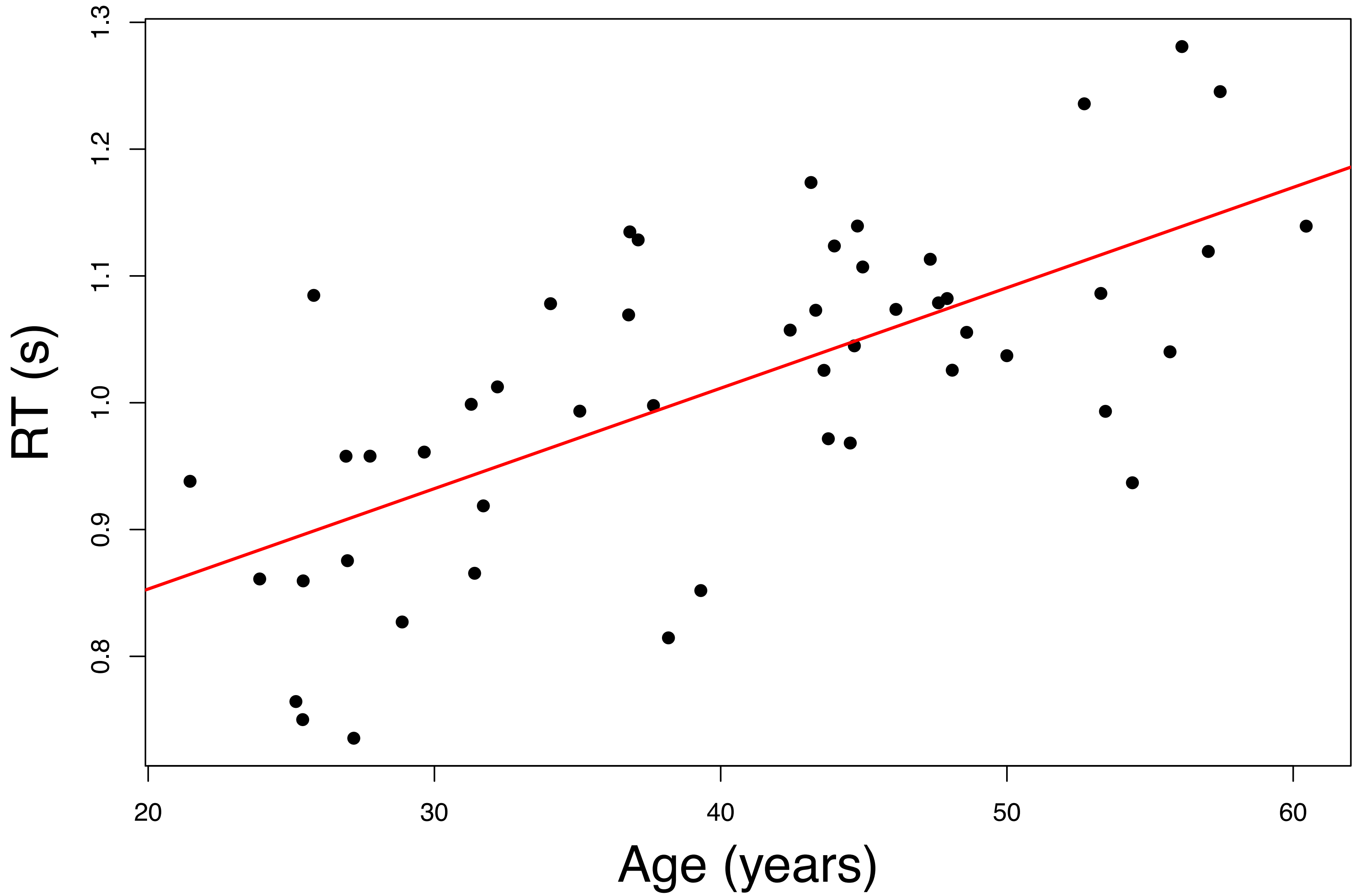
What do we need from previous lectures?

- Do you recall how we generate regressors for our time series models?
- Do you recall what collinearity is?
- Do you recall what the downside of collinearity is?

Getting started

- If you fully understand a simple linear regression, you can understand what parametric modulators are doing

My analogy

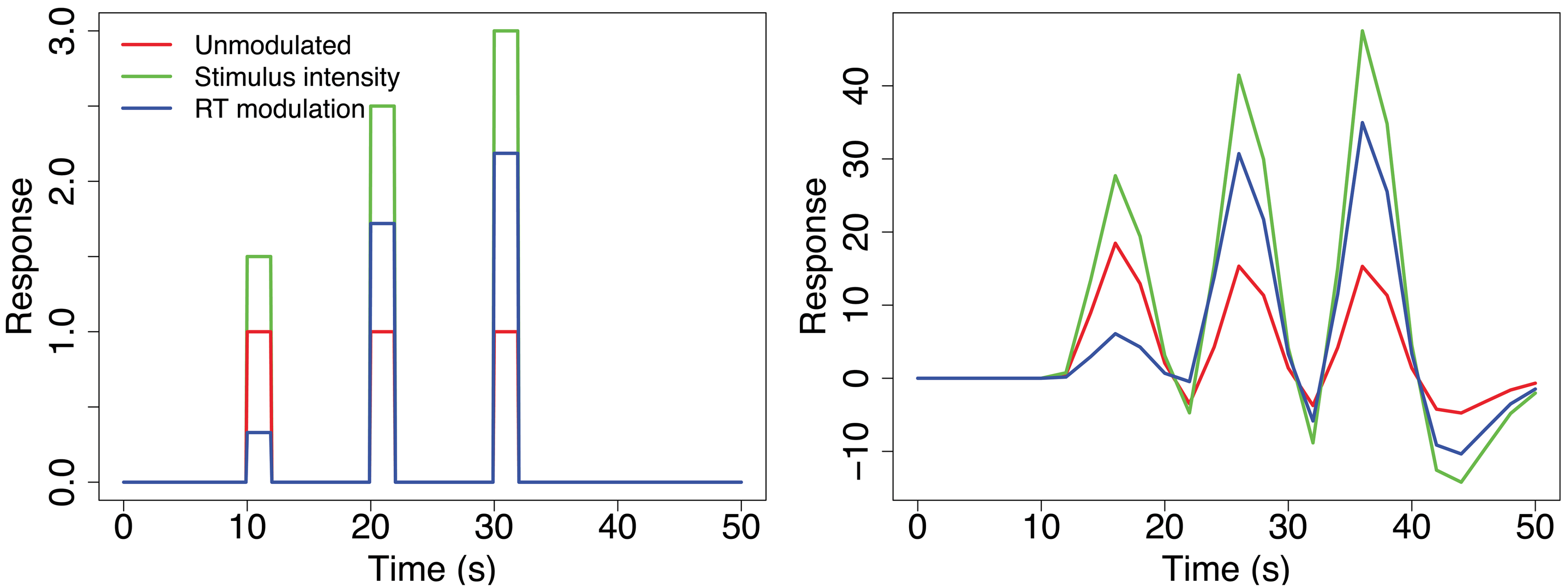


How do we make regressors?

Our boxcar regressor

Our boxcar regressor, modulated

Just add convolution!



Interpretation

- Just like a regular old regression slope!

- Hypothesis testing
  - reg 1 = unmodulated regressor
  - reg 2 = modulated regressor
  - c = [0, 1] tests positive slope
  - c = [0, -1] tests negative slope
  - c = [1, 0] Mean activation when the modulator = 0
    - More on this in a bit!!

Sometimes run into trouble with more than one modulator

- Modulators might be correlated

- Often orthogonalization is misused here

Reference

RESEARCH ARTICLE

Orthogonalization of Regressors in fMRI Models

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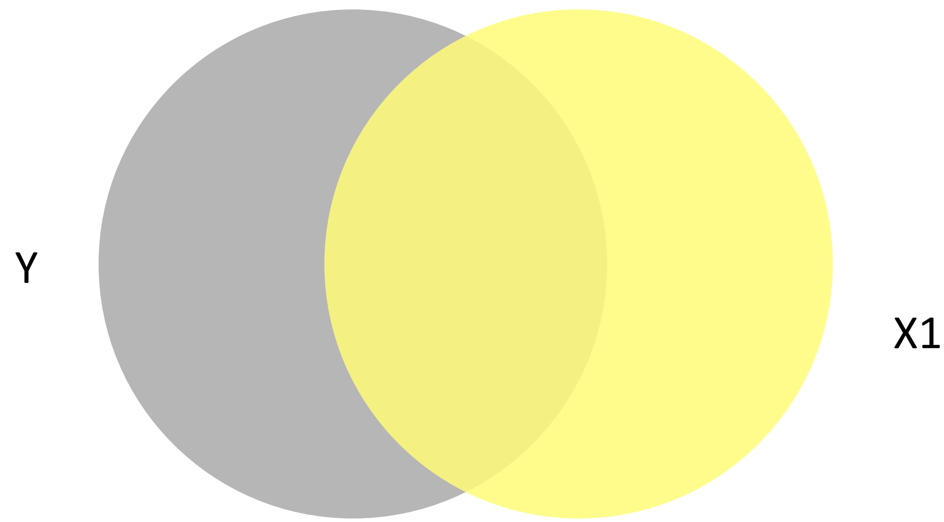
How regression naturally works

- Each regressor's p-value only reflects its unique variability



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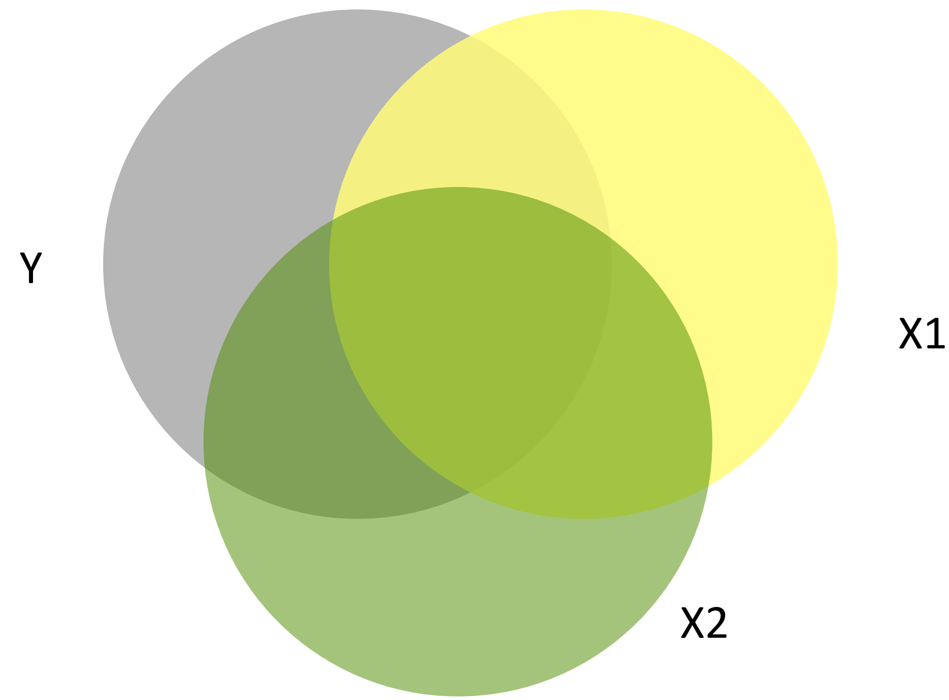

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- Giving that shared portion to one of the regressors
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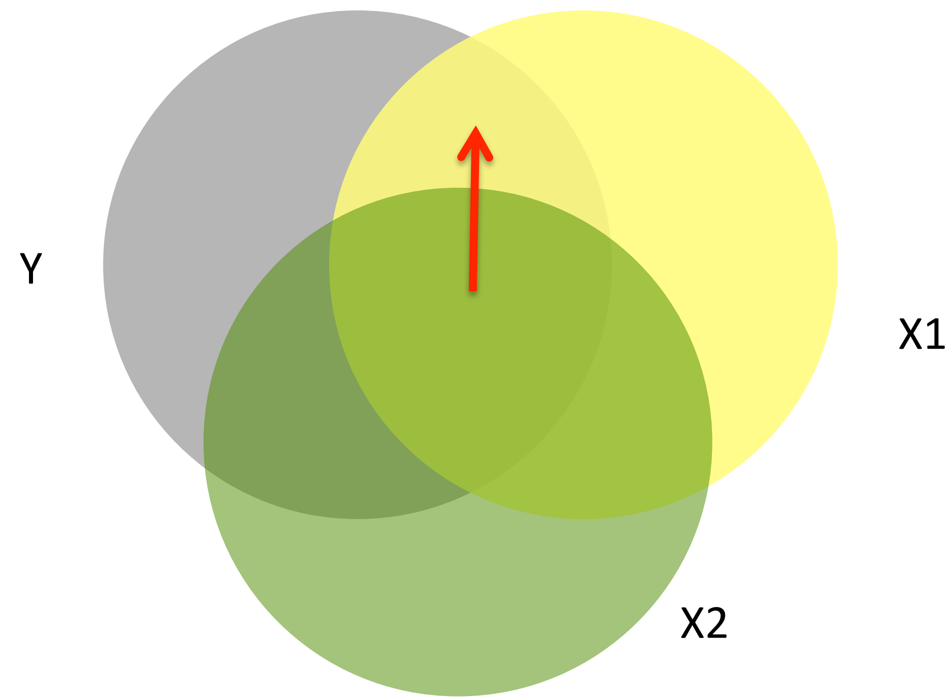
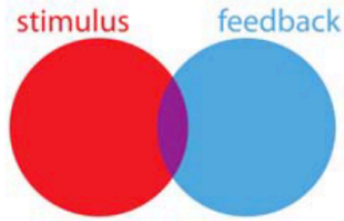
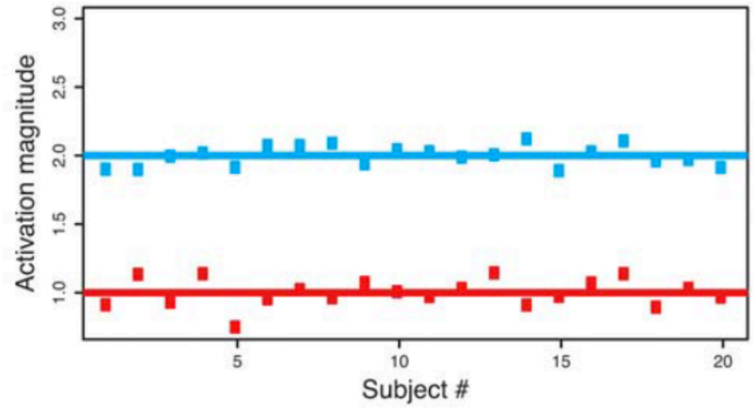


What happens to estimates?

- Same design as before (stimulus followed by feedback)

Low collinearity
ISI=3s





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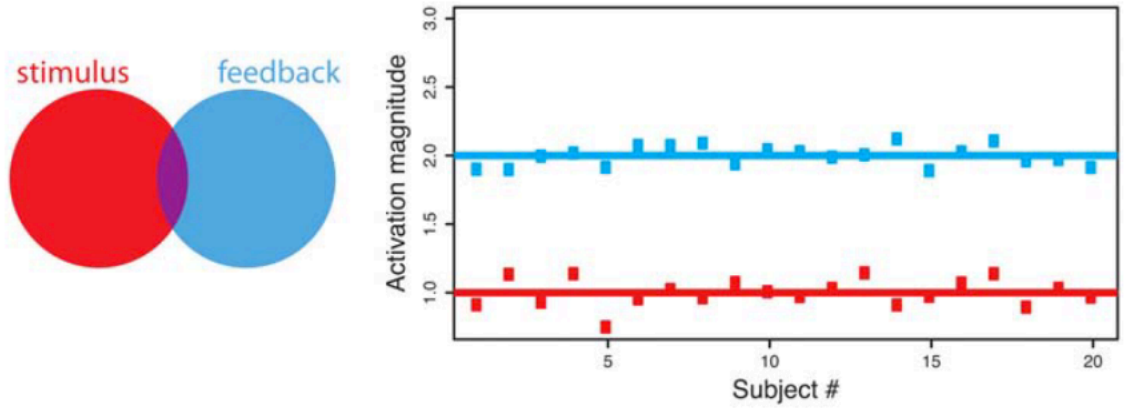
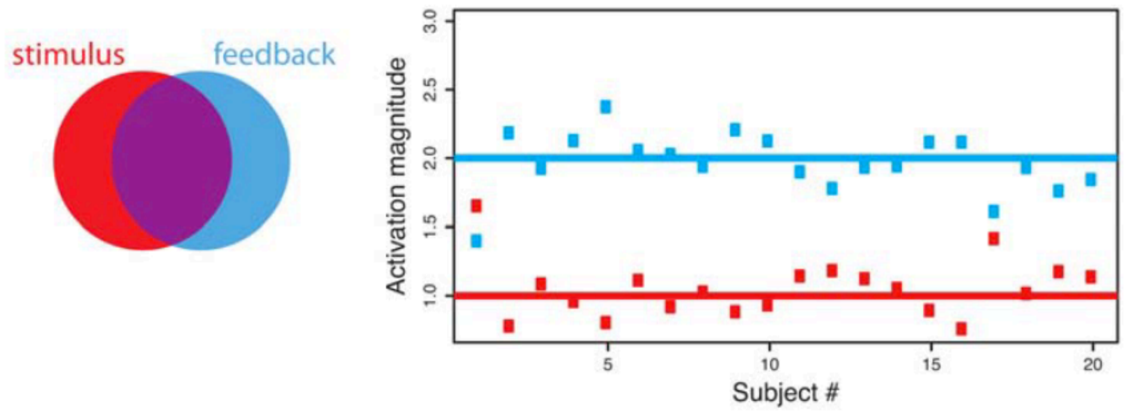
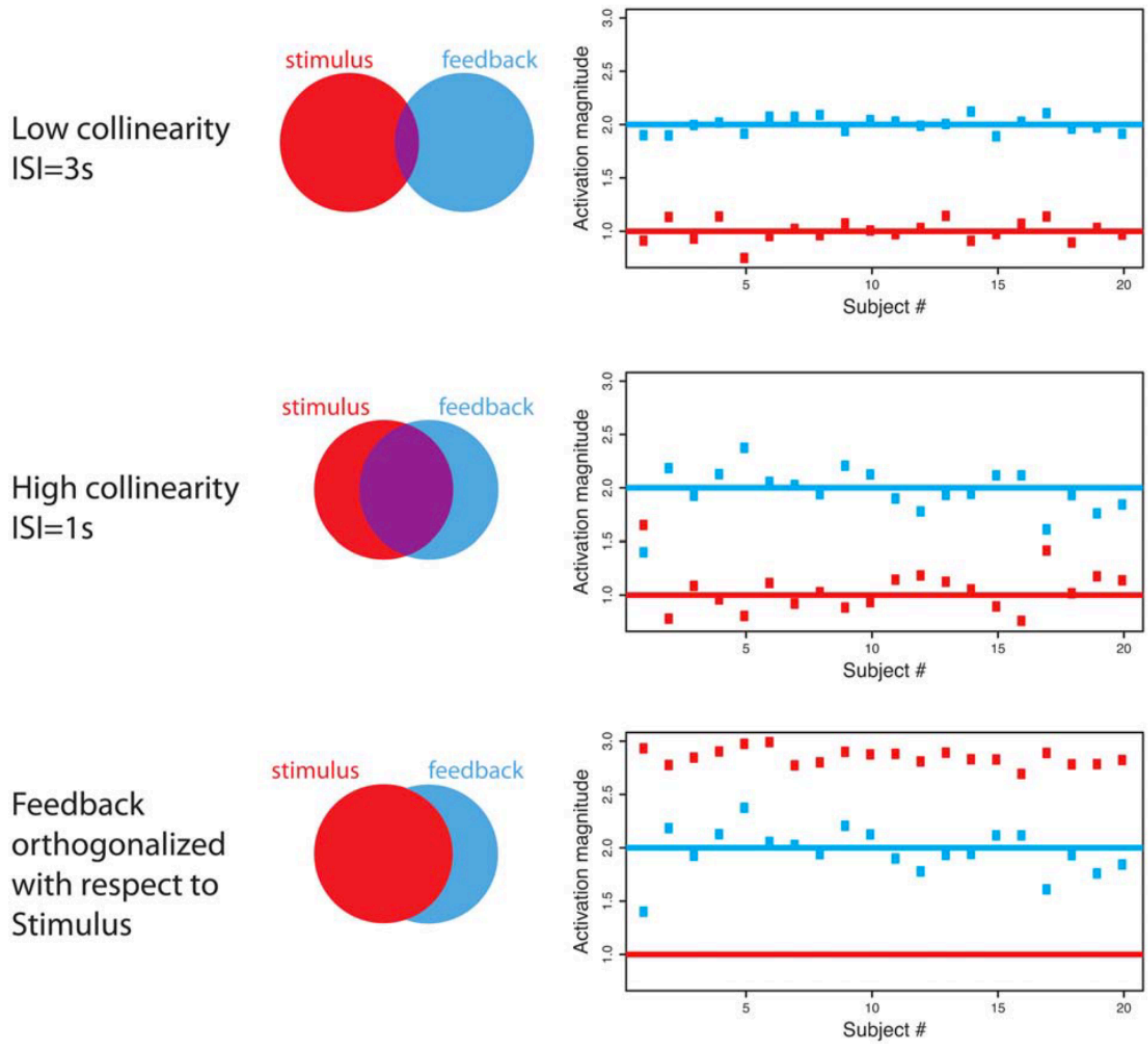


High collinearity
ISI=1s




Low collinearity
ISI=3s
stimulus
feedback
Activation magnitude
Subject #
High collinearity
ISI=1s
stimulus
feedback
Activation magnitude
Subject #
Feedback
orthogonalized
with respect to
Stimulus
stimulus
feedback
Activation magnitude
Subject #

Orthogonalization can lead to very misleading results

- Basically “un-controls” one covariate for the other
  - But that’s the entire reason we model multiple regressors!
- If you orthogonalize “motion” with respect to task, you are not “fixing” collinearity

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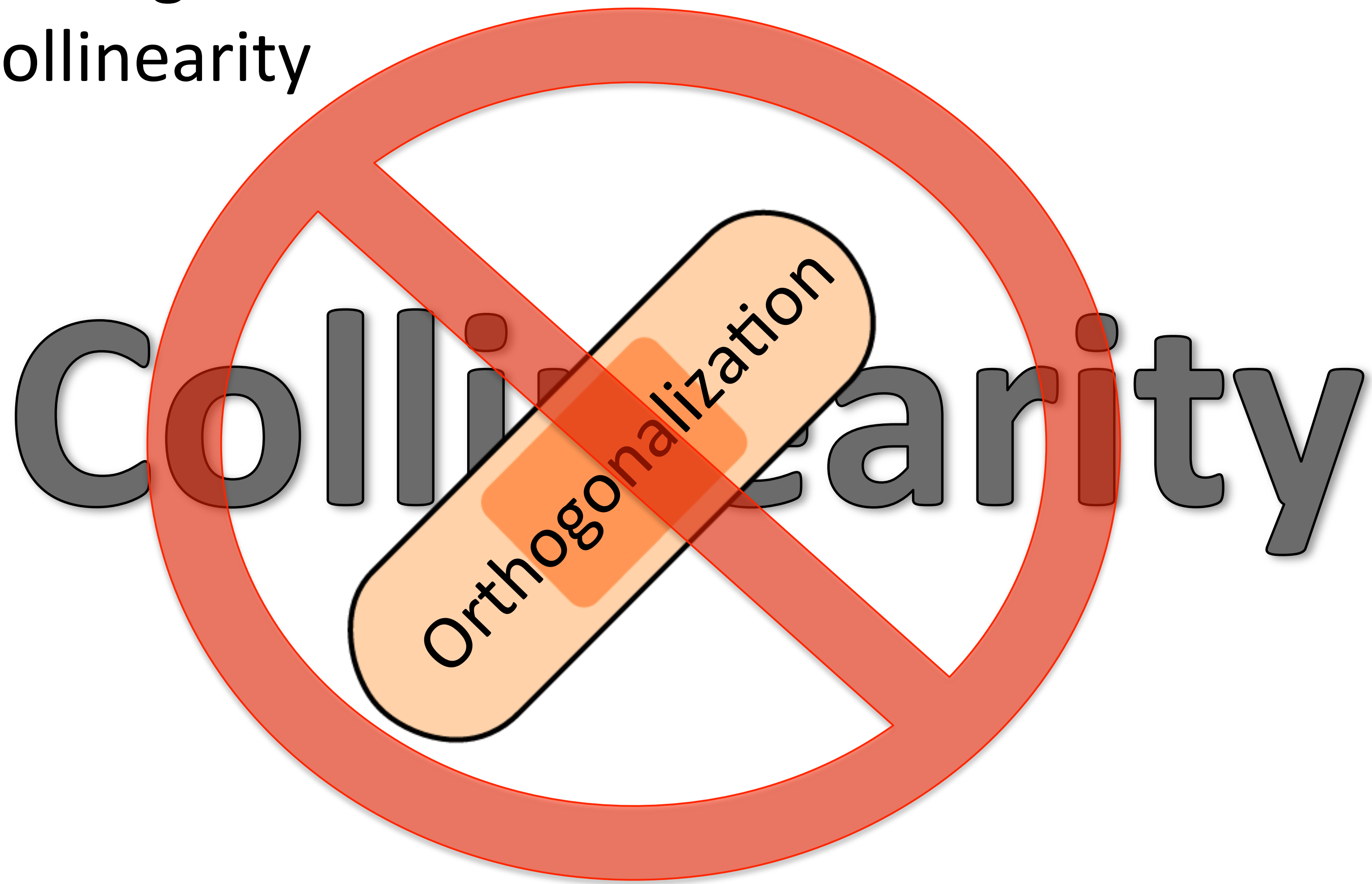
  - Please don't do it
  - Your orthogonalized model behaves, basically, as if you omitted motion

Recap

- Orthogonalization is NOT a band-aid for collinearity



Is orthogonalization ever okay?

- Yes!
  - Mean centering covariates!
  - Parametric modulation!
    - Same idea as mean centering
    - Unmodulated regressor should represent mean activation for that task
    - Modulation regressors should reflect unique variability of that modulation value

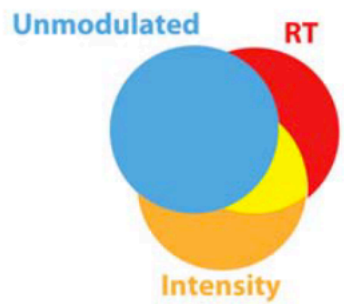
Beware of what your software does!

- Setup: Modeling stimulus intensity and RT as parametric modulators
- Orthogonalization is *okay* if done properly
- Goal: Orthogonalize each of RT and intensity with respect to unmodulated regressor

Regressors without orthogonalization

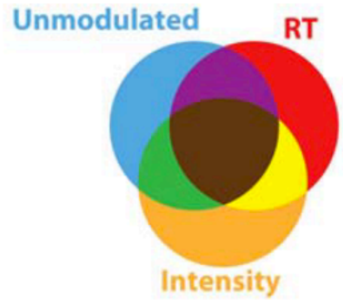
Regressors without orthogonalization

Correct orthogonalization for interpretable Unmodulated



RT wrt Unmod
Intensity wrt Unmod

Regressors without orthogonalization



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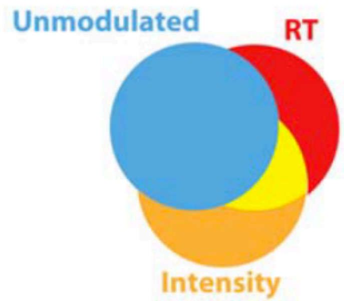
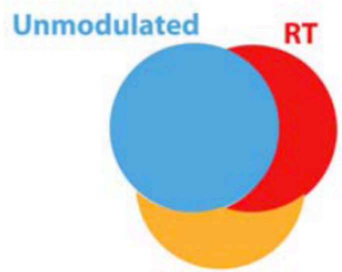


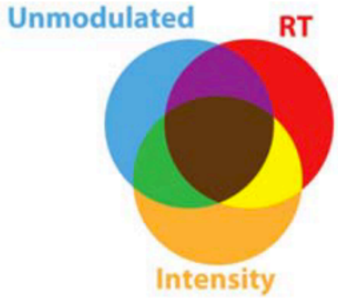
RT wrt Unmod
Intensity wrt Unmod

SPM
RT first
Intensity second



RT wrt Unmod
Intensity wrt Unmod and RT

Regressors without orthogonalization



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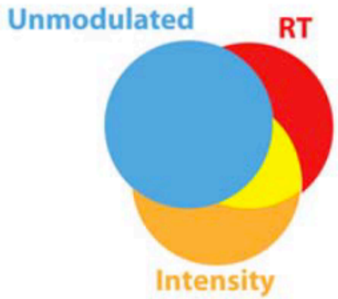

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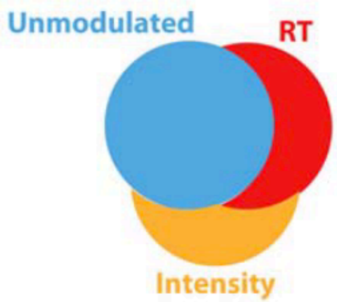

RT wrt Unmod
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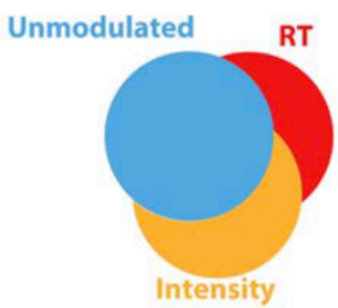

RT wrt Unmod and Intensity
Intensity wrt Unmod

Aw no, SPM ☹

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- There's a fix
  - mean center modulators

- What seems like a fix, but isn't
  - SPM's "No orthogonalization" option alone
  - We still need the modulated regressors to be orthogonalized with respect to the unmodulated regressor and to keep the unmodulated regressor's parameters interpretable

Aw no, SPM ☹

- Let me write out the different combos on the board! You help me determine the interpretations of the parameter estimates in each case.

Today in lab

- What will happen if you let SPM do the default thing with 2 sets of modulators?
  - i.e. what's the interpretation of the parameter estimates for the unmodulated regressor, first added modulation and second added modulation?
  - What would the correlation between the regressors look like?

Today in lab

- How do we make SPM do what we’d like it to do?

Summary

- If you do orthogonalize
  - Your p-value for the regressor you orthogonalized with respect TO will change
    - It will almost always decrease….this is not good

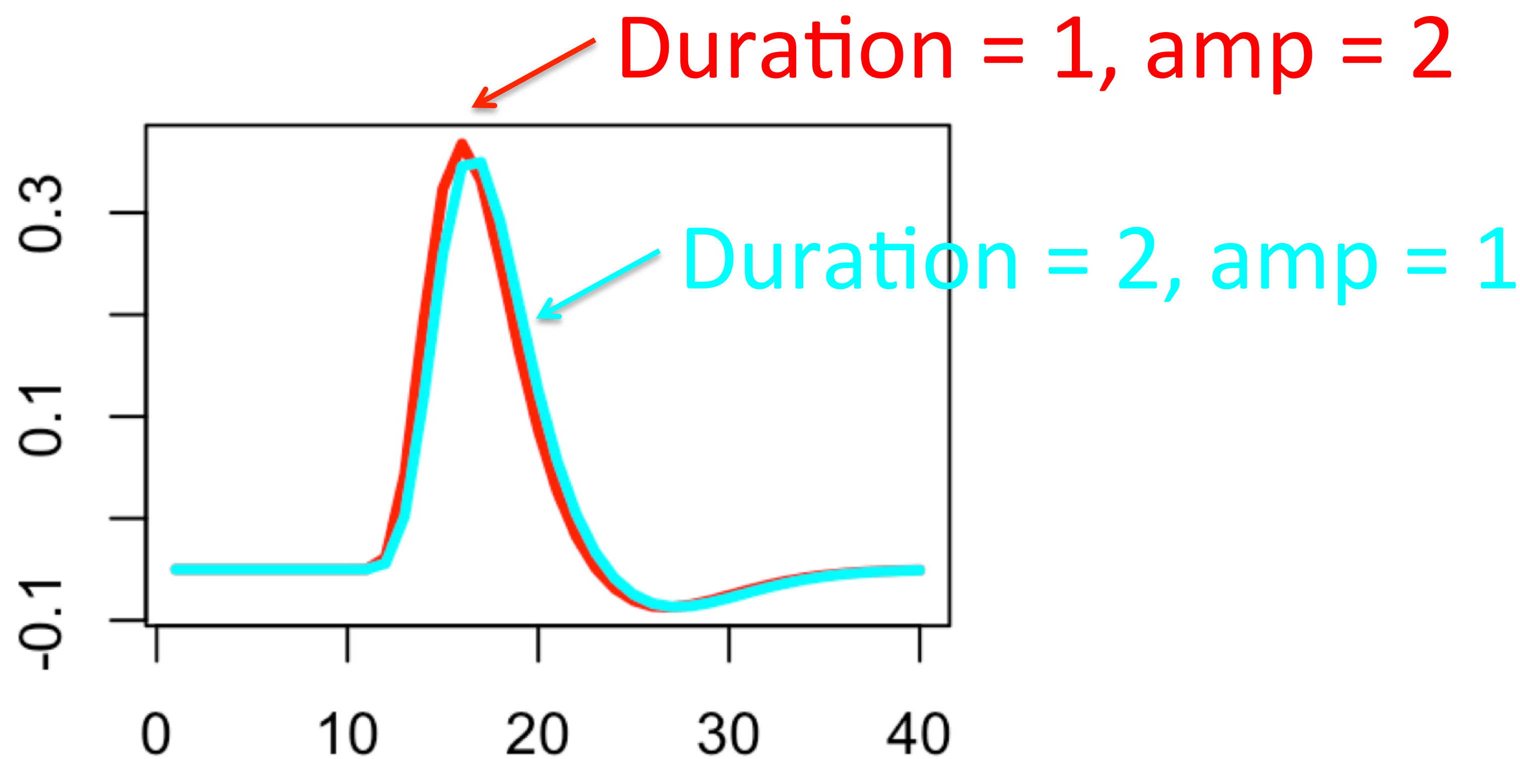
  - The regressor that was actually changed will have the same p-value!

RT explanation

- Setup: You have two tasks (A&B) and you know there are RT differences (A has longer RT), but the hypothesis of interest is A>B… duration and amplitude are almost perfectly confounded, so you want to be sure the A>B comparison is not reflecting RT differences, but is reflecting amplitude differences
  - Solution: Model RT as a nuisance regressor to adjust your A-B comparison

Both the problem and the solution to our problem

- Duration and amplitude of response are almost perfectly confounded.



What if we did use duration?

- Regressor 1 : Unmodulated task A
- Regressor 2: Unmodulated task B
- Regressor 3: RT modeled via duration

What is the interpretation of regressor 1's Parameter estimate?

Orthogonlization *could* work

- We'd need to simultaneously orthogonalize RT with respect to all other trials (A and B, combined).
  - Then the interpretation of A, alone, would be mean activation during trial A
  - Interpretation of A-B would be RT-adjusted difference between A and B

Problem: software doesn’t allow us to do that orthogonalization!

- Only allows orthogonalizing with respect to one and then the other, but not both at the same time
  - True for SPM and FSL
- Solution: Use the parametric modulation and mean center RT!
  - Equivalent to the proper orthogonalization!!

Questions?