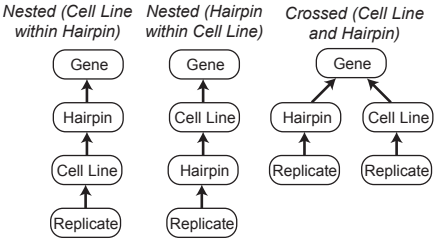
A

Alternatives for organizing variables into hierarchies ("Random Effects" hierarchies)

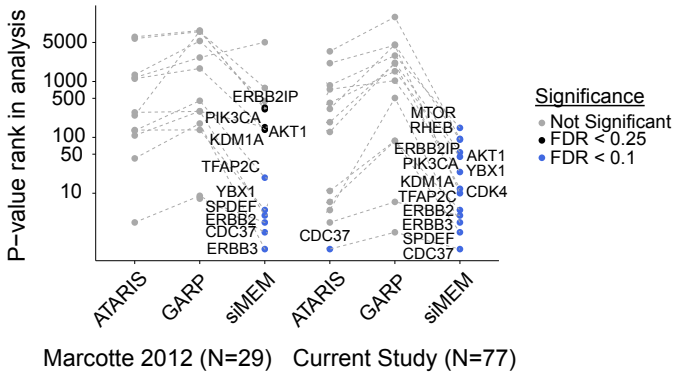


Each variable can be associated with an intercept and/or slope adjustment

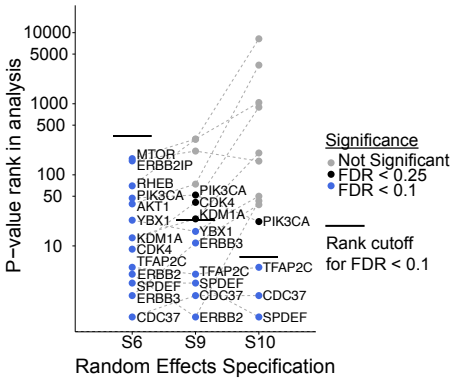
B

Structure Name	Relation Between Variables	Variables Included in Structure	Detailed Description	Compared to siMEM (S6)
S1	Single variable	Hairpin	Hairpin (random intercept)	Simpler
S2	Single variable	Hairpin	Hairpin (random slope)	Simpler
S3	Single variable	Hairpin	Hairpin (random intercept+slope)	Simpler
S4	Nested variables	Cell Line, Hairpin	Nested: Cell Line (random intercept), nested in Hairpin (random intercept+slope)	Simpler
S5	Nested variables	Cell Line, Hairpin	Nested: Cell Line (random slope), nested in Hairpin (random intercept+slope)	Simpler
S6 (siMEM)	Nested variables	Cell Line, Hairpin	Nested: Cell Line (random intercept+slope), nested in Hairpin (random intercept+slope)	Same
S7	Nested variables	Cell Line, Hairpin, Replicate	Nested: Replicate (random interept), nested in Cell Line (random intercept+slope), nested in Hairpin (random intercept+slope)	More complex
S8	Nested variables	Cell Line, Hairpin, Replicate	Nested: Replicate (random slope), nested in Cell Line (random intercept+slope), nested in Hairpin (random intercept+slope)	More complex
S9	Nested variables	Cell Line, Hairpin	Nested: Hairpin (random intercept+slope), nested in Cell Line (random intercept+slope)	Different – nested variables
S10	Crossed variables	Cell Line, Hairpin	Crossed Cell Line(random intercept+slope) and Hairpin (random intercept+slope)	Different – crossed variables

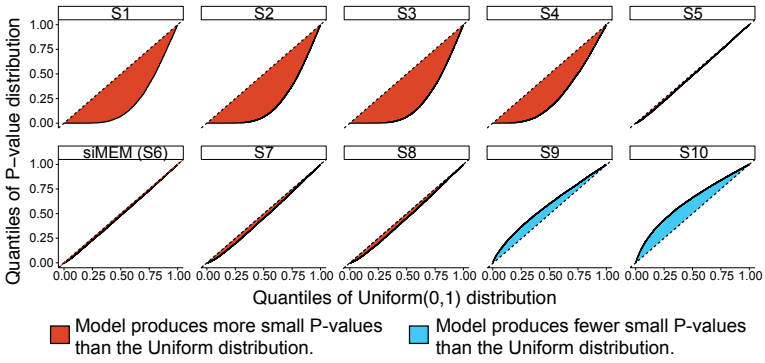
C



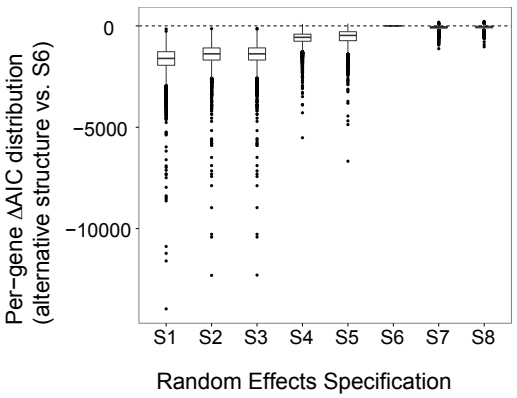
F



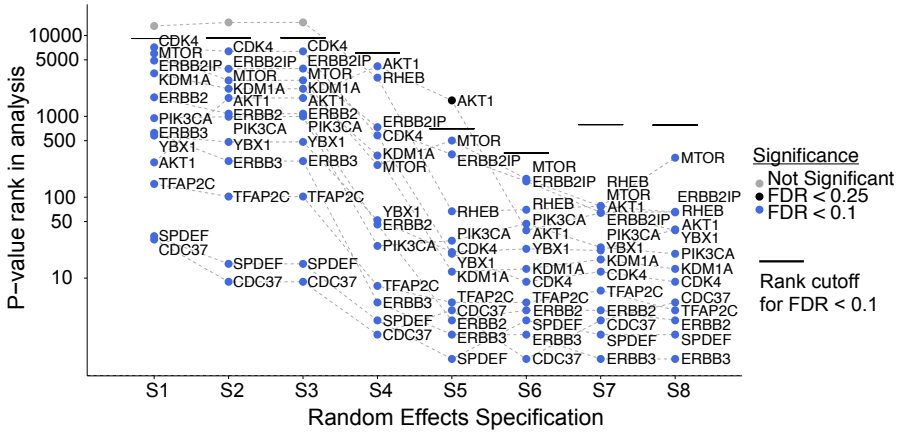
D



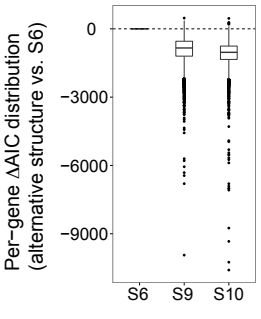
G



E



H



Supplementary Figure 2