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Origins of sloppiness in biological models. JOSHUA WATERFALL, FERGAL CASEY, RYAN GUTENKUNST, Cornell University, KEVIN BROWN, Harvard University, CHRISTOPHER MYERS, JAMES SETHNA, Cornell University — Models of biological networks such as those involved in signal transduction, development, and the cell cycle routinely contain dozens of parameters. Even if high quality data on the dynamics of every form of every chemical species were available for such networks, some parameter combinations would be orders of magnitude more constrained than other combinations – a feature we term sloppiness. In order to understand this shared, possibly universal, behavior we turn to mathematically well-defined classes of models – multiple linear regression, sums of polynomials and sums of exponentials. The origins of sloppiness turn out to have nothing to do with how much data is available or how many parameters a model has, but are instead the scale of description at which a model is constructed and how the parameters of the model map to the data. Thus describing a cloud of points by a plane, the core of linear regression, is not sloppy while describing complex biological networks by the biochemical reactions, just as fitting sums of exponentials or polynomials, is unavoidably sloppy.

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