



oving boundaries	
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Modeling toolbox 10 Stochastic processes -**Biochemical reaction networks** 10^{2} How does it work? 10 Coarse-grained models Number of structures -- Optimization frameworks What is it doing? (functionally) 10 - Complex interacting systems Randomness as disorder - 10^{2} Where is it in the space of possibilities? 101 10 10 100 Number of sequences that fold into a particular structure (N_s)

Li et al. Science (1996)



6

How might machine learning help us find principles?

The Bitter Lesson

Rich Sutton

March 13, 2019

The biggest lesson that can be read from 70 years of AI research is that general methods that leverage computation are ultimately the most effective, and by a large margin. The ultimate reason for this is

Moving boundaries, boosting productivity, raising questions \rightarrow Try to cut through the hype!



Some hopes, or how to *not* find principles...

- Try to avoid fact- or theory-free biology!
 - Representatives: Paul Nurse, Sydney Brenner
 - Are your models grounded in experiments and questions?
 - Are your experiments guided by questions and theory?
 - Might your computations also generate questions?

1-2 weeks planning	2-5 years of execution		
Time			
			Fischbach. <i>Cell</i> (2024) Wikipedia

Modeling toolbox where is your research?
 Stochastic processes Biochemical reaction networks How does it work?
 Coarse-grained models Optimization frameworks What is it doing? (functionally)
 Complex interacting systems Randomness as disorder Where is it in the space of possibilities?
 Evolutionary dynamics Bioinformatics and machine learning How did it get here and where will it go?

