The Robot Scientist or:
How I learned to stop worrying and love automated model inference

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The complexity of biological systems arises from highly nonlinear structural, metabolic, and signaling networks that span multiple spatiotemporal scales. Massively parallel experiments provide ever more dynamic data. As we acquire complete, reductionist parts list for simple biological systems, we must ascertain how these pieces interact – a mathematical model of a functioning animal might require Avogadro's number of partial differential equations, termed a Leibnitz. One might worry about the limitations of the human mind in designing and interpreting multivariable experiments on complex, non-linear systems. The key could be robot scientists that independently design and conduct experiments to infer automatically models describing the dynamics of simultaneous interactions between hundreds of biological variables. This presents significant challenges: sensors and actuators with adequate spatial and temporal resolution to acquire the necessary data from living cells and organisms, and computer algorithms that specify initial conditions, the variables to measure for each experiment, and the desired perturbations/actuations. The experiments themselves should be conducted on small numbers of cells to minimize cost, achieve the required time response, capture paracrine and autocrine signaling, quantify cell-to-cell variation, and enable large numbers of simultaneous experiments. We are developing an integrated measurement and modeling system in which a computer specifies an experiment on isolated cells, the dynamic responses of the cells to a controlled stimulus are recorded using multiple real-time analytical techniques, and the computer then uses these data to select among possible models of the system and propose the next experiment for further model refinement. Preliminary results are encouraging.