Why use optimization?

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Why and how to model?

- to understand (descriptive process, validate principles and/or explore underlying mechanisms)
- to predict (and/or discover new system features)
- to decide (engaging groups in a decision, make decisions, operate/control a system of interacting parts)
- to design (strategic planning, investigate new designs, can they be economical given price of raw materials, production process, etc)

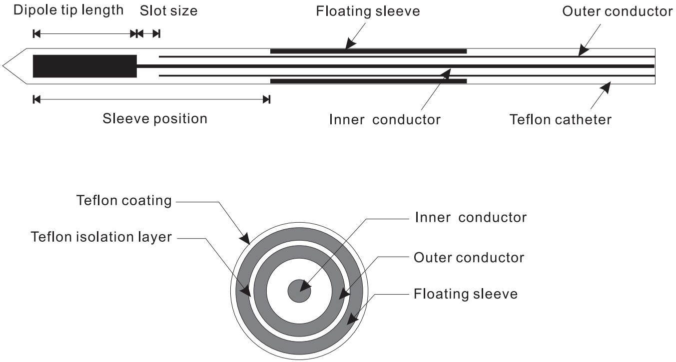
Simulation Optimization

- Computer simulations are used as substitutes to understand or predict the behavior of a complex system when exposed to a variety of realistic, stochastic input scenarios
- Widely used in epidemiology, engineering design, manufacturing, supply chain management, medical treatment and many other fields (calibration, parameter tuning, inverse optimization)

$$\min_{p \in P} f(p) = \mathbb{E}[S(p, \xi)],$$

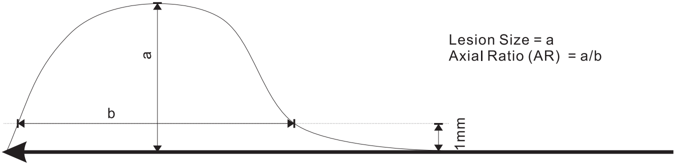
- The sample response function $S(p, \xi)$
  - typically does not have a closed form, thus cannot provide gradient or Hessian information
  - is normally computationally expensive
  - is affected by uncertain factors in simulation

Design a coaxial antenna for hepatic tumor ablation



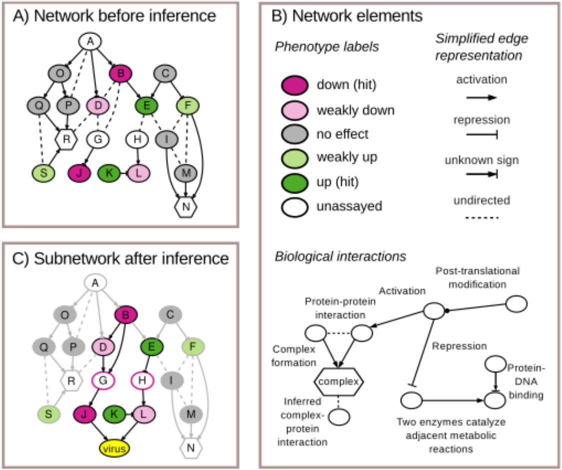
Simulation of the electromagnetic radiation profile

Finite element models (COMSOL MultiPhysics) are used to generate the electromagnetic (EM) radiation fields in liver given a particular design



Metric	Measure of	Goal
Lesion radius	Size of lesion in radial direction	Maximize
Axial ratio	Proximity of lesion shape to a sphere	Fit to 0.5
S_{11}	Tail reflection of antenna	Minimize

Network inference



- Given prior knowledge, select paths, color nodes and sign arcs to explain as many hits as possible
- e.g. sign of a relevant edge is consistent with the phenotypes of nodes it connects

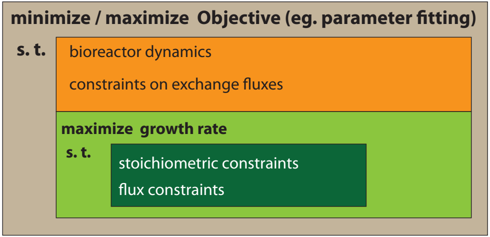
- Can model (propositional) logic constraints in a mixed integer program
- Key issue is to determine objective

Biological Hierarchical Models

I: Opt knock (a bilevel program)

max	bioengineering objective (through gene knockouts)	
s.t.	max cellular objective (over fluxes)	
	s.t.	fixed substrate uptake
		network stoichiometry
		blocked reactions (from outer problem)
	number of knockouts $\leq$ limit	

II: Bio-reactor dynamics:



Different mathematical programming techniques are used to transform the problem to a nonlinear program. The differential equations are transformed into nonlinear constraints using collocation methods.

Parameter estimation

Example (Crombach):

$$\min_{p} J(x(p) - \bar{x}) \text{ s.t. } \frac{\partial x}{\partial t} = D\Delta x + f(x, p), p \in P$$

Key points:

- Constraints on parameter choice $p \in P$
- Can solve using PDE constrained optimization. Huge literature in applied mathematics. Key computational idea for optimization is that of the adjoint operator
- Can discretize/optimize, and then add L_1 penalization to get "sparse" (parameter) solution via nonlinear optimization
- Extension to nonsmooth f - DVI, and MPEC, allows for switching

Conclusions

- Optimization helps understand what drives a system
- Constraints are a crucial design/modeling tool
- Uncertainty is present everywhere: we need to hedge/control/ameliorate it
- Collections of, and interactions between, models are critical
- Modern computational optimization tools can be very fast, deal with large amounts of data and variables, address non-convex and discrete issues, interact with dynamics