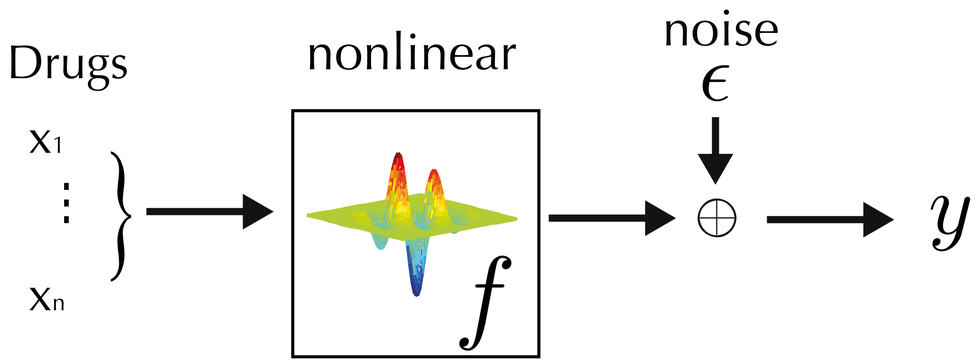
Adaptive Experimental Design For Drug Combinations

Mijung Park , Marcel Nassar, Brian L. Evans, Haris Vikalo

Electrial and Computer Engineering, The University of Texas at Austin

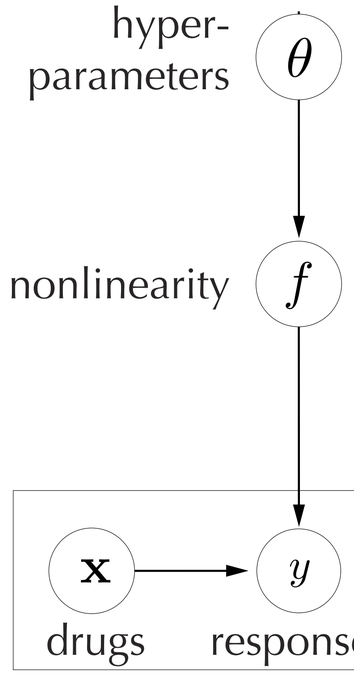
1. Drug combinations problem



biological system

2. Respose modeling using Gaussian processes

generative model



noise variance, overall scale

flat hyper-prior on $\theta = \{\sigma^2, \rho, \tau\}$

correlation scale

Gaussian process prior

$$f|\theta \sim \mathcal{N}(0, K)$$

$$k(\mathbf{x}_i, \mathbf{x}_j) = \rho \exp\left(-\frac{||\mathbf{x}_i - \mathbf{x}_j||^2}{(2\tau)}\right)$$

likelihood

$$y|\mathbf{x} \sim \mathcal{N}(f(\mathbf{x}), \sigma^2)$$

MAP inference: at test points $P(\mathbf{f}^*|X^*, X, \mathbf{y}, \theta) \sim \mathcal{N}(\mu, \Sigma)$

$$\mu = K(X^*, X)(K + \sigma^2 I)^{-1}\mathbf{y}$$

$$\Sigma = K(X^*, X^*) - K(X^*, X)(K + \sigma^2 I)^{-1}K(X, X^*)$$

Hyperparameter estimation:

$$\theta_{ml} = \arg\max_{\theta} P(\mathbf{y}|\theta) = \int P(\mathbf{y}|X, \mathbf{f})P(\mathbf{f}|X, \theta)d\mathbf{f}.$$

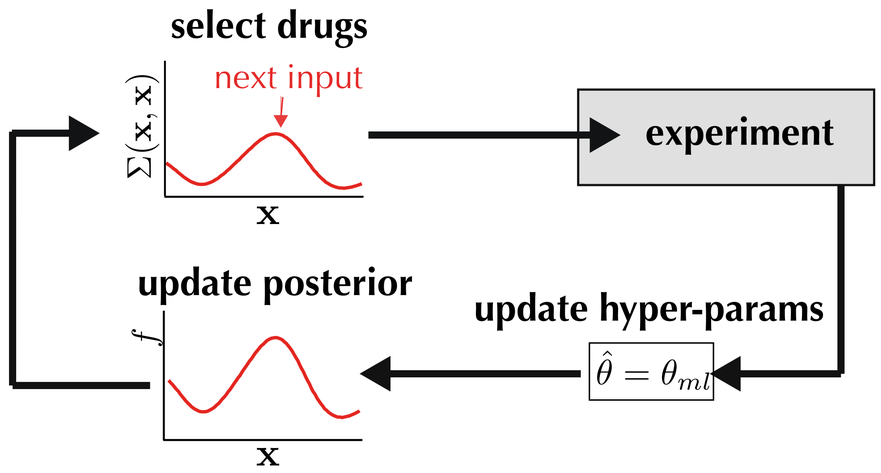
3. Info-theoretic Active Learning

- maximize expected info gain about f

$$\mathbf{x}^* = \arg\max_{\mathbf{x}} \mathbb{E}_{p(y|\mathbf{x},D_t)}\left[H(\mathbf{f}|D_t) - H(\mathbf{f}|D_t, \mathbf{x}, y)\right]$$

$$= \arg\max_{\mathbf{x}} \Sigma(\mathbf{x}, \mathbf{x}) \quad \text{uncertainty sampling}$$

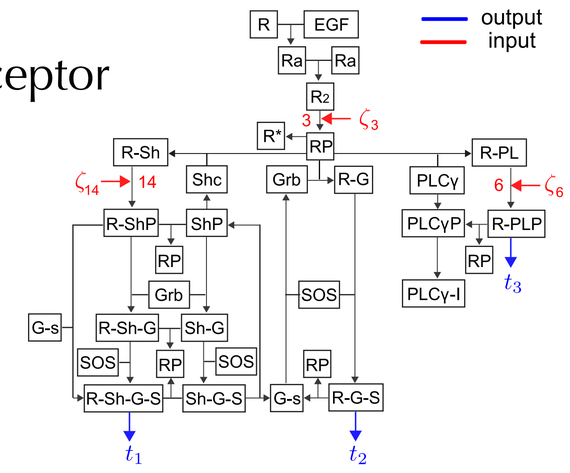
- sequential active learning



4. Application to EGFR network

- Epidermal Growth Factor Receptor
- Inhibiting EGFR desired

select drugs
minimizing target: $t = \exp(\sum_{i=1}^{3} t_i)$



5. Results