# Bayesian approaches for multiscale modeling

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- $\pi(\theta|y)$ quantifies uncertainty about $\theta$ & functionals $f(\theta)$

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- Markov chain Monte Carlo (MCMC) constructs a Markov chain with stationary distribution $\pi(\theta|y)$
- Bypasses ever needing to calculate $L(y)$ & highly complex models can be considered

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- Bayesian paradigm potentially very useful for solving such problems

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  1. Use a usual solver without considering UQ & put solution in as 'center' of simple statistical distribution
  2. Use approximate Bayes computation (ABC) methods, which only require a forward simulator & not an explicit likelihood

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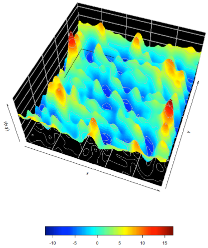
- $\mu \sim \text{GP}(\hat{g}, c)$ = unknown function, $\epsilon_i$ = measurement error

# Gaussian process (GP) overview

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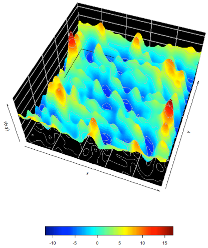


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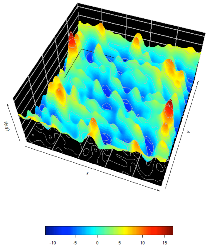


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- Realizations $\mu \sim \mathrm{GP}(\hat{g}, c)$ are random functions/stochastic processes centered on $\hat{g}$ on average
- Variance and smoothness of the realizations controlled by the covariance function:

$$\mathrm{cov}\{\mu(x), \mu(x')\} = c_\phi(x, x'),$$

where $\phi$ are (potentially unknown) parameters

# Some comments on GPs

- Often a default covariance is used that doesn't include mechanistic information; eg,

$$c_\phi(x, x') = \phi_1 \exp\{-\phi_2 ||x, x'||_2^2\},$$

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$$\{\mu(x_1), \ldots, \mu(x_n)\} \sim N_n(\{\hat{g}(x_1), \ldots, \hat{g}(x_n)\}, C_n),$$

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- This prior for $\mu$ evaluated at a finite number of inputs is *conjugate* to the normal likelihood of the measurements $\{y_i\}$
- The posterior for $\mu | y_1, \ldots, y_n, \hat{g}, \phi$ has a simple analytic form

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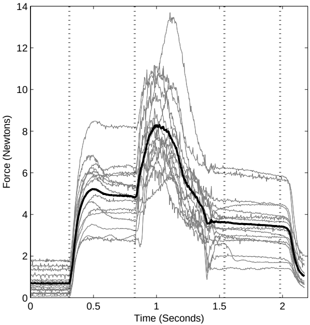
- Broadly *mechanistic nonparametric Bayes* models can be designed for these problems
- Literature is under-developed- will give a simple case study here

# Mechanistic GPs - muscle activation example

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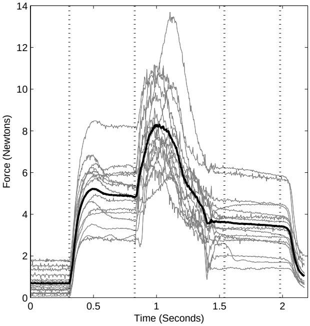


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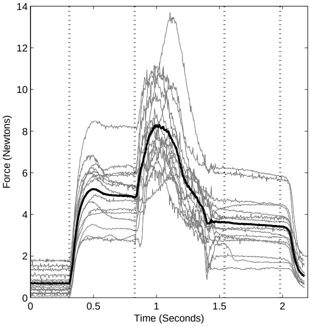


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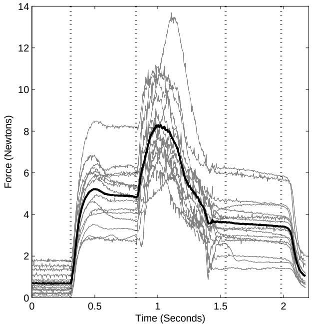


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- Solutions to ODEs would need to be specific to each replicate & do not fit observed data perfectly

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- As the integral operator is linear, if $r(t) \sim \mathrm{GP}(0, c)$ then $h(t)$ is also a GP
- Covariance kernel of induced GP is obtained by the convolution of Green's function for the ODE & the covariance kernel of $r(t)$.

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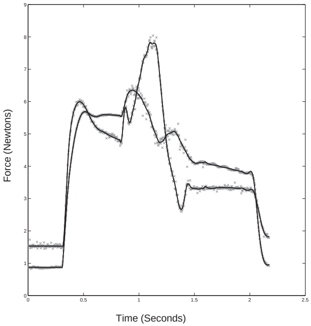
- Sample individual curves from GPs with mean curve specific to each group.

# Muscle force application

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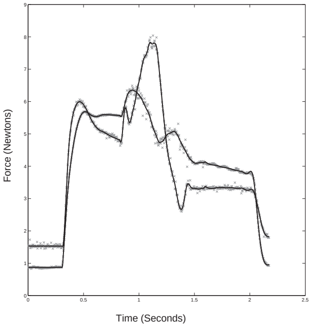


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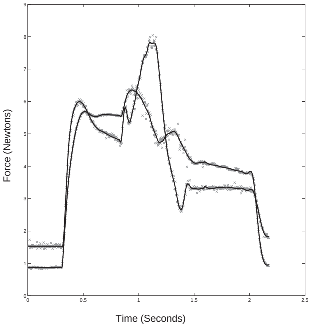


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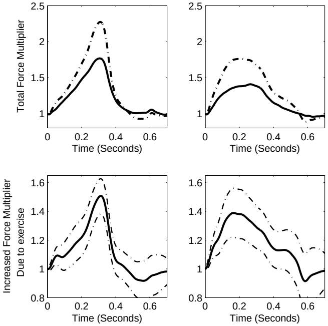
- The above figure shows our model fits for one animal pre- and post-

# Some results

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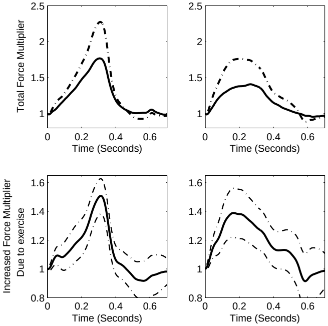


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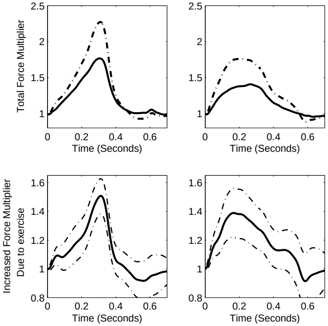
- Top row: mean isometric contraction for pre- (dashed) & post- (solid) exercise in old (top left) & young (top right)

# Some results




- Bayesian mechanistic hierarchical model can produce uncertainty estimates in any functional of interest
- Top row: mean isometric contraction for pre- (dashed) & post- (solid) exercise in old (top left) & young (top right)
- Figure bottom row = differences & 95% intervals are shown in the bottom row (old left & young right)

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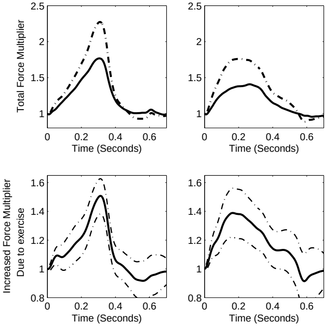


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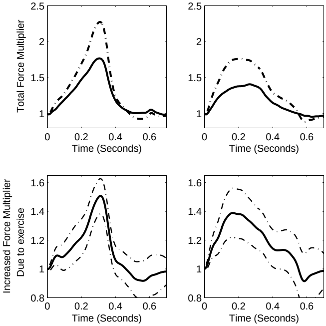


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- Can also do inferences on individual differences

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- However, GPs are remarkably flexible and can incorporate quite rich dynamics including multiscale structure

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- One of the STAN developers (Michael Betancourt) is here & interested in helping facilitate implementation