Efficient Multiple Output Convolution Processes for Multiple Task Learning

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Outline

1. Introduction
2. Gaussian Process Review
3. Covariance Functions
4. Discussion and Future Work

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Dimensionality Reduction I

- Linear relationship between the data, $\mathbf{X} \in \Re^{N\times d}$, and a reduced dimensional representation, $\mathbf{F} \in \Re^{N\times q}$, where $q \ll d$.

$$\mathbf{X} = \mathbf{F}\mathbf{W} + \boldsymbol{\epsilon},$$

$$\boldsymbol{\epsilon} \sim \mathcal{N}\left(\mathbf{0}, \boldsymbol{\Sigma}\right)$$

- Integrate out $\mathbf{F}$, optimize with respect to $\mathbf{W}$.
- For temporal data and a particular Gaussian prior in the latent space: Kalman filter/smoother.
- More generally consider a Gaussian process (GP) prior,

$$p\left(\mathbf{F}|\mathbf{t}\right) = \prod_{i=1}^{q} \mathcal{N}\left(\mathbf{f}_{:,i}|\mathbf{0}, \mathbf{K}_{f_{:,i},f_{:,i}}\right).$$

Dimensionality Reduction II

- Given the covariance functions for $\{f_i(t)\}$ the implied covariance functions for $\{x_i(t)\}$ — semi-parametric latent factor model (Teh et al., 2005).
- Kalman filter/smoother approach has been preferred
  - linear computational complexity in N.
  - Advances in sparse approximations have made the general GP framework practical. (Titsias, 2009; Snelson and Ghahramani, 2006; Quiñonero Candela and Rasmussen, 2005).

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Gaussian Distribution

Zero mean Gaussian distribution

- A multi-variate Gaussian distribution is defined by a mean and a covariance matrix.

$$N\left(\mathbf{f}|\mu,\mathbf{K}\right)=\frac{1}{\left(2\pi\right)^{\frac{N}{2}}\left|\mathbf{K}\right|^{\frac{1}{2}}}\exp\left(-\frac{\left(\mathbf{f}-\mu\right)^{\mathrm{T}}\mathbf{K}^{-1}\left(\mathbf{f}-\mu\right)}{2}\right).$$

- We will consider the special case where the mean is zero,

$$N\left(\mathbf{f}|\mathbf{0},\mathbf{K}\right)=\frac{1}{\left(2\pi\right)^{\frac{N}{2}}\left|\mathbf{K}\right|^{\frac{1}{2}}}\exp\left(-\frac{\mathbf{f}^{\mathrm{T}}\mathbf{K}^{-1}\mathbf{f}}{2}\right).$$

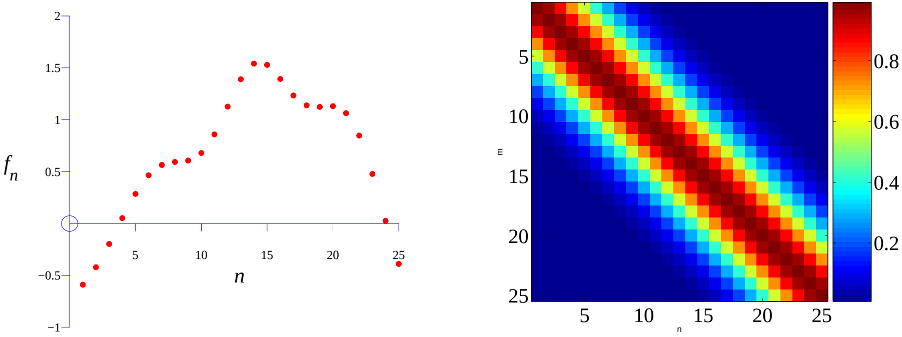
Sampling a Function

Multi-variate Gaussians

- We will consider a Gaussian with a particular structure of covariance matrix.
- Generate a single sample from this 25 dimensional Gaussian distribution, $\mathbf{f} = [f_1, f_2 \dots f_{25}]$.
- We will plot these points against their index.

Gaussian Distribution Sample

`demGPSample`



(a) (b)

Figure: (a) 25 instantiations of a function, f_n, (b) colormap of covariance matrix.

Covariance Function

The covariance matrix

- Covariance matrix shows correlation between points f_m and f_n if n is near to m.
- Less correlation if n is distant from m.
- Our ordering of points means that the *function appears smooth*.
- Let's focus on the joint distribution of two points form the 25.

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Prediction of f_2 from f_1

```
demGpCov2D([1 2])
```

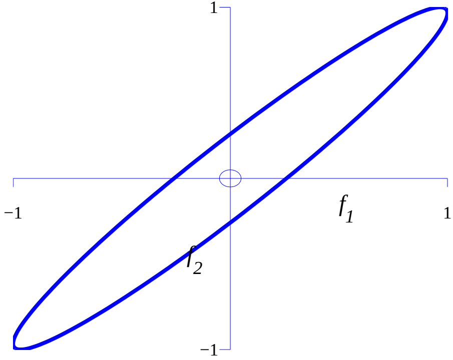

Figure: Covariance for $\begin{bmatrix} f_1 \\ f_2 \end{bmatrix}$ is $\mathbf{K}_{12} = \begin{bmatrix} 1 & 0.966 \\ 0.966 & 1 \end{bmatrix}$.

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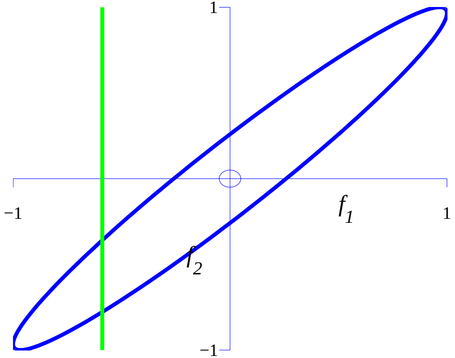

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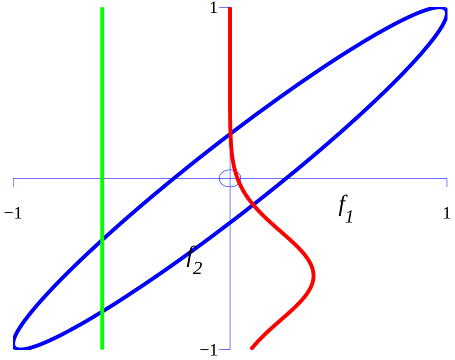

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Prediction of f_5 from f_1

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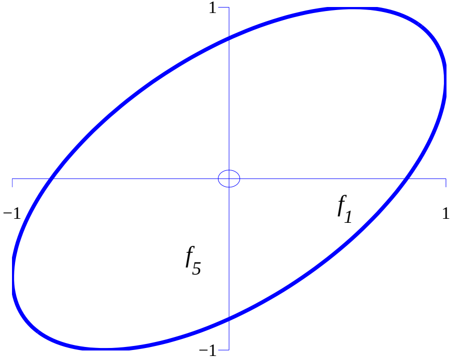

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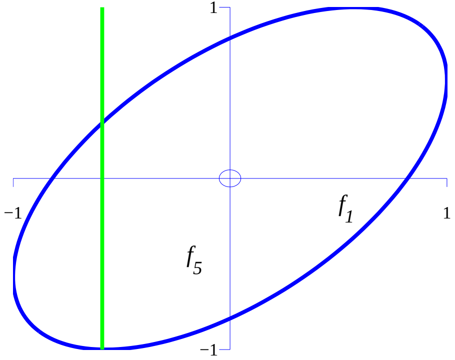

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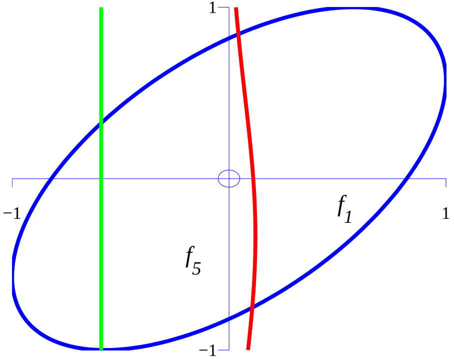

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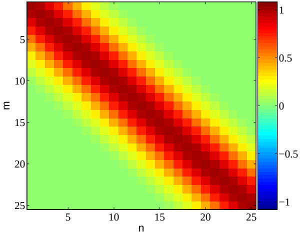
Covariance Functions

Where did this covariance matrix come from?

RBF Kernel Function

$$k\left(t, t'\right) = \alpha \exp\left(-\frac{\left\|t - t'\right\|^2}{2l^2}\right)$$

- Covariance matrix is built using the *inputs* to the function t.
- For the example above it was based on Euclidean distance.
- The covariance function is also know as a kernel.



Covariance Samples

`demCovFuncSample`

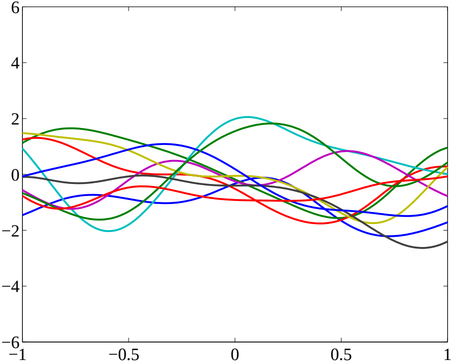


Figure: RBF kernel with $l = 10^{-\frac{1}{2}}$, $\alpha = 1$

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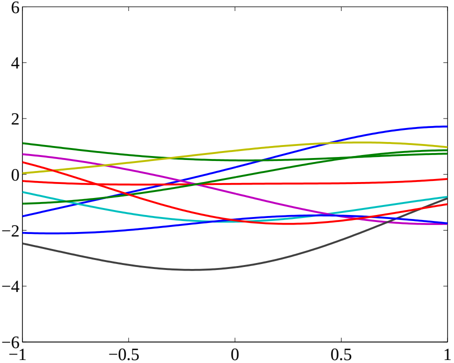

Figure: RBF kernel with $l = 1$, $\alpha = 1$

Covariance Samples

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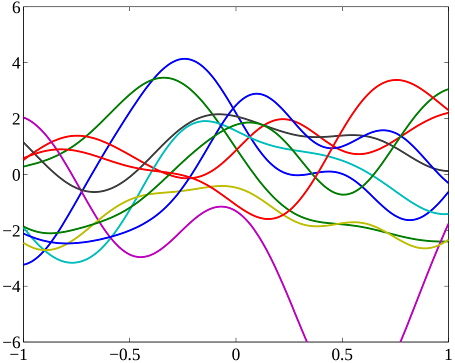

Figure: RBF kernel with $l = 0.3$, $\alpha = 4$

Gaussian Process Regression

`demRegression`

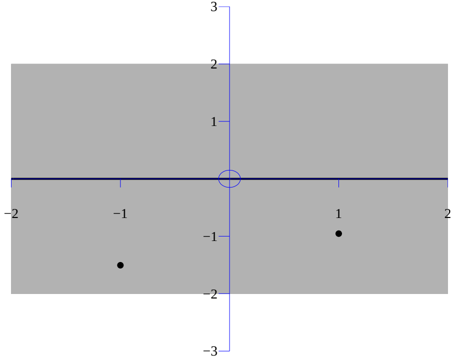

Figure: Examples include WiFi localization, C14 callibration curve.

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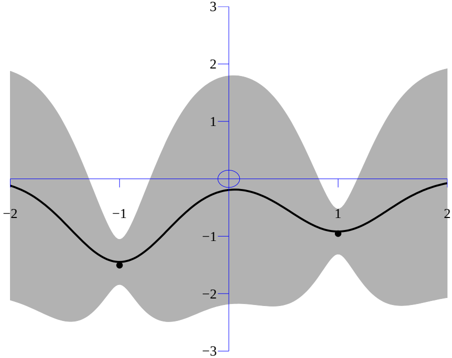

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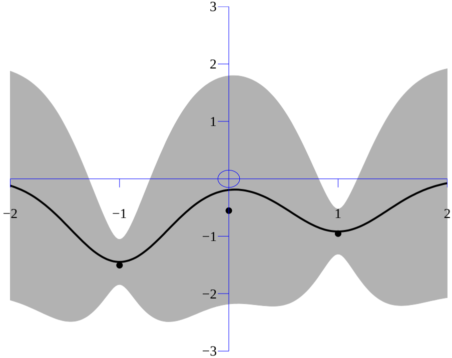

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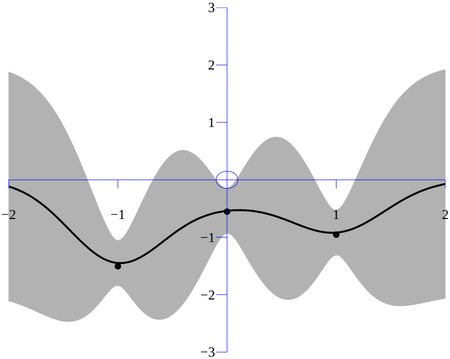

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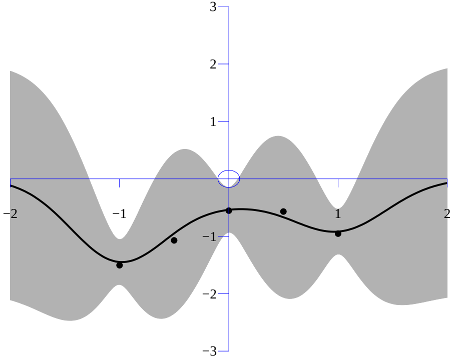

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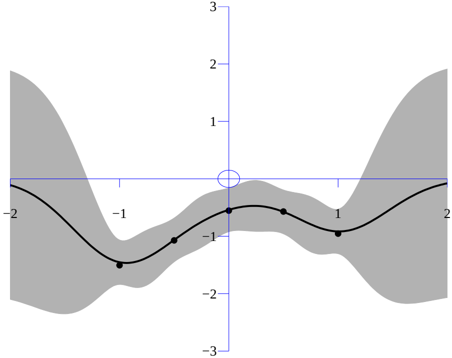

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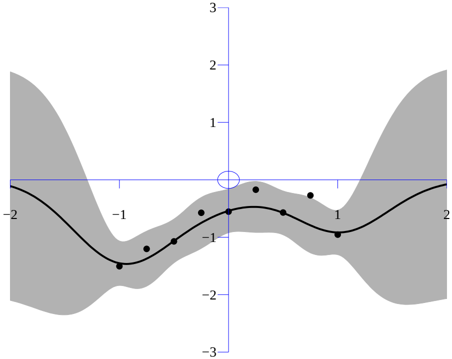

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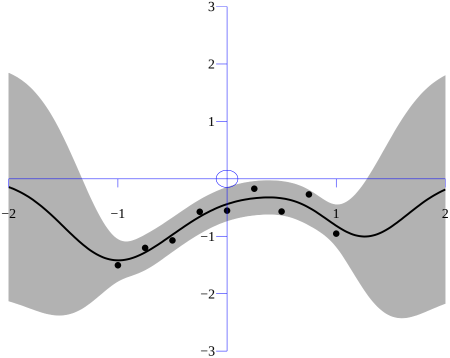

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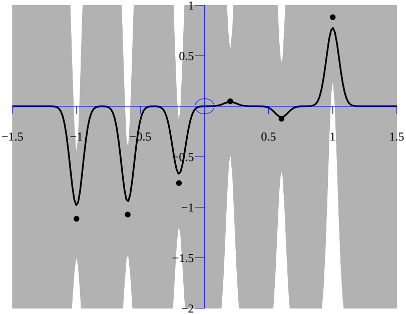
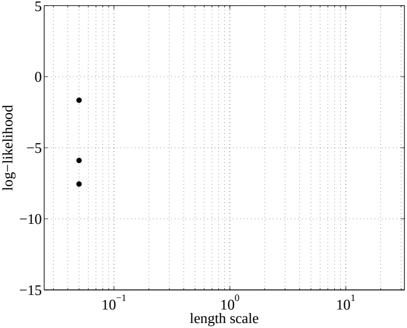
Learning Kernel Parameters

Can we determine length scales and noise levels from the data?

demOptimiseGp





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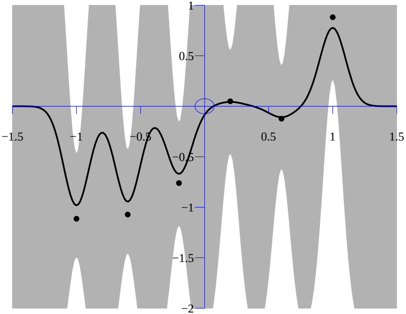

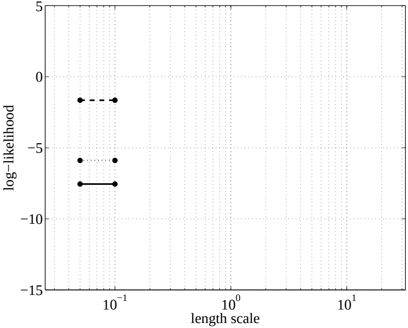

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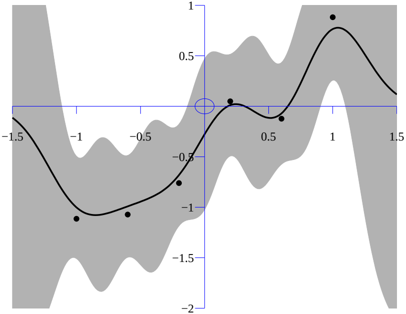

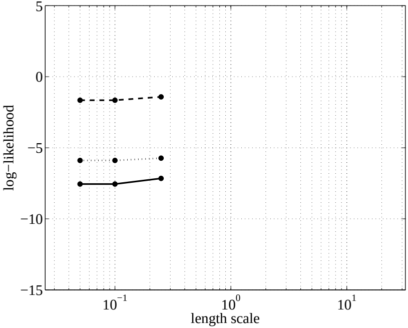

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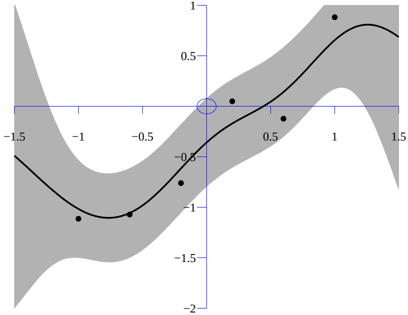

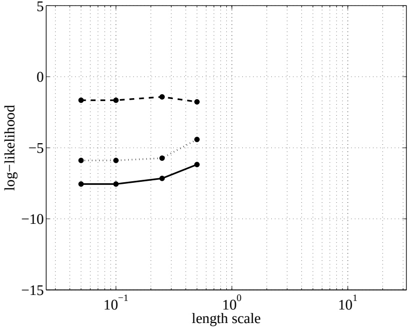

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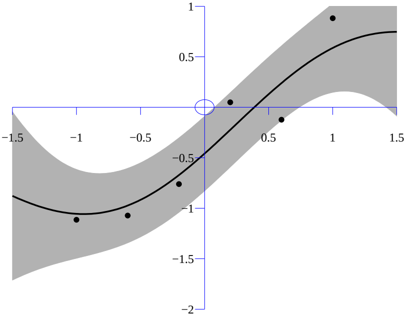

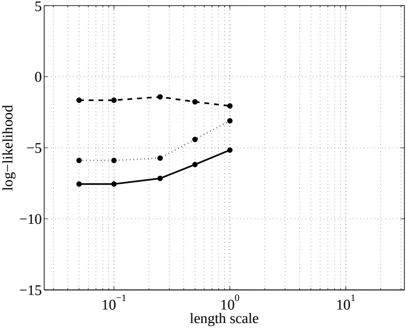

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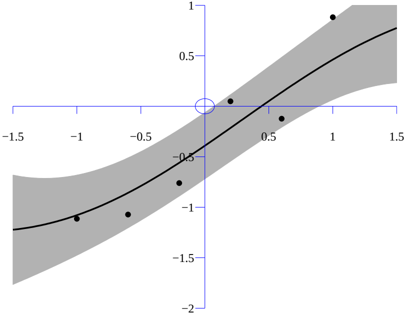

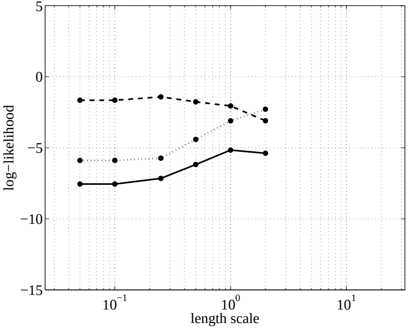

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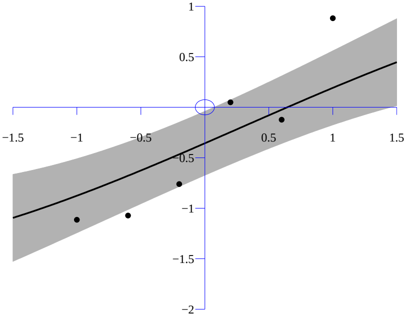

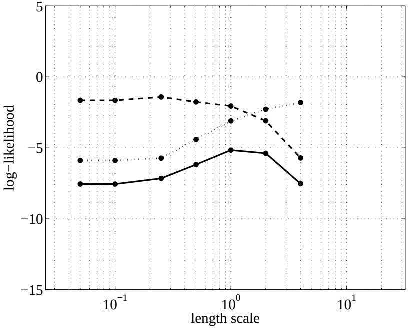

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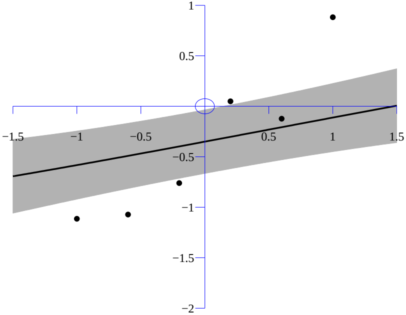

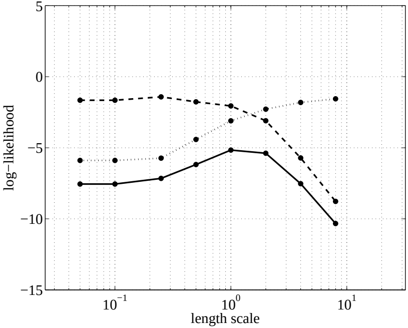

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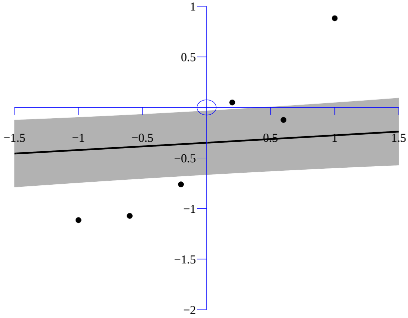

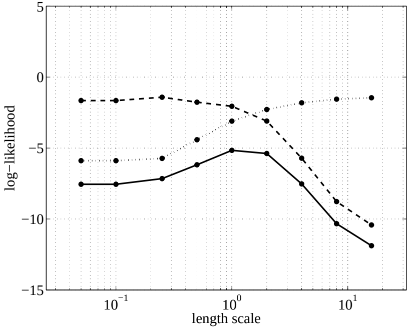

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Mechanical Analogy

Back to Latent Force Models!

- These models rely on the latent variables to provide the dynamic information.
- We now introduce a further dynamical system with a *mechanistic* inspiration.
- Physical Interpretation:
  - the latent functions, $f_i(t)$ are q forces.
  - We observe the displacement of d springs to the forces.,
  - Interpret system as the force balance equation, $\mathbf{XD} = \mathbf{FS} + \boldsymbol{\epsilon}$.
  - Forces act, e.g. through levers — a matrix of sensitivities, $\mathbf{S} \in \Re^{q \times d}$.
  - Diagonal matrix of spring constants, $\mathbf{D} \in \Re^{d \times d}$.
  - Original System: $\mathbf{W} = \mathbf{SD}^{-1}$.

Extend Model

- Add a damper and give the system mass.

$$\mathbf{FS} = \ddot{\mathbf{X}}\mathbf{M} + \dot{\mathbf{X}}\mathbf{C} + \mathbf{XD} + \epsilon.$$

- Now have a second order mechanical system.
- It will exhibit inertia and resonance.
- There are many systems that can also be represented by differential equations.
    - When being forced by latent function(s), $\{f_i(t)\}_{i=1}^{q}$, we call this a *latent force model*.

- For Gaussian process we can compute the covariance matrices for the output displacements.
- For one displace the model is

$$m_k \ddot{x}_k(t) + c_k \dot{x}_k(t) + d_k x_k(t) = b_k + \sum_{i=0}^{M} s_{ik} f_i(t), \tag{1}$$

  where, m_k is the kth diagonal element from $\mathbf{M}$ and similarly for c_k and d_k. s_{ik} is the i, kth element of $\mathbf{S}$.
- Model the latent forces as q independent, GPs with RBF covariances

$$k_{f_i f_l}(t, t') = \exp\left(-\frac{(t-t')^2}{\sigma_i^2}\right)\delta_{il}.$$

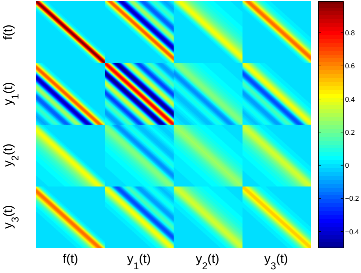
Covariance for ODE Model

- RBF Kernel function for $f(t)$

$$x_j(t) = \frac{1}{m_j\omega_j}\sum_{i=1}^{q} S_{ji}\exp(-\alpha_j t)\int_0^t f_i(u)\exp(\alpha_j u)\sin(\omega_j(t-u))\mathrm{d}u$$

- Joint distribution for $x_1(t)$, $x_2(t)$, $x_3(t)$ and $f(t)$. Damping ratios:

ζ_1	ζ_2	ζ_3
0.125	2	1



Joint Sampling of $x(t)$ and $f(t)$

- `demLfmSample`

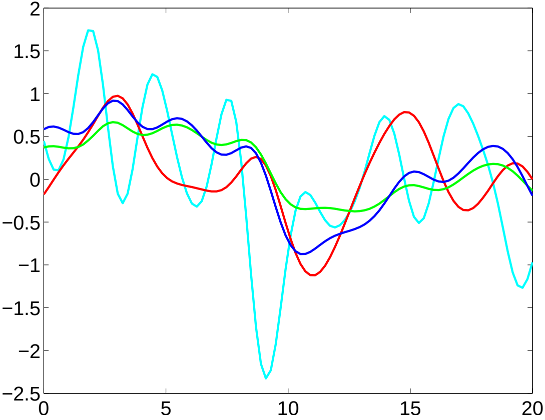


Figure: Joint samples from the ODE covariance, *cyan*: $f(t)$, *red*: $x_1(t)$(underdamped) and *green*: $x_2(t)$ (overdamped) and *blue*: $x_3(t)$ (critically damped).

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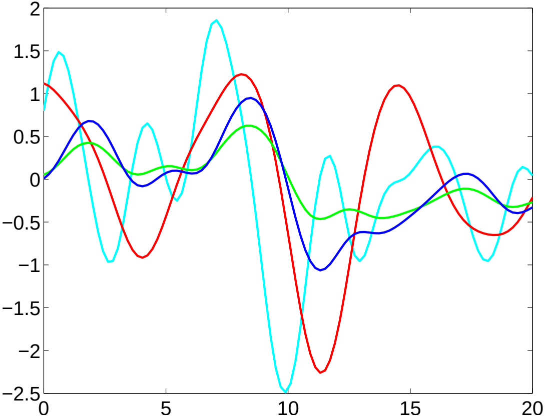

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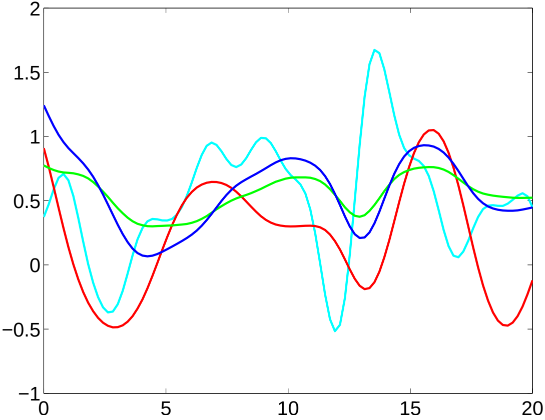

Figure: Joint samples from the ODE covariance, *cyan*: $f(t)$, *red*: $x_1(t)$(underdamped) and *green*: $x_2(t)$ (overdamped) and *blue*: $x_3(t)$ (critically damped).

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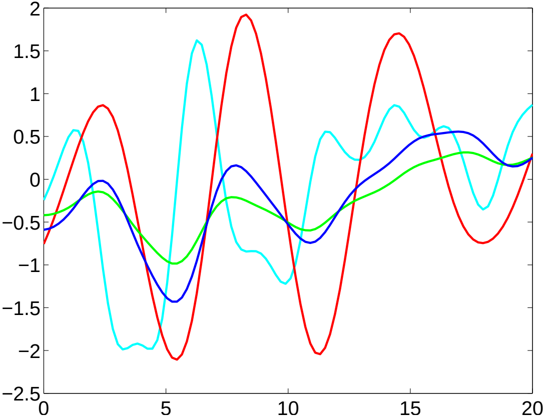

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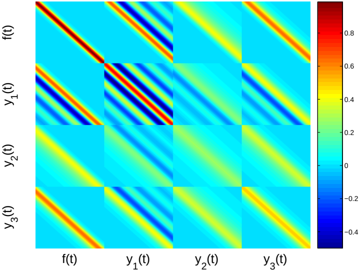
Covariance for ODE

- RBF Kernel function for $f\left(t\right)$

$$x_j(t) = \frac{1}{m_j \omega_j} \sum_{i=1}^{q} S_{ji} \exp(-\alpha_j t) \int_0^t f_i(u) \exp(\alpha_j u) \sin(\omega_j (t-u)) \mathrm{d}u$$

- Joint distribution for $x_1\left(t\right)$, $x_2\left(t\right)$, $x_3\left(t\right)$ and $f\left(t\right)$.
- Damping ratios:

ζ_1	ζ_2	ζ_3
0.125	2	1



Example: Motion Capture

Mauricio Alvarez and David Luengo (Álvarez et al., 2009)

- Motion capture data: used for animating human motion.
- Multivariate time series of angles representing joint positions.
- Objective: generalize from training data to realistic motions.
- Use 2nd Order Latent Force Model with mass/spring/damper (resistor inductor capacitor) at each joint. `demAistats`

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Example: Transcriptional Regulation

- First Order Differential Equation

$$\frac{\mathrm{d}x_j\left(t\right)}{\mathrm{d}t} = B_j + S_j f\left(t\right) - D_j x_j\left(t\right)$$

- Can be used as a model of gene transcription: Barenco et al., 2006; Gao et al., 2008.
- $x_j(t)$ – concentration of gene j's mRNA
- $f(t)$ – concentration of active transcription factor
- Model parameters: baseline B_j, sensitivity S_j and decay D_j
- Application: identifying co-regulated genes (targets)
- Problem: how do we fit the model when $f(t)$ is not observed?

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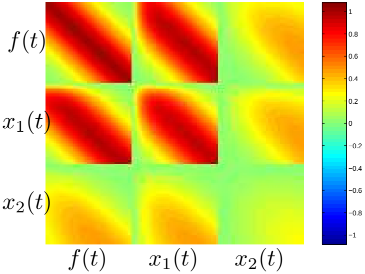
[labels=skipGPProperties]Covariance for Transcription Model

RBF covariance function for $f(t)$

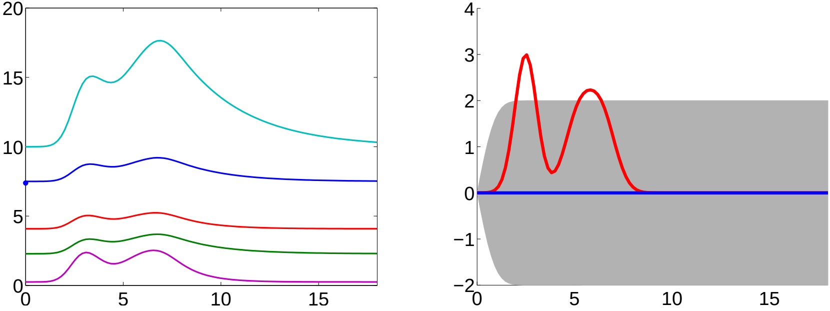
$$x_i(t) = \frac{B_i}{D_i} + S_i \exp(-D_i t) \int_0^t f(u) \exp(D_i u) \, \mathrm{d}u.$$

- Joint distribution for $x_1(t)$, $x_2(t)$ and $f(t)$.
    - Here:

D_1	S_1	D_2	S_2
5	5	0.5	0.5



Artificial Example: Inferring $f(t)$



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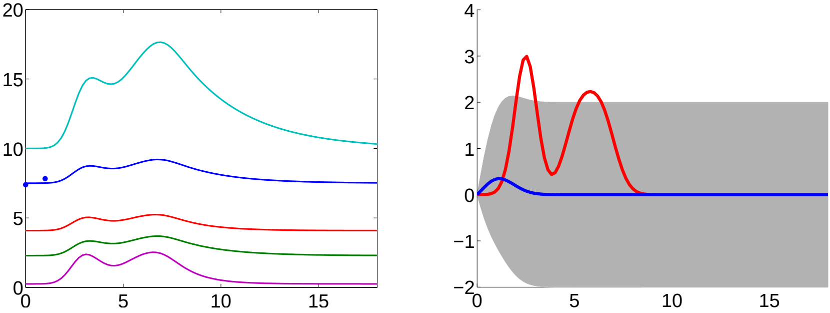

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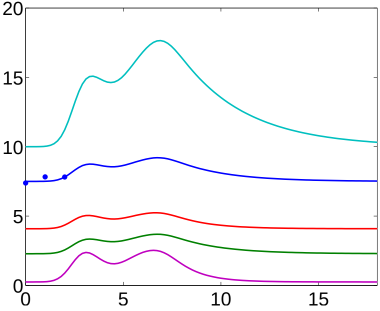

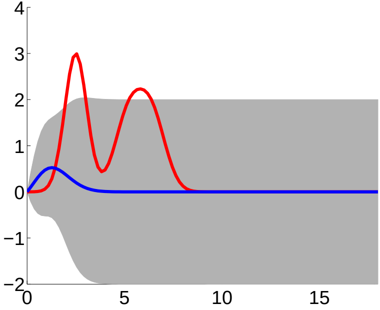

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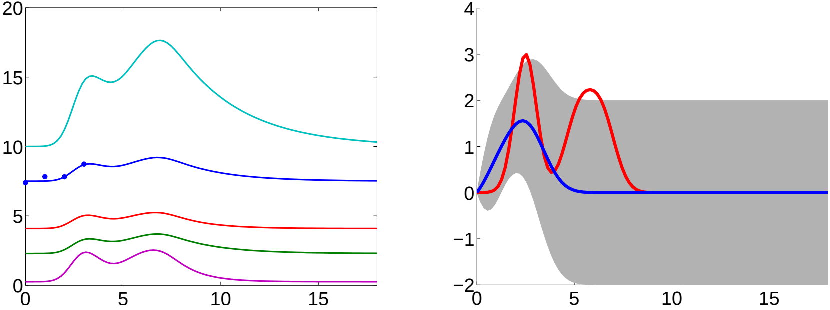

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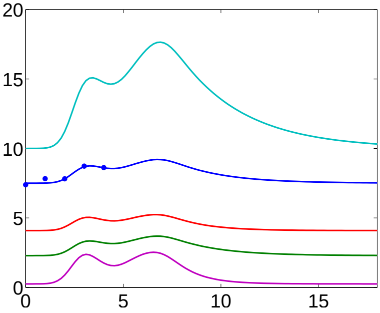

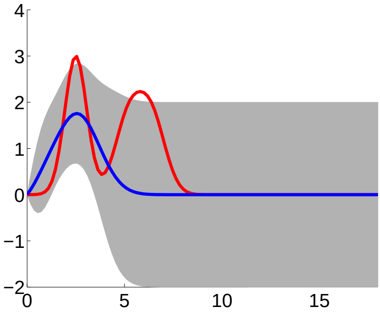

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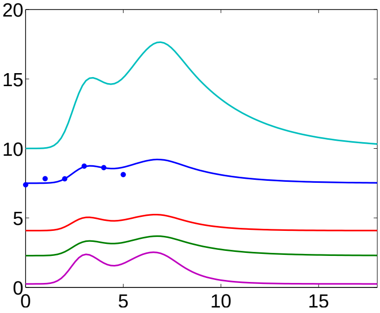

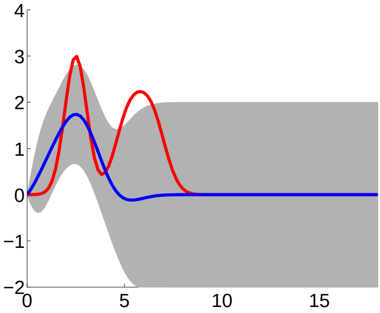

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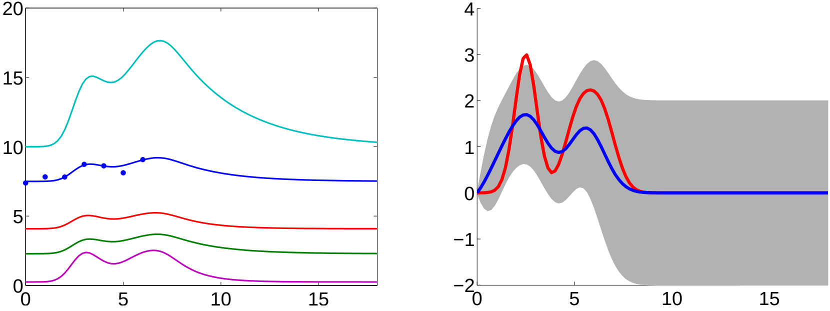

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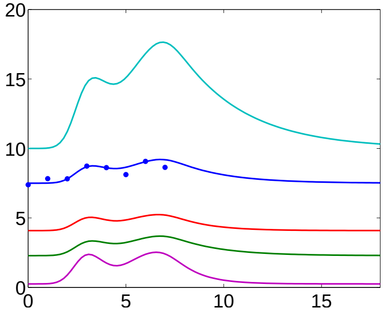

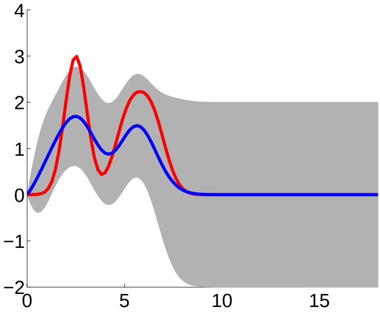

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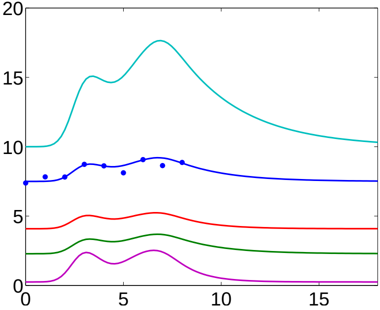

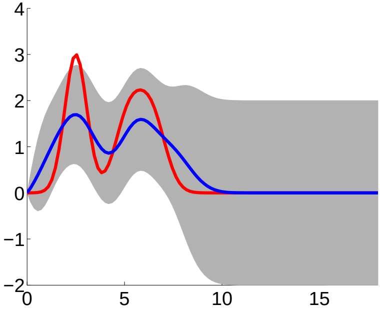

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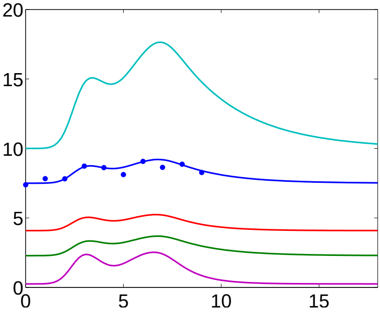

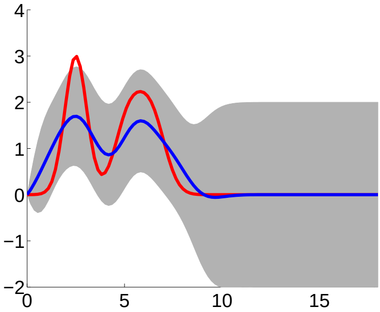

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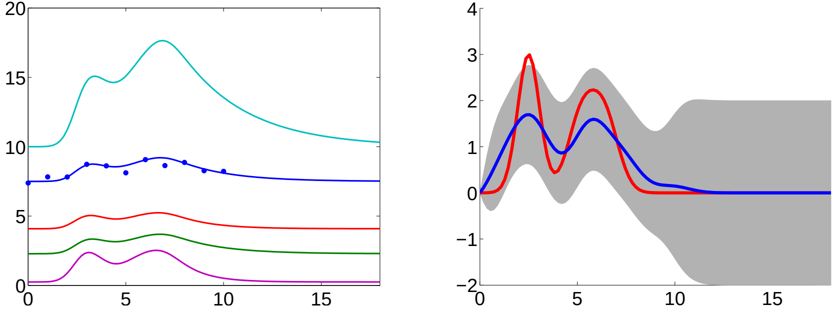

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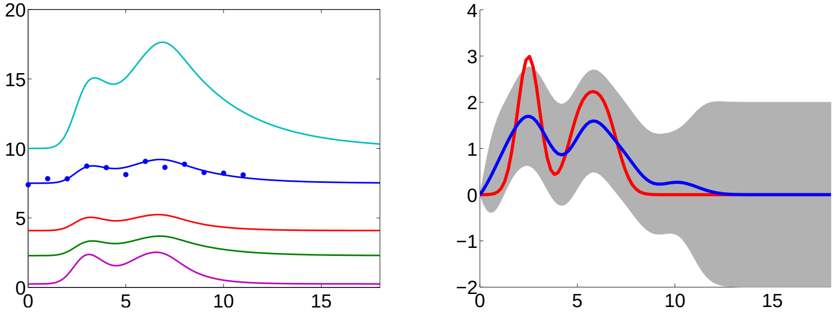

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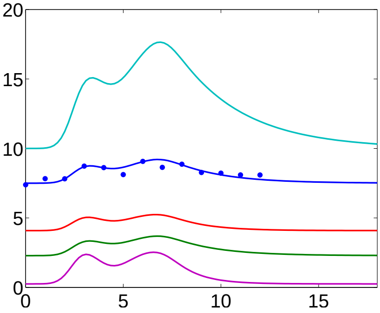

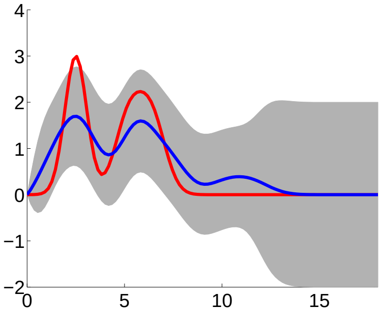

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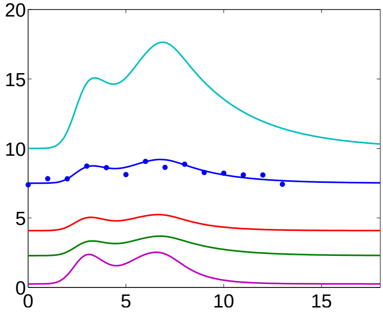

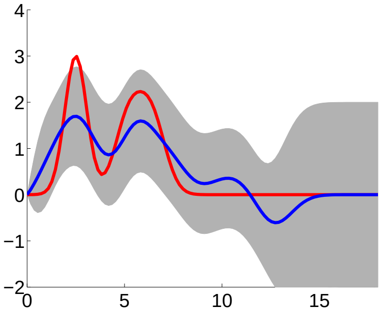

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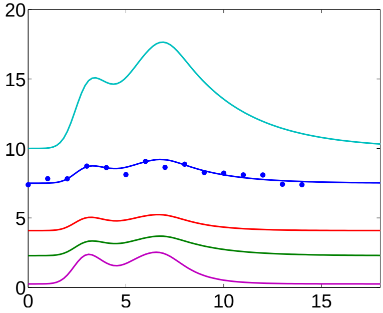

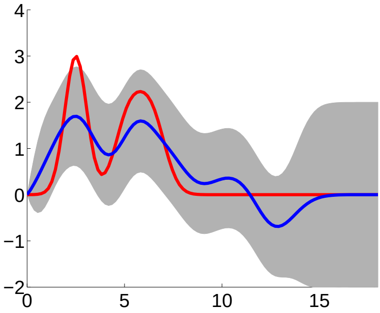

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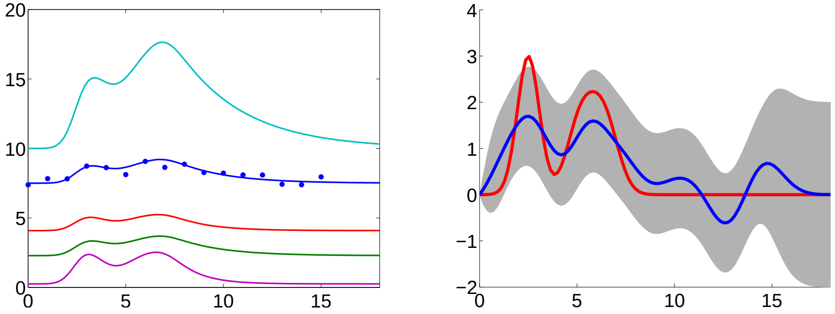

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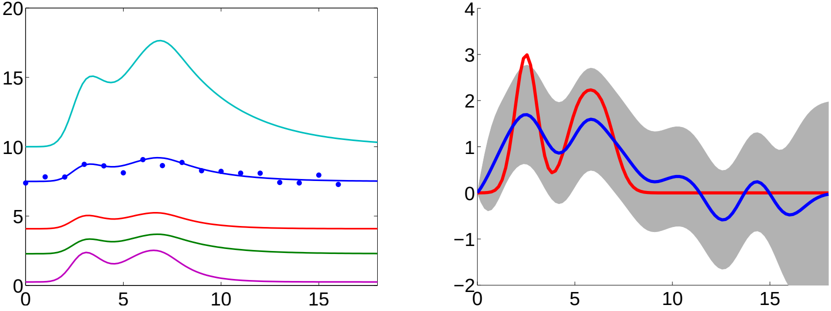

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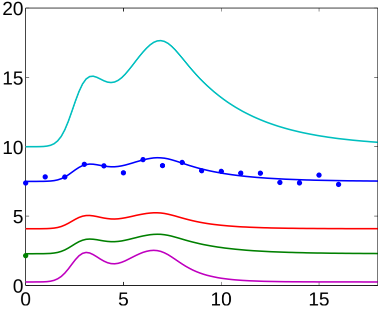

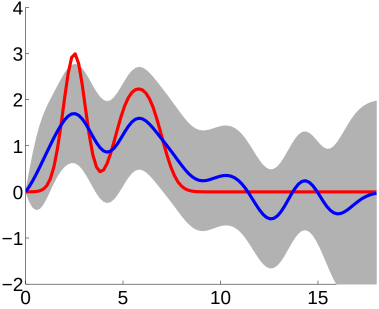

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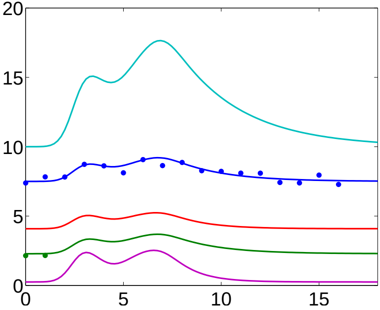

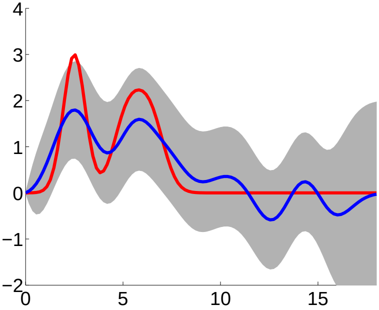

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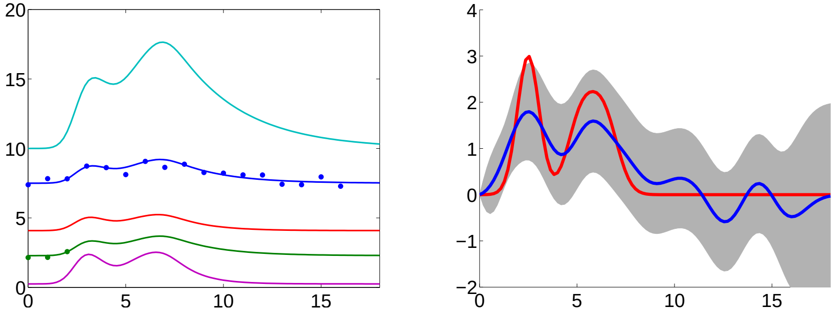

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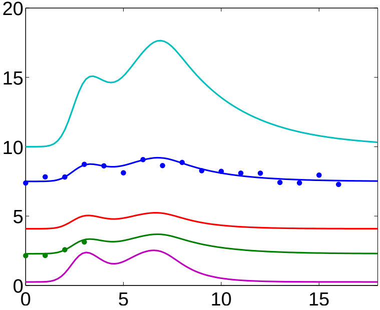

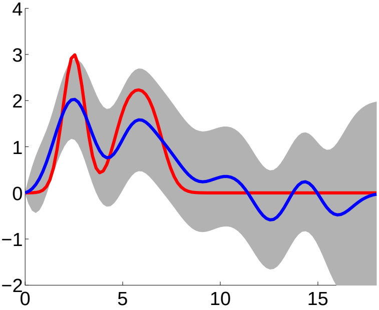

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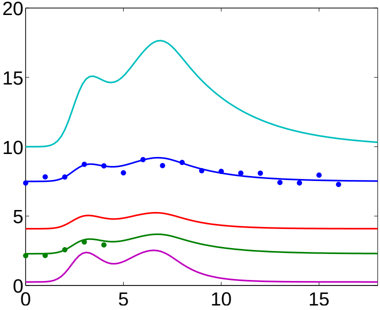

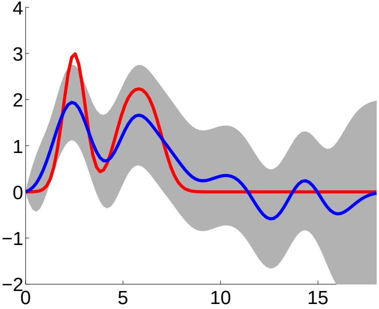

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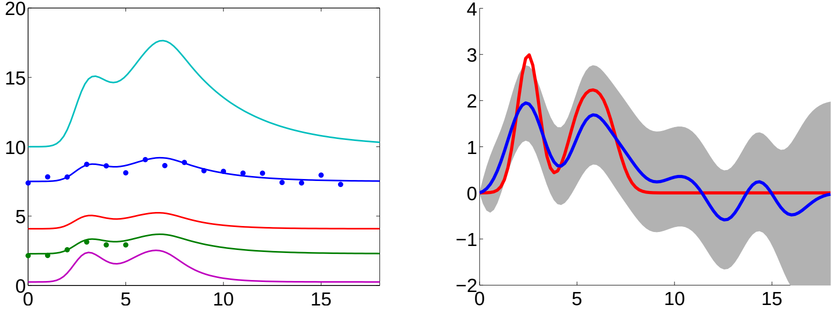

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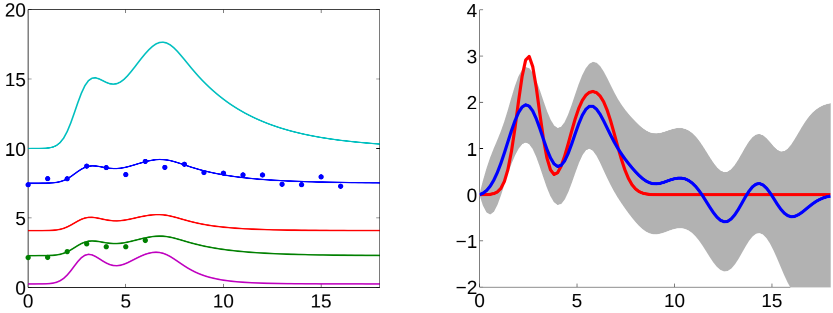

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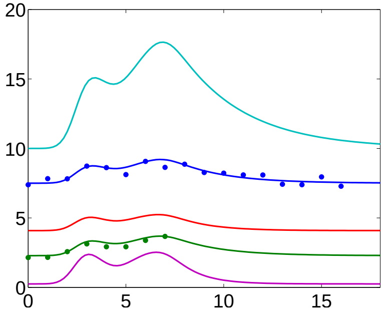

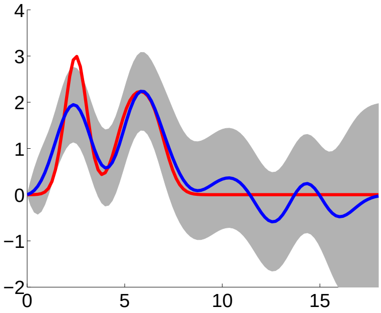

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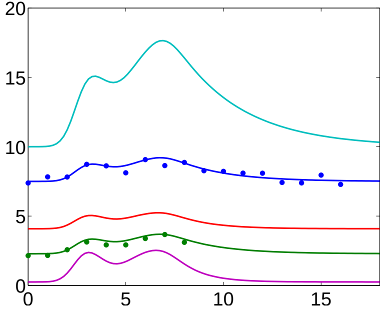

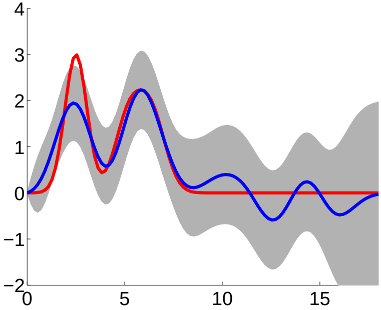

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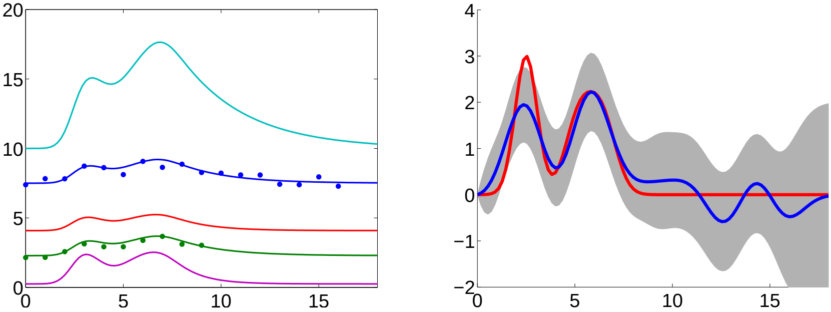

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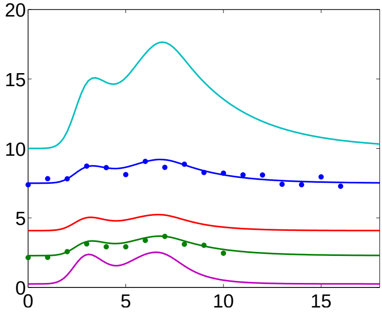

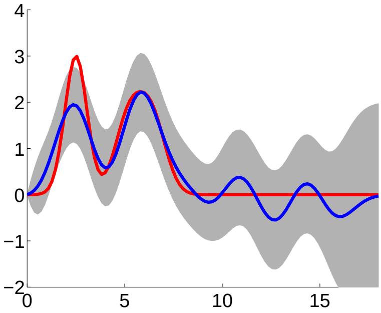

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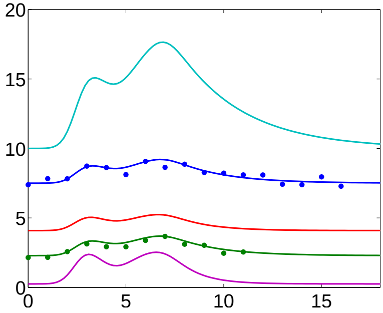

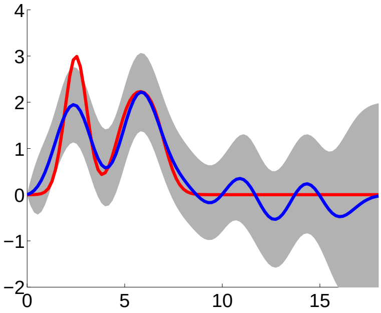

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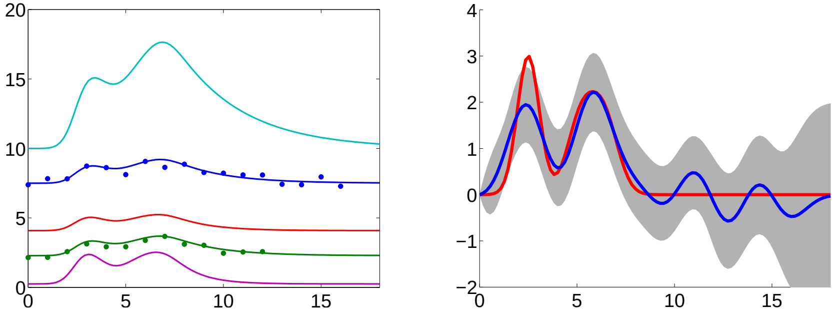

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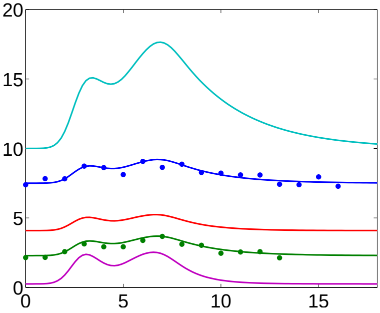
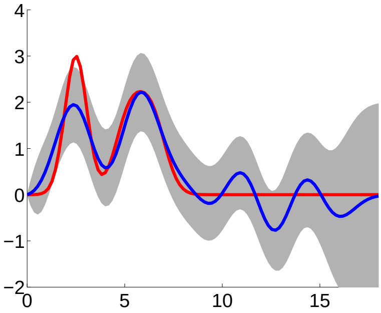
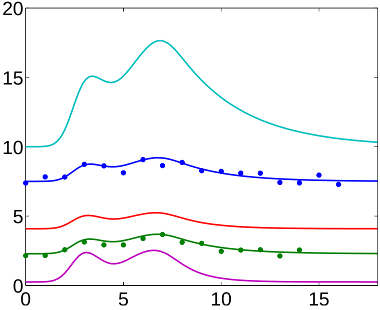
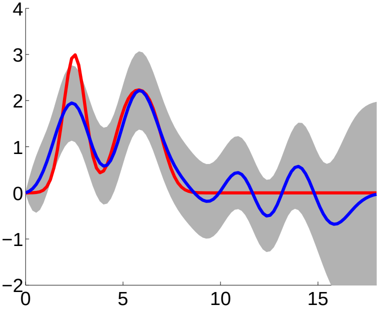


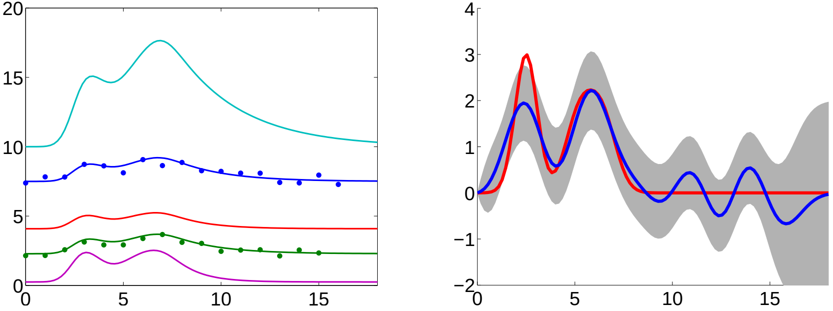


Artificial Example: Inferring $f(t)$

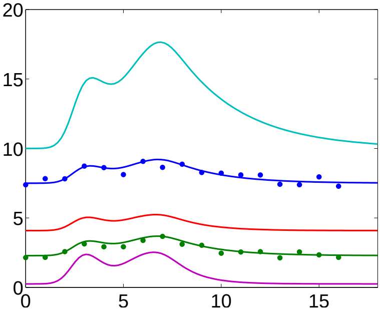


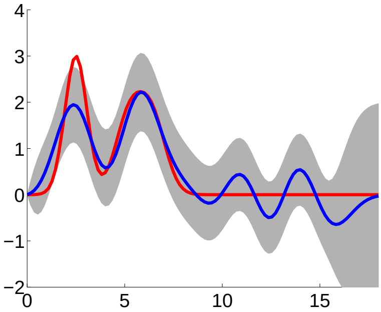


Artificial Example: Inferring $f(t)$

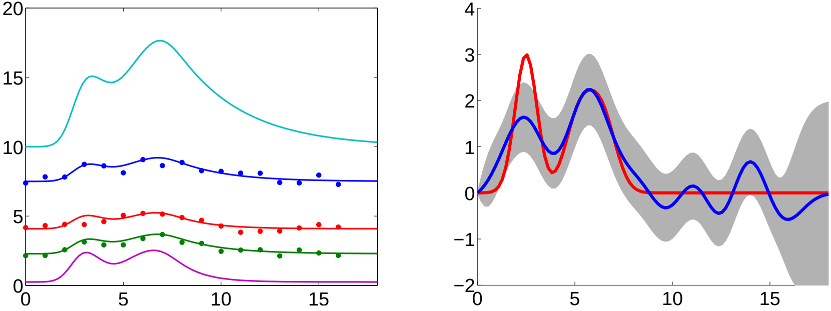


Artificial Example: Inferring $f(t)$

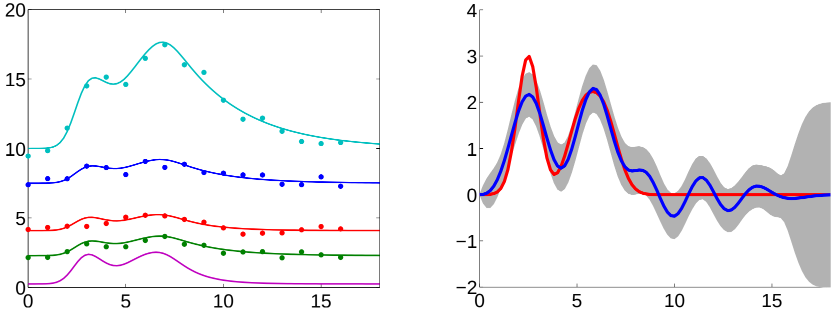




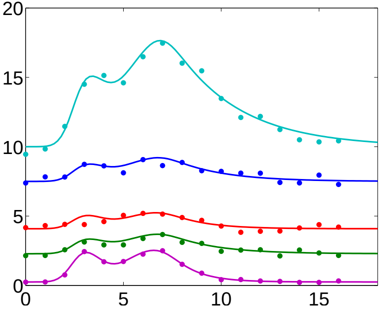
Artificial Example: Inferring $f(t)$

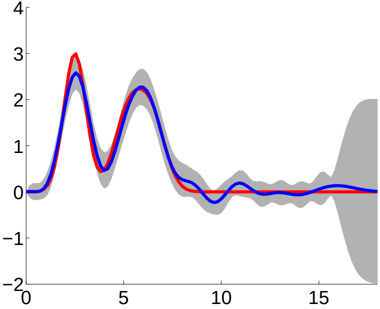


Artificial Example: Inferring $f(t)$



Artificial Example: Inferring $f(t)$





p53 “Guardian of the Cell”

- Responsible for Repairing DNA damage
- Activates DNA Repair proteins
- Pauses the Cell Cycle (prevents replication of damage DNA)
- Initiates *apoptosis* (cell death) in the case where damage can’t be repaired.
- Large scale feeback loop with NF-κB.

p53 DNA Damage Repair

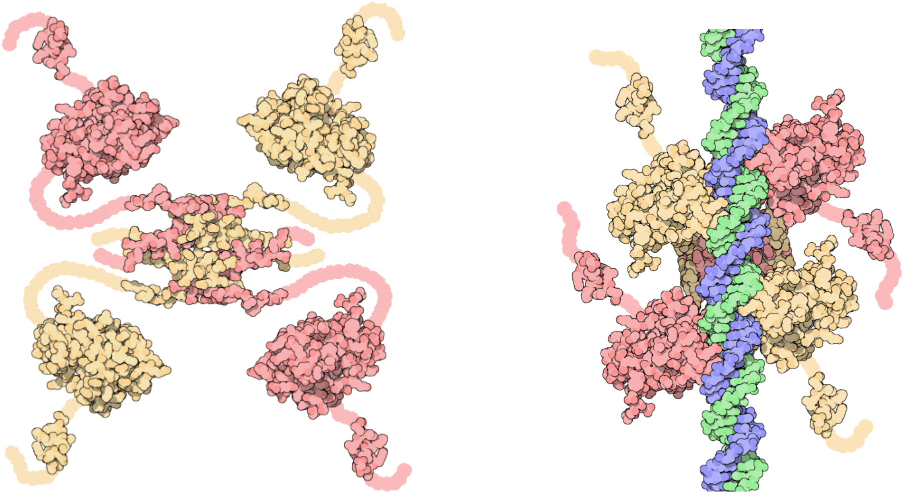


Figure: p53. *Left* unbound, *Right* bound to DNA. Images by David S. Goodsell from `http://www.rcsb.org/` (see the “Molecule of the Month” feature).

p53

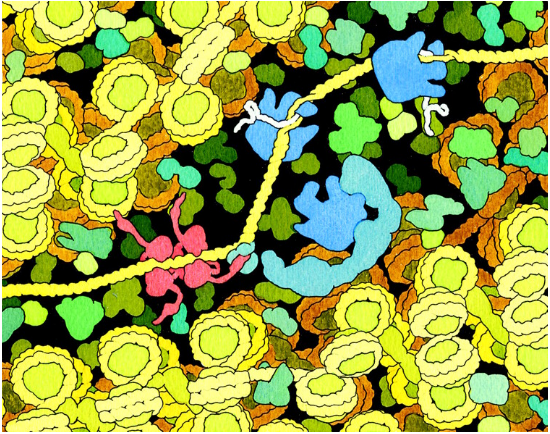


Figure: Repair of DNA damage by p53. Image fromGoodsell (1999).

Modelling Assumption

- Assume p53 affects targets as a single input module network motif (SIM).

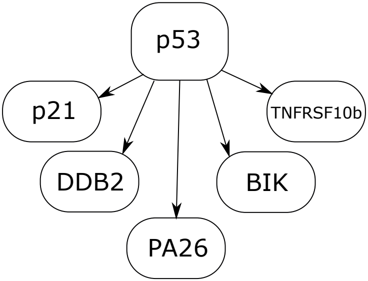
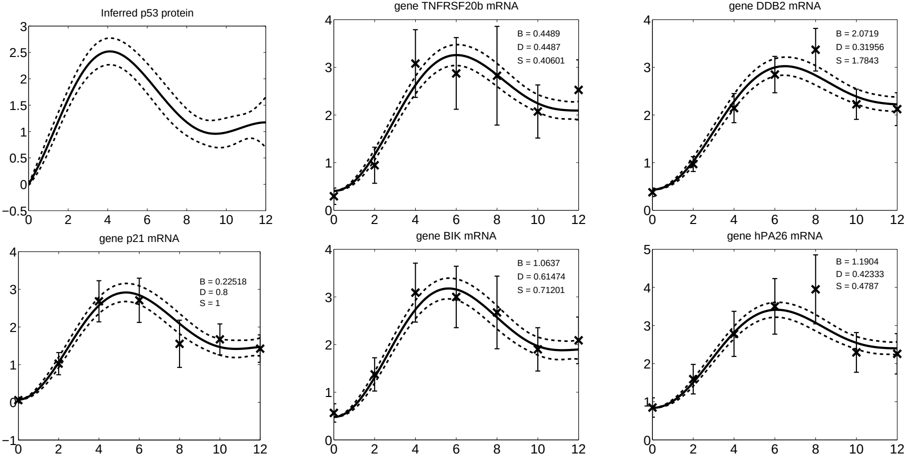


Figure: p53 SIM network motif as modelled by Barenco et al. 2006.

p53 (RBF covariance)

Pei Gao

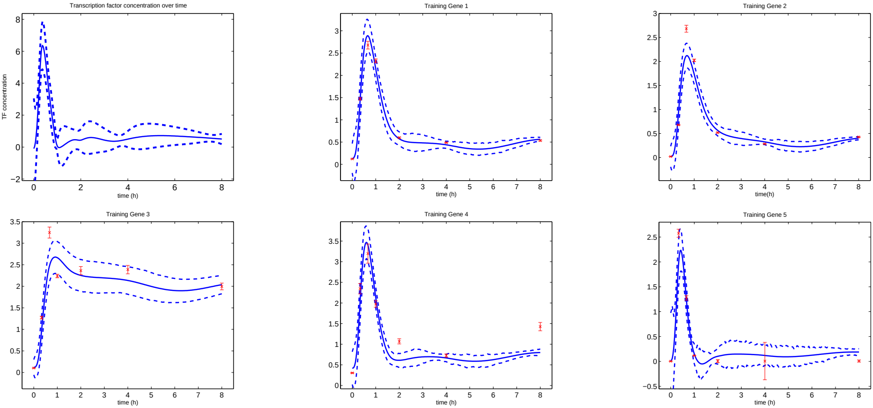


Ranking with ERK Signalling

- Target Ranking for Elk-1.
- Elk-1 is phosphorylated by ERK from the EGF signalling pathway.
- Predict concentration of Elk-1 from known targets.
- Rank other targets of Elk-1.

Elk-1 (MLP covariance)

Jennifer Withers



Transcription factor concentration over time

Training Gene 1

Training Gene 2

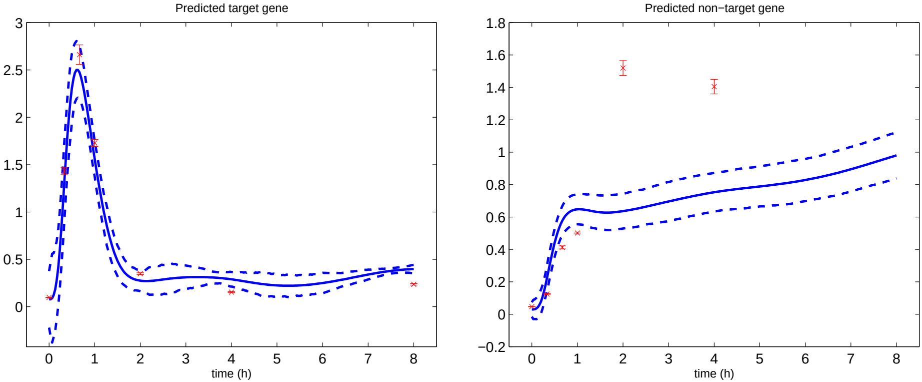
Training Gene 3

Training Gene 4

Training Gene 5

Elk-1 target selection

Fitted model used to rank potential targets of Elk-1



Outline

1. Introduction

2. Gaussian Process Review

3. Covariance Functions

4. Discussion and Future Work

Discussion and Future Work

- Integration of probabilistic inference with mechanistic models.
- These results are small simple systems.
- Ongoing work:
  - Scaling up to larger systems
  - Applications to other types of system, *e.g.* non-steady-state metabolomics, spatial systems etc.
  - Improved approximations.
  - Stochastic differential equations

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- Researchers: Peo Gao, Antti Honkela, Michalis Titsias, Mauricio Alvarez, David Luengo and Jennifer Withers
- Charles Girardot and Eileen Furlong of EMBL in Heidelberg (mesoderm development in *D. Melanogaster*).
- Martino Barenco and Mike Hubank at the Institute of Child Health in UCL (p53 pathway).

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Outline

5. Convolutions and Computational Complexity

6. Non-linear Response Models

7. Cascaded Differential Equations

Convolutions and Computational Complexity

Mauricio Alvarez

- Solutions to these differential equations is normally as a convolution.

$$x_i\left(t\right) = \int f\left(u\right) k_i\left(u - t\right) \mathrm{d}u + h_i\left(t\right)$$

$$x_i\left(t\right) = \int_0^t f\left(u\right) g_i\left(u\right) \mathrm{d}u + h_i\left(t\right)$$

- Convolution Processes (Higdon, 2002; Boyle and Frean, 2005).
- Convolutions lead to $N \times d$ size covariance matrices $O\left(N^3 d^3\right)$ complexity, $O\left(N^2 d^2\right)$ storage.
- Model is conditionally independent over $\left\{x_i\left(t\right)\right\}_{i=1}^{d}$ given $f\left(t\right)$.

Independence Assumption

Mauricio Alvarez

- Can assume conditional independence given given $\{f(t_i)\}_{i=1}^{k}$. (Álvarez and Lawrence, 2009)
  - Result is very similar to PITC approximation (Quiñonero Candela and Rasmussen, 2005).
  - Reduces to $O\left(N^3dk^2\right)$ complexity, $O\left(N^2dk\right)$ storage.
  - Can also do a FITC style approximation (Snelson and Ghahramani, 2006).
  - Reduces to $O\left(Ndk^2\right)$ complexity, $O\left(Ndk\right)$ storage.

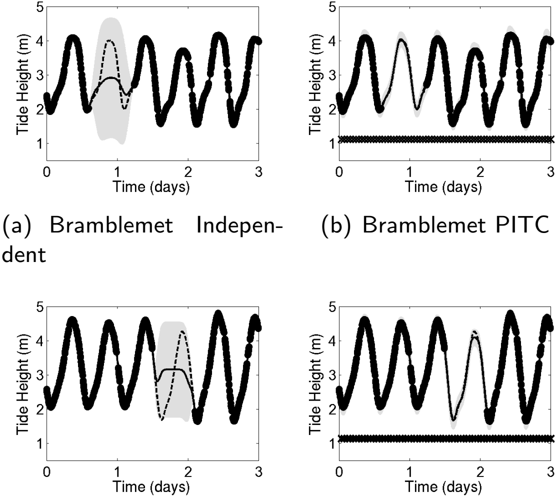
Tide Sensor Network

Mauricio Alvarez

- Network of tide height sensors in the solent — tide heights are correlated.
- Data kindly provided by Alex Rogers (see Osborne et al., 2008).
- $d = 3$ and $N = 1000$ of the 4320 for the training set.
- Simulate sensor failure by knocking out onse sensor for a given time.
- For the other two sensors we used all 1000 training observations.
- Take $k = 100$.

Tide Height Results

Mauricio Alvarez



(a) Bramblemet Independent

(b) Bramblemet PITC

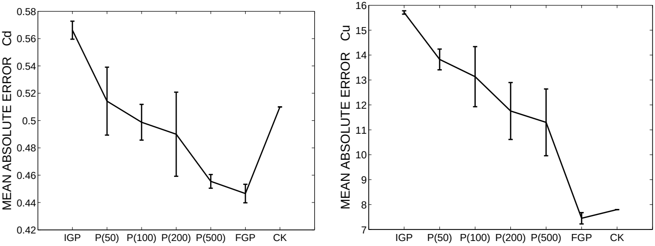
Cokriging Jura

Mauricio Alvarez

- Jura dataset — concentrations of several heavy metals.
- Prediction 259 data, validation 100 data points.
- Predict *primary variables* (cadmium and copper) at prediction locations in conjunction with some *secondary variables* (nickel and zinc for cadmium; lead, nickel and zinc for copper) (Goovaerts, 1997, p. 248,249).

Swiss Jura Results

Mauricio Alvarez



(a) Cadmium

(b) Copper

Figure: Mean absolute error. IGP stands for independent GP, P(M) stands for PITC with M inducing values, FGP stands for full GP and CK stands for ordinary co-kriging.

Outline

5 Convolutions and Computational Complexity

6 Non-linear Response Models

7 Cascaded Differential Equations

Models of non-linear regulation

- Non-linear Activation: Michaelis-Menten Kinetics

$$\frac{\mathrm{d}x_i\left(t\right)}{\mathrm{d}t} = B_i + \frac{S_i f\left(t\right)}{\gamma_i + f\left(t\right)} - D_i x_i\left(t\right)$$

used by Rogers and Girolami (2006)

- Non-linear Repression

$$\frac{\mathrm{d}x_i\left(t\right)}{\mathrm{d}t} = B_i + \frac{S_i}{\gamma_i + f\left(t\right)} - D_i x_i\left(t\right)$$

used by Khanin et al., 2006, PNAS 103

Models of non-linear regulation

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- Non-linear Repression

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  used by Khanin et al., 2006, PNAS 103

MAP Laplace Approximation

Consider the following modification to the model,

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = B_j + S_j g(f(t)) - D_j x_j(t),$$

where $g(\cdot)$ is a non-linear function. The differential equation can still be solved,

$$x_j(t) = \frac{B_j}{D_j} + S_j \int_0^t e^{-D_j(t-u)} g_j(f(u))\,\mathrm{d}u$$

Use Laplace's method (Laplace, 1774),

$$p(\mathbf{f} \mid \mathbf{x}) = N\left(\hat{\mathbf{f}}, \mathbf{A}^{-1}\right) \propto \exp\left(-\frac{1}{2}\left(\mathbf{f}-\hat{\mathbf{f}}\right)^{\top}\mathbf{A}\left(\mathbf{f}-\hat{\mathbf{f}}\right)\right)$$

where $\hat{\mathbf{f}} = \mathrm{argmax} p(\mathbf{f} \mid \mathbf{x})$ and $\mathbf{A} = -\nabla\nabla \log p(\mathbf{f} \mid \mathbf{y})\,|_{\mathbf{f}=\hat{\mathbf{f}}}$ is the Hessian of the negative posterior at that point.

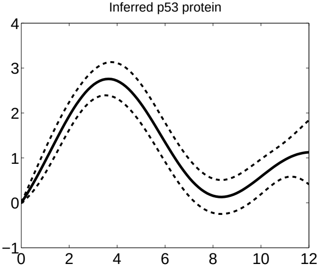
p53 and Michaelis-Menten Kinetics

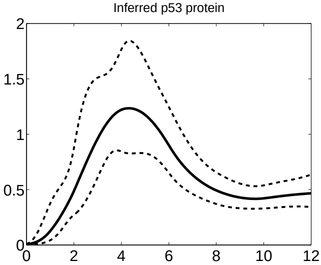
Pei Gao

- The Michaelis-Menten activation model uses the following non-linearity

$$g_j\left(f\left(t\right)\right) = \frac{e^{f(t)}}{\gamma_j + e^{f(t)}},$$

where we are using a GP $f\left(t\right)$ to model the log of the TF activity.





(a)

Valdiation of Laplace Approximation

Michalis Titsias

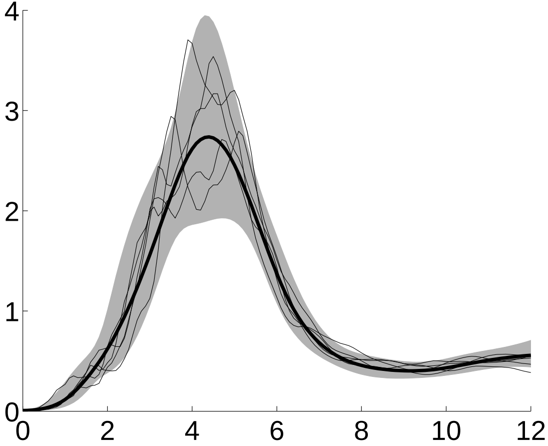


Figure: Laplace approximation error bars along with samples from the true posterior distribution.

Use Samples to Represent Posterior

Michalis Titsias

- Sample in Gaussian processes

$$p\left(\mathbf{f}|\mathbf{x}\right) \propto p\left(\mathbf{x}|\mathbf{f}\right) p\left(\mathbf{f}\right)$$

- Likelihood relates GP to data through

$$x_j\left(t\right) = \alpha_j e^{-D_j t} + \frac{B_j}{D_j} + S_j \int_0^t e^{-D_j(t-u)} g_j(f\left(u\right)) \mathrm{d}u$$

- We use *control points* for fast sampling. (Titsias et al., 2009)

Sampling using control points

- Separate the points in $\mathbf{f}$ into two groups:
  - few control points $\mathbf{f}_c$
  - and the large majority of the remaining points $\mathbf{f}_\rho = \mathbf{f} \setminus \mathbf{f}_c$
- Sample the control points $\mathbf{f}_c$ using a proposal $q\left(\mathbf{f}_c^{(t+1)}|\mathbf{f}_c^{(t)}\right)$
- Sample the remaining points $\mathbf{f}_\rho$ using the conditional GP prior $p\left(\mathbf{f}_\rho^{(t+1)}|\mathbf{f}_c^{(t+1)}\right)$
- The whole proposal is

$$Q\left(\mathbf{f}^{(t+1)}|\mathbf{f}^{(t)}\right) = p\left(\mathbf{f}_\rho^{(t+1)}|\mathbf{f}_c^{(t+1)}\right) q\left(\mathbf{f}_c^{(t+1)}|\mathbf{f}_c^{(t)}\right)$$

- Its like sampling from the prior $p(\mathbf{f})$ but imposing random walk behaviour through the control points.

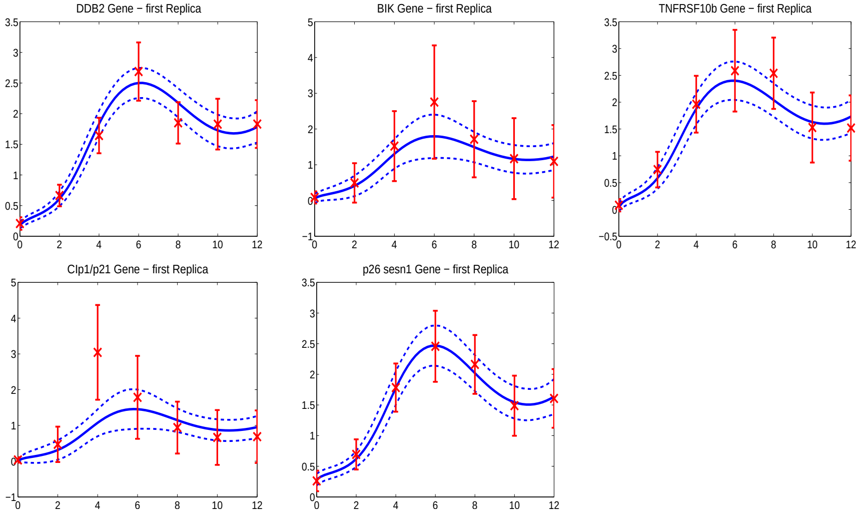
p53 System Again

- One transcription factor (p53) that acts as an activator. We consider the Michaelis-Menten kinetic equation

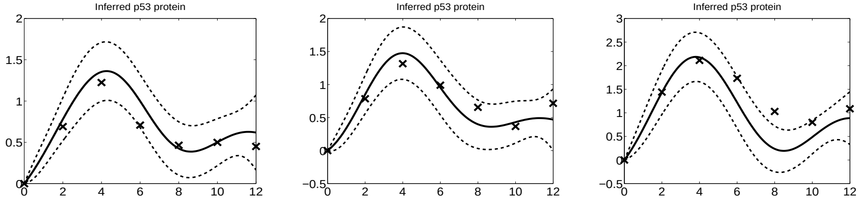
$$\frac{\mathrm{d}x_j(t)}{dt} = B_j + S_j \frac{\exp(f(t))}{\exp(f(t)) + \gamma_j} - D_j x_j(t)$$

- MCMC details:
  - 7 control points are used (placed in a equally spaced grid)
  - Running time 4/5 hours for 2 million sampling iterations plus burn in
  - Acceptance rate for **f** after burn in was between 15% – 25%

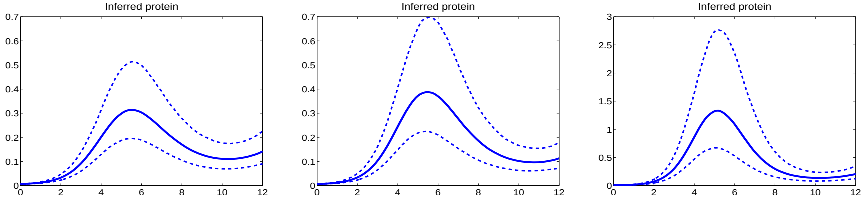
Data used by Barenco et al. (2006): Predicted gene expressions for the 1st replica



Data used by Barenco et al. (2006): Protein concentrations

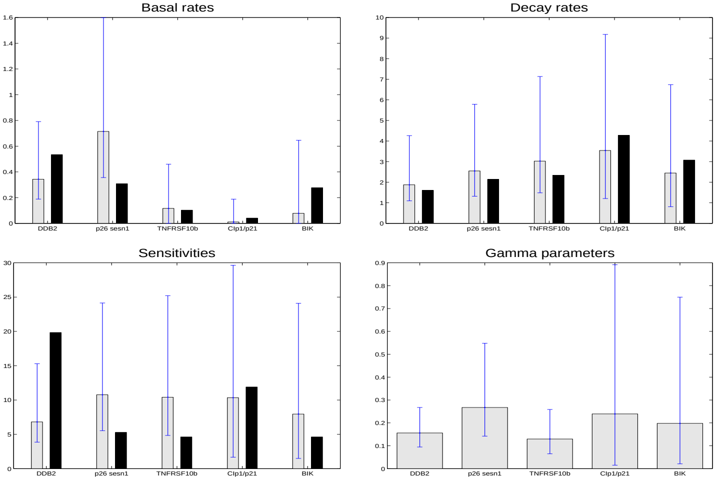


Linear model (Barenco et al. predictions are shown as crosses)



Nonlinear (Michaelis-Menten kinetic equation)

p53 Data Kinetic parameters



Our results (grey) compared with Barenco et al. (2006) (black). Note that Barenco et al. use a linear model

5. Convolutions and Computational Complexity

6. Non-linear Response Models

7. Cascaded Differential Equations

Cascaded Differential Equations

Antti Honkela

- Transcription factor protein also has governing mRNA.
- This mRNA can be measured.
- In signalling systems this measurement can be misleading because it is activated (phosphorylated) transcription factor that counts.
- In development phosphorylation plays less of a role.

Drosophila *Mesoderm* Development

Data from Furlong Lab in EMBL Heidelberg.

- Describe mesoderm development.

Cascaded Differential Equations

Antti Honkela

We take the production rate of active transcription factor to be given by

$$\frac{\mathrm{d}f\left(t\right)}{\mathrm{d}t} = \sigma y\left(t\right) - \delta f\left(t\right)$$
$$\frac{\mathrm{d}x_j\left(t\right)}{\mathrm{d}t} = B_j + S_j f\left(t\right) - D_j x_j\left(t\right)$$

The solution for $f(t)$, setting transient terms to zero, is

$$f(t) = \sigma \exp\left(-\delta t\right) \int_0^t y(u) \exp\left(\delta u\right) \mathrm{d}u \ .$$

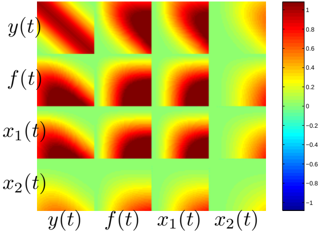
Covariance for Translation/Transcription Model

RBF covariance function for $y(t)$

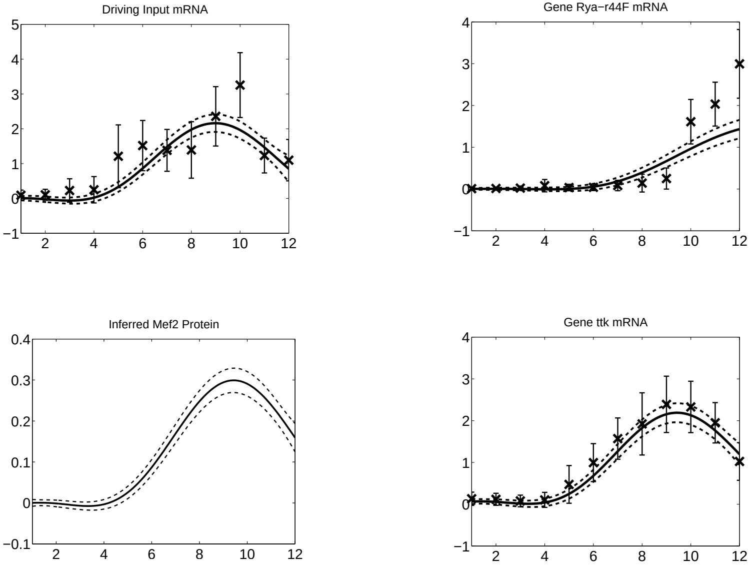
$$
\begin{aligned}
f(t) &= \sigma \exp(-\delta t) \int_0^t y(u) \exp(\delta u)\, \mathrm{d}u \\
x_i(t) &= \frac{B_i}{D_i} + S_i \exp(-D_i t) \int_0^t f(u) \exp(D_i u)\, \mathrm{d}u.
\end{aligned}
$$

- Joint distribution for $x_1(t)$, $x_2(t)$, $f(t)$ and $y(t)$.
- Here:

δ	D_1	S_1	D_2	S_2
0.1	5	5	0.5	0.5



Results for Mef2 using the Cascade model



Driving Input mRNA

Gene Rya−r44F mRNA

Inferred Mef2 Protein

Gene ttk mRNA