Latent Force Models

Neil D. Lawrence
work with Magnus Rattray, **Mauricio Alvarez**, Pei Gao, Antti Honkela, David Luengo, Guido Sanguinetti, Michalis Titsias, Jennifer Withers

University of Exeter
Talk at Mathematics and Computer Science

16th March 2011

Outline

Outline

- Urs Hölzle keynote talk at NIPS 2005.
    - Emphasis on massive data sets.
    - Let the data do the work—more data, less extrapolation.
- Alternative paradigm:
    - Very scarce data: computational biology, human motion.
    - How to generalize from scarce data?
    - Need to include more assumptions about the data (e.g. invariances).

data modeling

mechanistic modeling

data modeling

mechanistic modeling
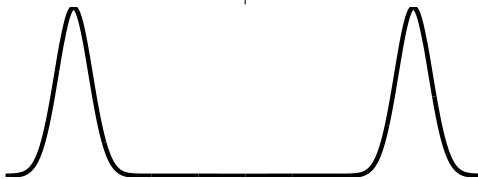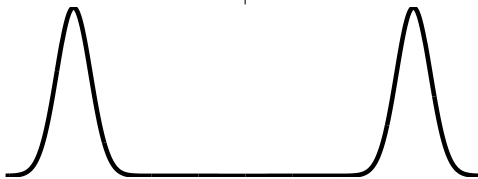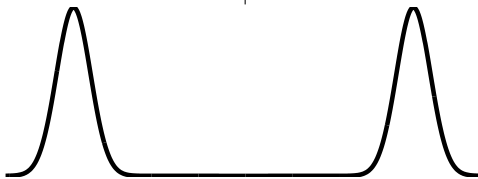
let the data "speak"

data modeling

let the data "speak"
data driven

mechanistic modeling
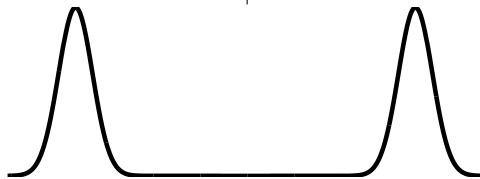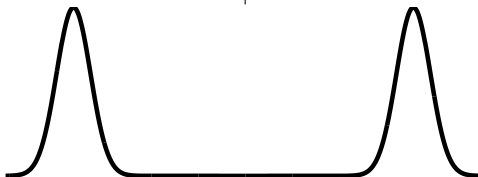
impose physical laws
knowledge driven

data modeling

let the data "speak"

data driven

adaptive models

digit recognition

mechanistic modeling

impose physical laws

knowledge driven

differential equations

data modeling

mechanistic modeling

let the data "speak"

data driven

adaptive models

digit recognition

impose physical laws

knowledge driven

differential equations

climate, weather models

Weakly Mechanistic

data modeling   *mechanistic modeling*

let the data "speak"   impose physical laws

data driven   knowledge driven

adaptive models   differential equations

digit recognition   climate, weather models
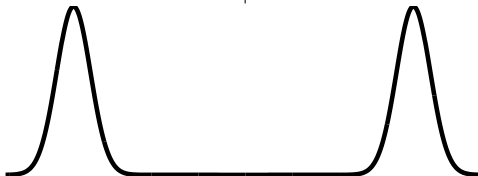
Weakly Mechanistic   Strongly Mechanistic
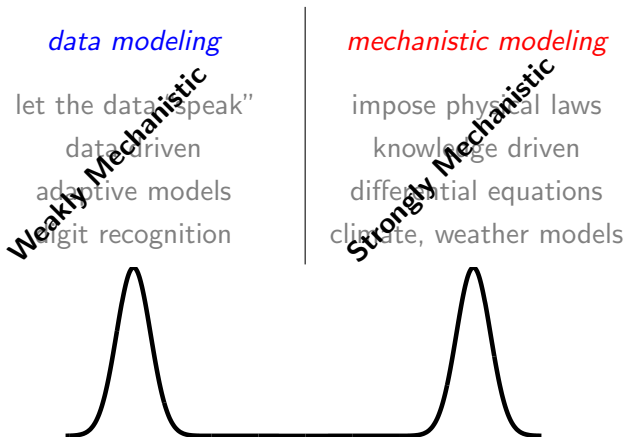
Weakly Mechanistic vs Strongly Mechanistic

- Underlying data modeling techniques there are *weakly mechanistic* principles (e.g. smoothness).
- In physics the models are typically *strongly mechanistic*.
- In principle we expect a range of models which vary in the strength of their mechanistic assumptions.
- This work is one part of that spectrum: add further mechanistic ideas to weakly mechanistic models.

Dimensionality Reduction

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

$$\mathbf{X} = \mathbf{FW} + \boldsymbol{\epsilon},$$

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

- Integrate out $\mathbf{F}$, optimize with respect to $\mathbf{W}$.
- For Gaussian prior, $\mathbf{F} \sim \mathcal{N}(\mathbf{0}, \mathbf{I})$
  - and $\Sigma = \sigma^2 \mathbf{I}$ we have probabilistic PCA (Tipping and Bishop, 1999; Roweis, 1998).
  - and Σ constrained to be diagonal, we have factor analysis.

Dimensionality Reduction: Temporal Data

- Deal with temporal data with a temporal latent prior.
- Independent Gauss-Markov priors over each $f_i(t)$ leads to : Rauch-Tung-Striebel (RTS) smoother (Kalman filter).
- More generally consider a Gaussian process (GP) prior,

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

- Given the covariance functions for $\{f_i(t)\}$ we have an implied covariance function across all $\{x_i(t)\}$—(ML: semi-parametric latent factor model (Teh et al., 2005), Geostatistics: linear model of coregionalization).
- Rauch-Tung-Striebel smoother 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).

Zero mean Gaussian distribution

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

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

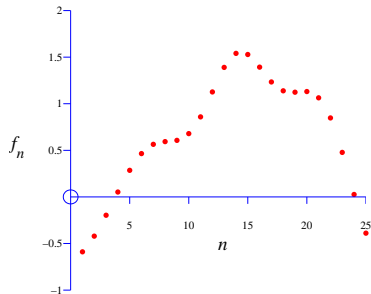▶ We will consider the special case where the mean is zero,

$$\mathcal{N}\left(\mathbf{f}|\mathbf{0}, \mathbf{K}\right) = \frac{1}{(2\pi)^{\frac{n}{2}} |\mathbf{K}|^{\frac{1}{2}}} \exp\left(-\frac{\mathbf{f}^{\top}\mathbf{K}^{-1}\mathbf{f}}{2}\right).$$
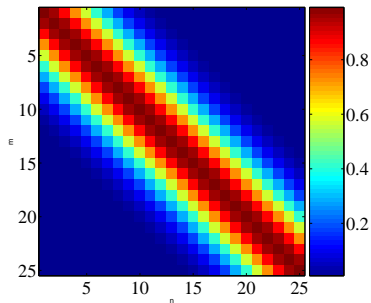
Multi-variate Gaussians

▶ We will consider a Gaussian with a particular structure of covariance matrix.

▶ Generate a single sample from this 25 dimensional Gaussian distribution, $\mathbf{f} = [f_1, f_2 \ldots f_{25}]$.

▶ We will plot these points against their index.

Gaussian Distribution Sample

(a) A 25 dimensional correlated random variable (values ploted against index)

(b) colormap showing correlations between dimensions

Figure: A sample from a 25 dimensional Gaussian distribution.

The covariance matrix

- ▶ Covariance matrix shows correlation between points f_i and f_j if i is near to j.
- ▶ Less correlation if i is distant from j.
- ▶ Our ordering of points means that the *function appears smooth*.
- ▶ Let's focus on the joint distribution of two points from the 25.

The covariance matrix

- Covariance matrix shows correlation between points f_i and f_j if i is near to j.
- Less correlation if i is distant from j.
- Our ordering of points means that the *function appears smooth*.
- Let's focus on the joint distribution of two points from the 25.

The covariance matrix

- ► Covariance matrix shows correlation between points f_i and f_j if i is near to j.
- ► Less correlation if i is distant from j.
- ► Our ordering of points means that the *function appears smooth*.
- ► Let's focus on the joint distribution of two points from the 25.

The covariance matrix

- Covariance matrix shows correlation between points f_i and f_j if i is near to j.
- Less correlation if i is distant from j.
- Our ordering of points means that the *function appears smooth*.
- Let's focus on the joint distribution of two points from the 25.

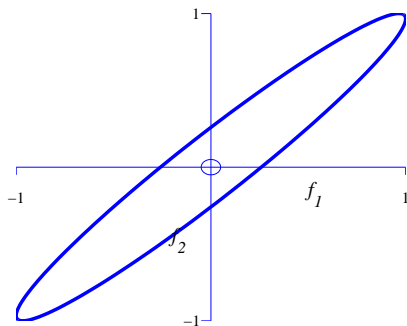# Prediction of f_2 from f_1
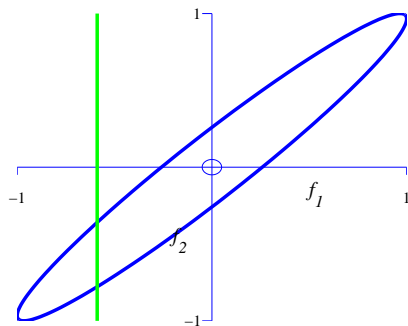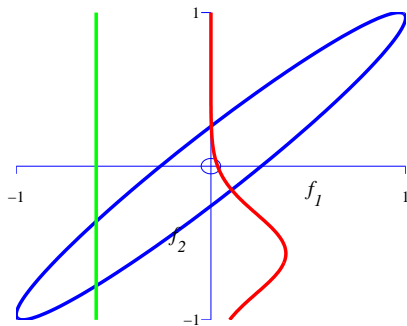
```
demGpCov2D([1 2])
```


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

Prediction of f_2 from f_1

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


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

Prediction of f_2 from f_1

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


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

```
demGpCov2D([1 5])
```

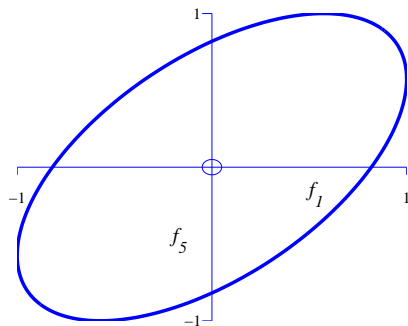

Figure: Covariance for $\begin{bmatrix} f_1 \\ f_5 \end{bmatrix}$ is $\mathbf{K}_{15} = \begin{bmatrix} 1 & 0.574 \\ 0.574 & 1 \end{bmatrix}$.
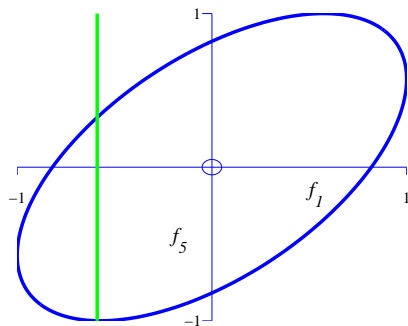
```
demGpCov2D([1 5])
```


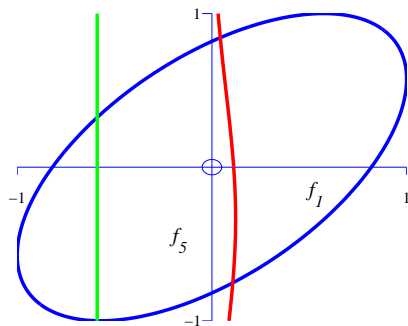
Figure: Covariance for $\begin{bmatrix} f_1 \\ f_5 \end{bmatrix}$ is $\mathbf{K}_{15} = \begin{bmatrix} 1 & 0.574 \\ 0.574 & 1 \end{bmatrix}$.

Prediction of f_5 from f_1

```
demGpCov2D([1 5])
```


Figure: Covariance for $\begin{bmatrix} f_1 \\ f_5 \end{bmatrix}$ is $\mathbf{K}_{15} = \begin{bmatrix} 1 & 0.574 \\ 0.574 & 1 \end{bmatrix}$.
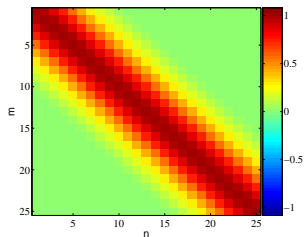
Exponentiated Quadratic Kernel Function (RBF, Squared Exponential, Gaussian)

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

- ▶ 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.

`demCovFuncSample`

Figure: Exponentiated quadratic kernel with $\ell = 0.3$, $\alpha = 1$
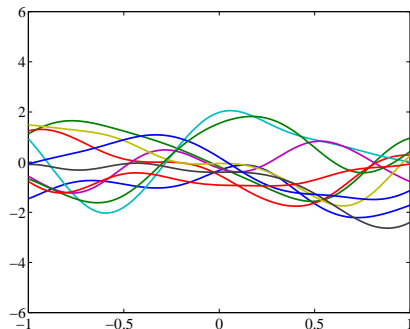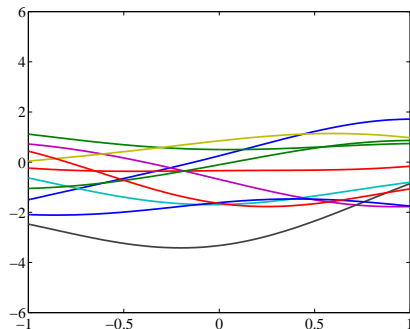
`demCovFuncSample`

Figure: Exponentiated quadratic kernel with $\ell = 1$, $\alpha = 1$

Covariance Samples
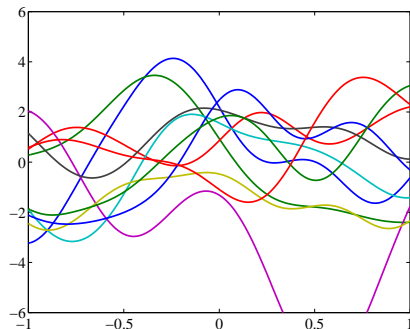
`demCovFuncSample`

Figure: Exponentiated quadratic kernel with $\ell = 0.3$, $\alpha = 4$
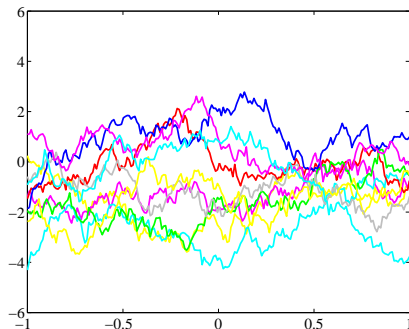
Covariance Samples

`demCovFuncSample`

Figure: Ornstein-Uhlenbeck (stationary Gauss-Markov) covariance function $\ell = 1$, $\alpha = 4$
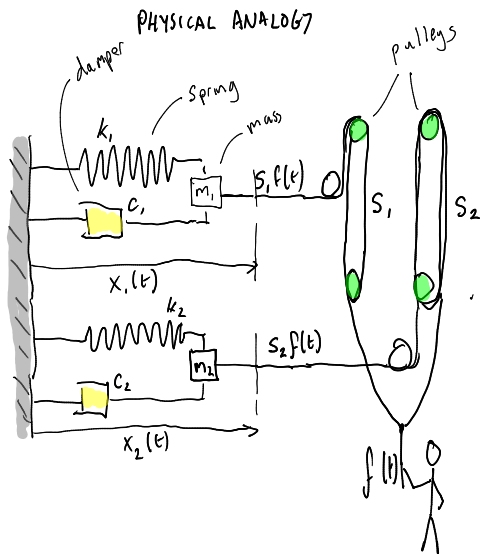
Outline

Back to Mechanistic 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 p springs to the forces.,
    - Interpret system as the force balance equation, $\mathbf{XD} = \mathbf{FS} + \epsilon$.
    - Forces act, e.g. through levers — a matrix of sensitivities, $\mathbf{S} \in \Re^{q \times p}$.
    - Diagonal matrix of spring constants, $\mathbf{D} \in \Re^{p \times p}$.
    - Original System: $\mathbf{W} = \mathbf{SD}^{-1}$.

- Add a damper and give the system mass.

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

- 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*.

Physical Analogy

PHYSICAL ANALOGY

damper

spring

mass

k_1

c_1

m_1

$S_1 f(t)$

$X_1(t)$

k_2

m_2

$S_2 f(t)$

c_2

$X_2(t)$

pulleys

S_1

S_2

$f(t)$

MARIONETTE

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

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

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 exponentiated quadratic covariances

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

Covariance for ODE Model

▶ Exponentiated Quadratic Covariance function for $f(t)$

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

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

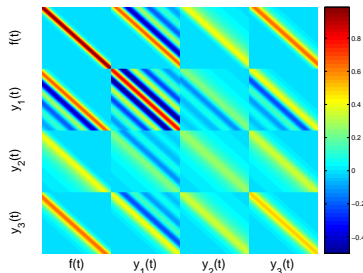| ζ_1	ζ_2	ζ_3
0.125	2	1
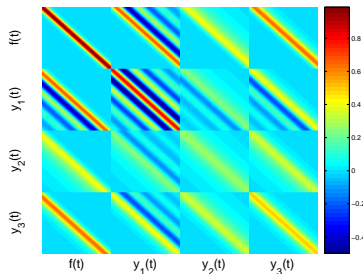
Covariance for ODE Model

▶ Analogy

$$x = \sum_i \mathbf{e}_i^\top \mathbf{f}_i \quad \mathbf{f}_i \sim \mathcal{N}\left(\mathbf{0}, \Sigma_i\right) \rightarrow x \sim \mathcal{N}\left(0, \sum_i \mathbf{e}_i^\top \Sigma_i \mathbf{e}_i\right)$$

▶ Joint distribution for $x_1(t)$, $x_2(t)$, $x_3(t)$ and $f(t)$. Damping ratios:
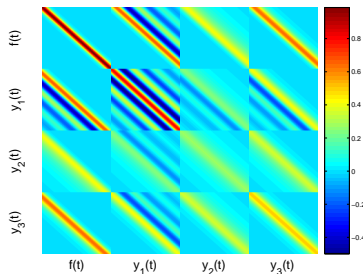
ζ_1	ζ_2	ζ_3
0.125	2	1

Covariance for ODE Model

▶ Exponentiated Quadratic Covariance function for $f(t)$

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

▶ 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 $f(t)$
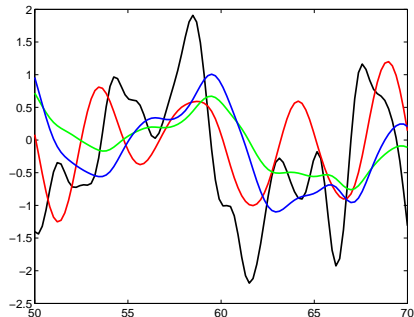
- `lfmSample`

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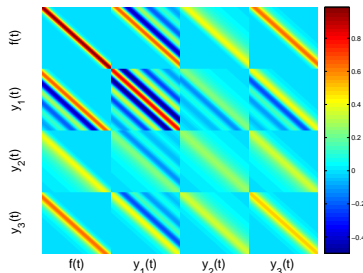
Joint Sampling of $x(t)$ and $f(t)$

- `lfmSample`

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

Joint Sampling of $x(t)$ and $f(t)$
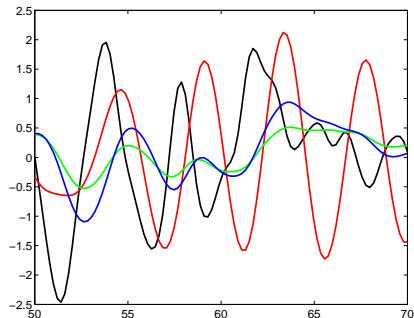
- `lfmSample`

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

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

▶ `lfmSample`

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

Covariance for ODE

- Exponentiated Quadratic Covariance function for $f(t)$

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

- 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

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.

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.

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.

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.

- Model left arm only.
- 3 balancing motions (18, 19, 20) from subject 49.
- 18 and 19 are similar, 20 contains more dramatic movements.
- Train on 18 and 19 and testing on 20
- Data was down-sampled by 32 (from 120 fps).
- Reconstruct motion of left arm for 20 given other movements.
- Compare with GP that predicts left arm angles given other body angles.

Mocap Results

Table: Root mean squared (RMS) angle error for prediction of the left arm's configuration in the motion capture data. Prediction with the latent force model outperforms the prediction with regression for all apart from the radius's angle.

Angle	Latent Force Error	Regression Error
Radius	4.11	4.02
Wrist	6.55	6.65
Hand X rotation	1.82	3.21
Hand Z rotation	2.76	6.14
Thumb X rotation	1.77	3.10
Thumb Z rotation	2.73	6.09

Mocap Results II
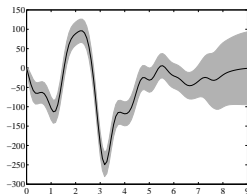
(a) Inferred Latent Force
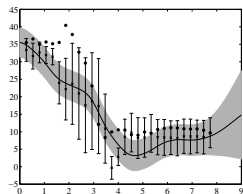
(b) Wrist
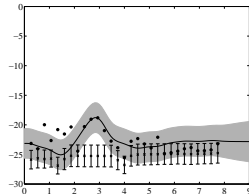
(c) Hand X Rotation
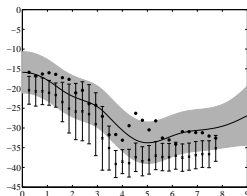
(d) Hand Z Rotation
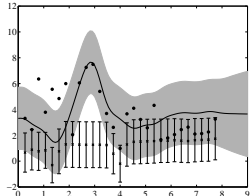
(e) Thumb X Rotation
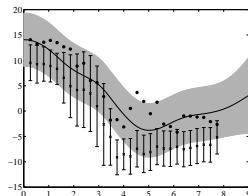
(f) Thumb Z Rotation

Figure: Predictions from LFM (solid line, grey error bars) and direct regression (crosses with stick error bars).

- First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

- 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)
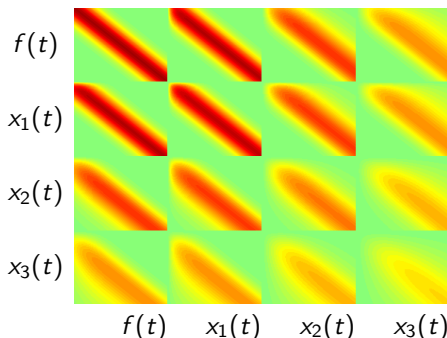- Problem: how do we fit the model when $f(t)$ is not observed?

Example: Transcriptional Regulation

- First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

- 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?

- First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

- 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?

Example: Transcriptional Regulation

- First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

- 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?

Example: Transcriptional Regulation

- First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

- 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?

Example: Transcriptional Regulation

- First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

- 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?

Example: Transcriptional Regulation

- First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

- 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?

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 $x_1(t)$, $x_2(t)$, $x_3(t)$, and $f(t)$.
- Here:

d_1	s_1	d_2	s_2	d_3	s_3
5	5	1	1	0.5	0.5

RBF covariance function for $f(t)$

$$x = b/d + \sum_i \mathbf{e}_i^\top \mathbf{f} \quad \mathbf{f} \sim \mathcal{N}\left(\mathbf{0}, \Sigma_i\right) \rightarrow x \sim \mathcal{N}\left(b/d, \sum_i \mathbf{e}_i^\top \Sigma_i \mathbf{e}_i\right)$$

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

d_1	s_1	d_2	s_2	d_3	s_3
5	5	1	1	0.5	0.5
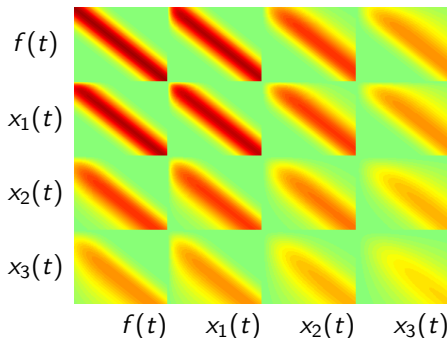
Covariance for Transcription Model

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 $x_1(t)$, $x_2(t)$, $x_3(t)$, and $f(t)$.
- Here:

d_1	s_1	d_2	s_2	d_3	s_3
5	5	1	1	0.5	0.5

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

- simSample

Figure: Joint samples from the ODE covariance, *black*: $f(t)$, *red*: $x_1(t)$ (high decay/sensitivity), *green*: $x_2(t)$ (medium decay/sensitivity) and *blue*: $x_3(t)$ (low decay/sensitivity).

- `simSample`

Figure: Joint samples from the ODE covariance, *black*: $f(t)$, *red*: $x_1(t)$ (high decay/sensitivity), *green*: $x_2(t)$ (medium decay/sensitivity) and *blue*: $x_3(t)$ (low decay/sensitivity).

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

- simSample

Figure: Joint samples from the ODE covariance, *black*: $f(t)$, *red*: $x_1(t)$ (high decay/sensitivity), *green*: $x_2(t)$ (medium decay/sensitivity) and *blue*: $x_3(t)$ (low decay/sensitivity).

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

- simSample

Figure: Joint samples from the ODE covariance, *black*: $f(t)$, *red*: $x_1(t)$ (high decay/sensitivity), *green*: $x_2(t)$ (medium decay/sensitivity) and *blue*: $x_3(t)$ (low decay/sensitivity).

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

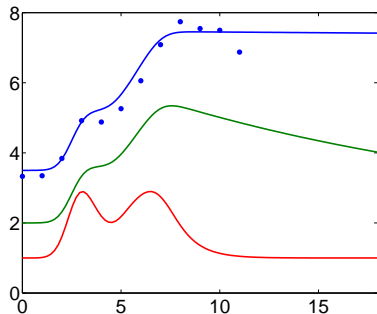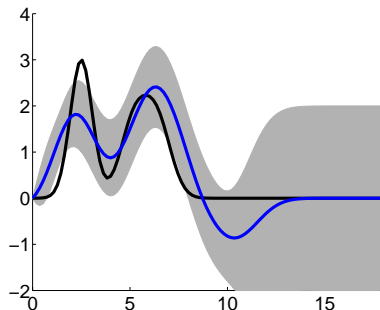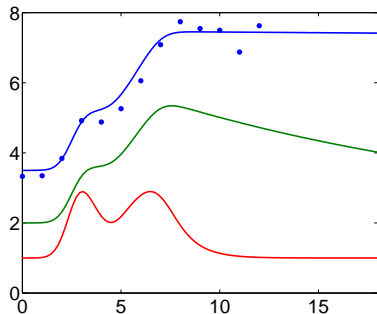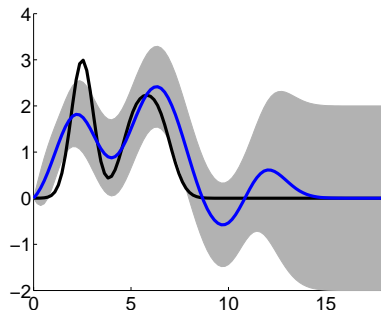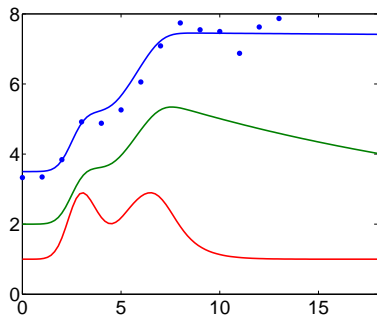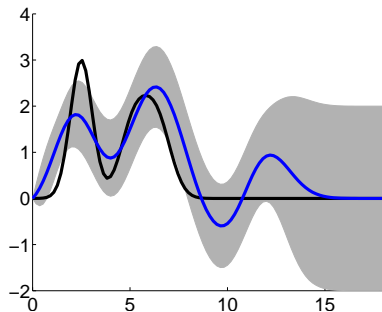Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

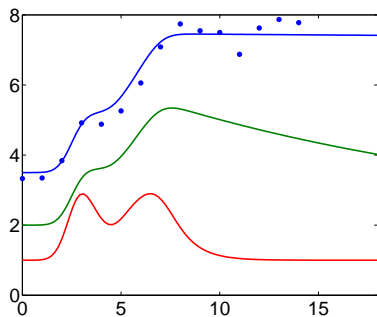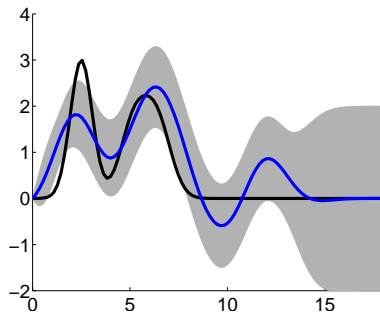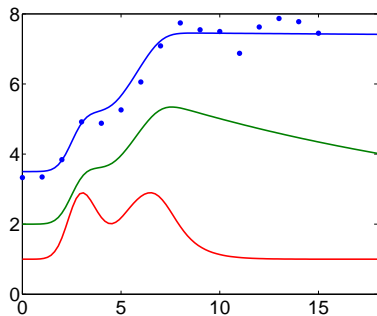Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

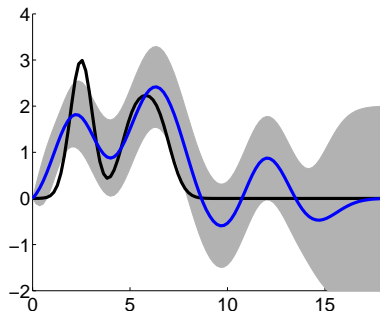True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

Inferring TF activity from artificially sampled genes.
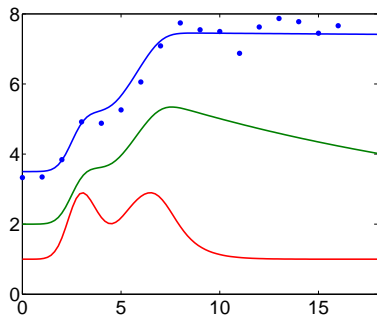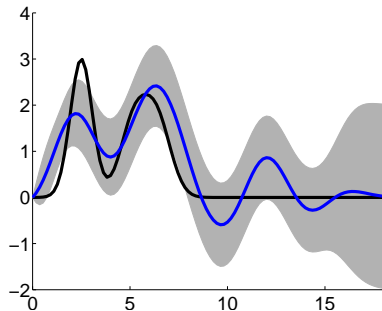

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

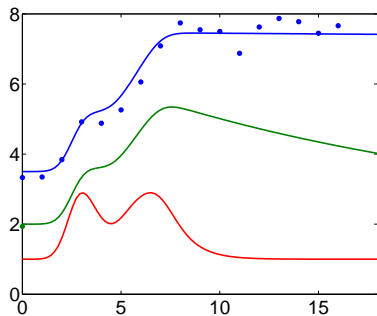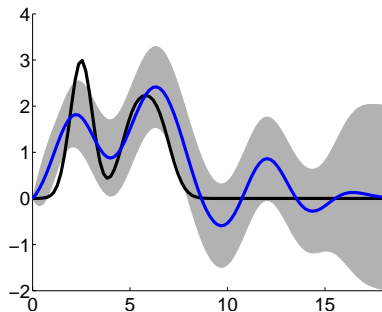Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

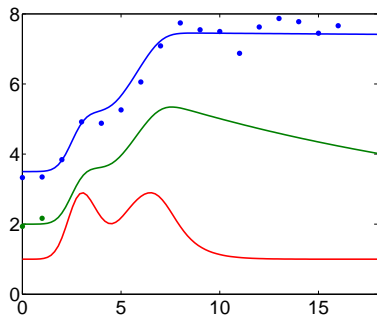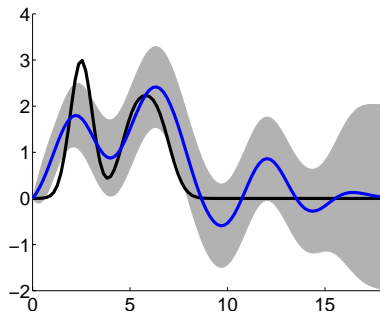Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

Inferring TF activity from artificially sampled genes.
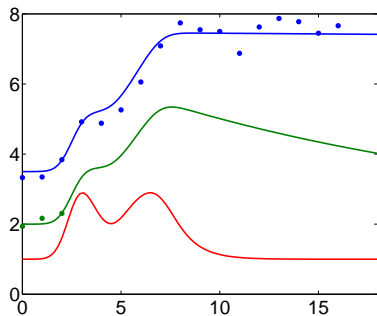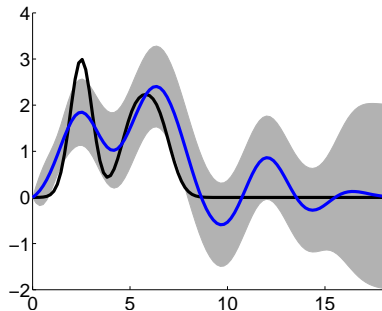

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

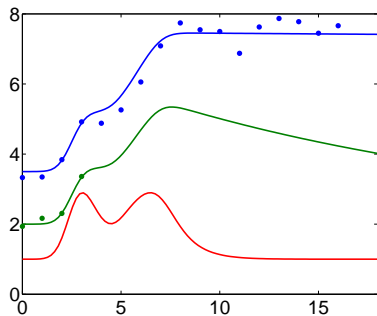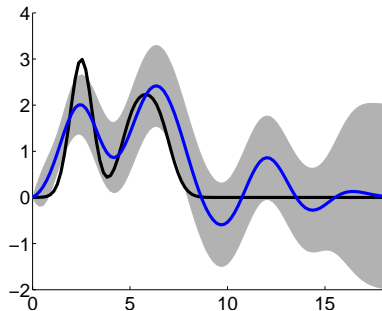Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

Inferring TF activity from artificially sampled genes.
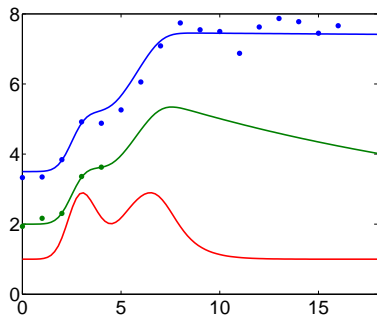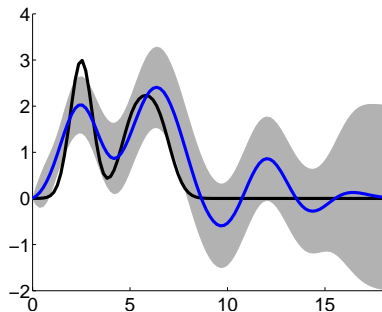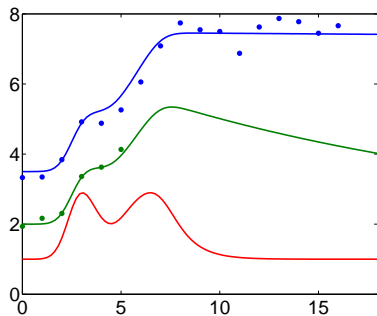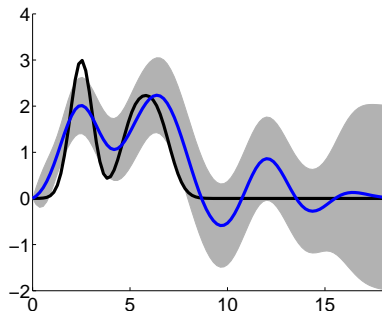

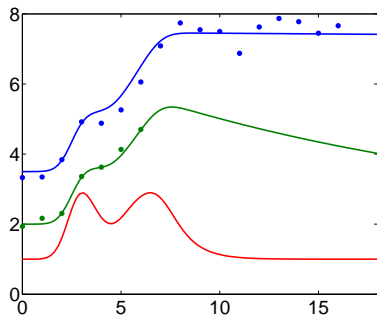True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.
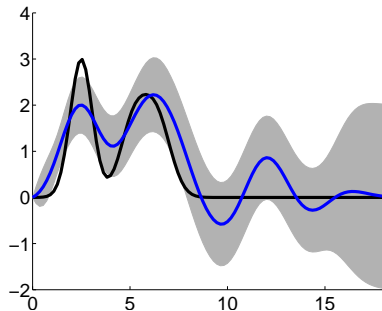
True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

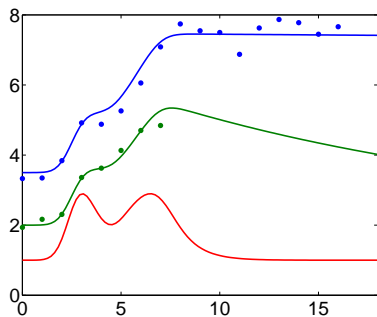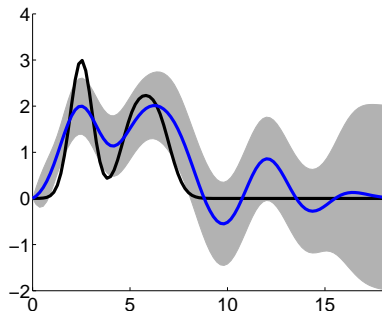Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

Inferring TF activity from artificially sampled genes.
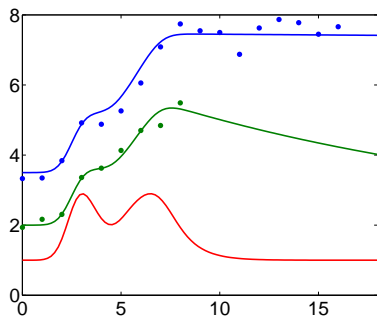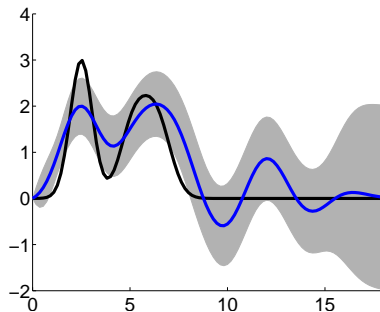

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

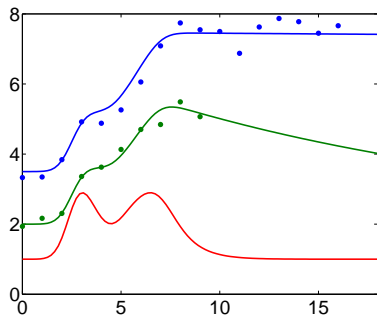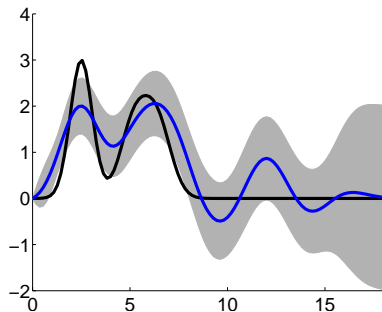Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

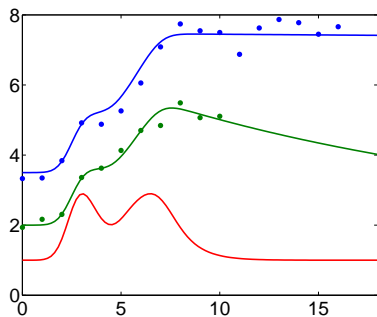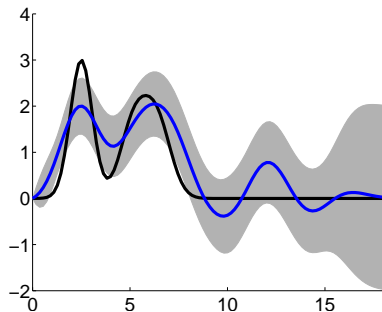Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

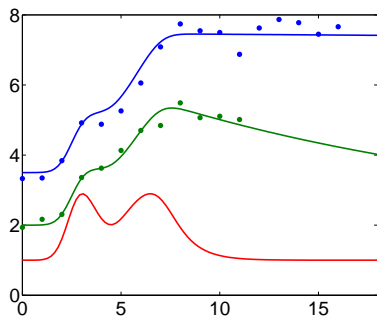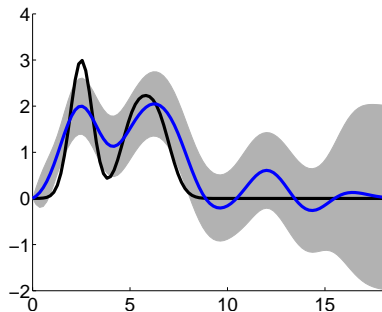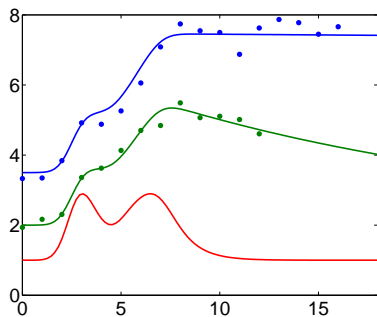Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

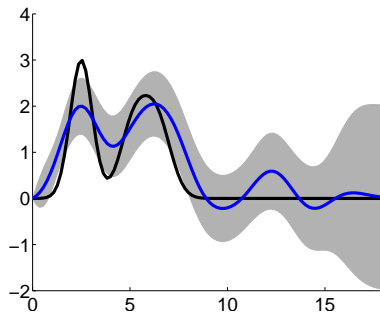True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

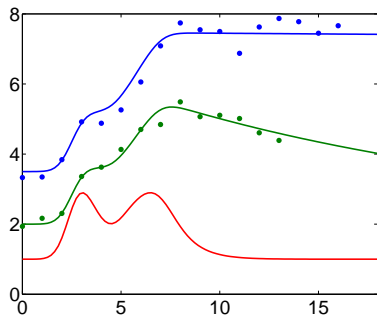Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

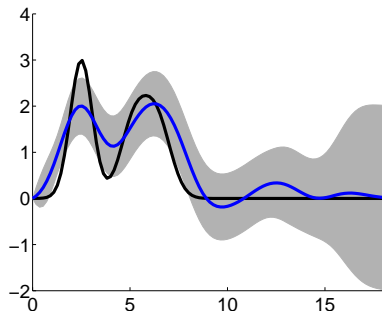True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

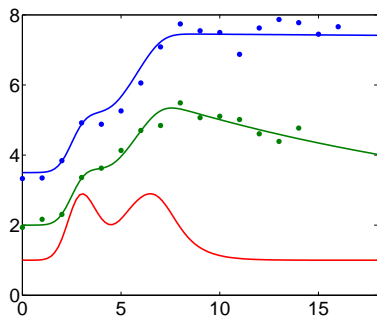Inferring TF activity from artificially sampled genes.

True "gene profiles" and noisy observations.
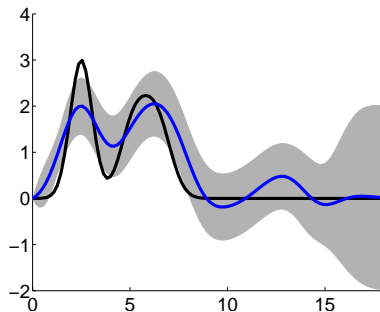

Inferred transcription factor activity.

Artificial Example: Inferring $f(t)$

Inferring TF activity from artificially sampled genes.
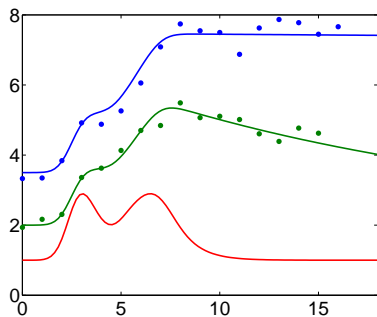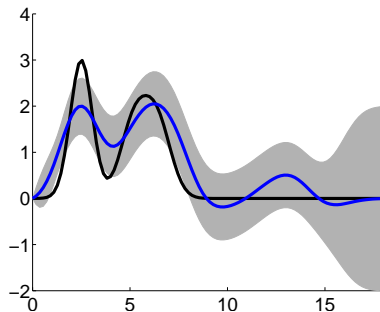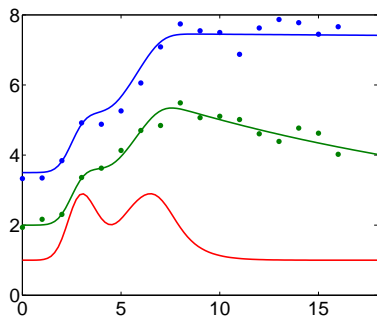

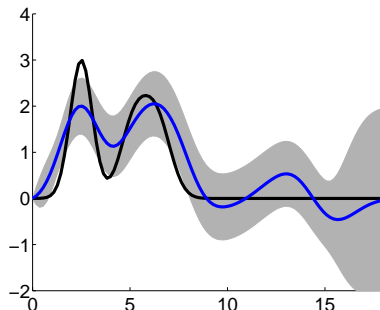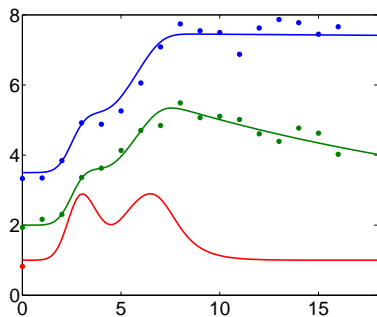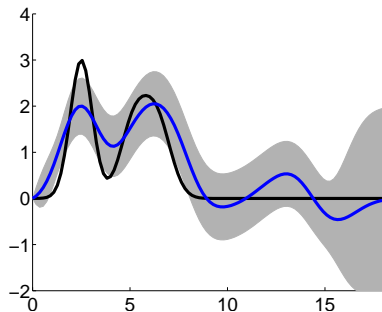True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

True "gene profiles" and noisy observations.

Inferred transcription factor activity.

Radiation Damage in the Cell

- Radiation can damages molecules including DNA.
- Most DNA damage is quickly repaired—single strand breaks, backbone break.
- Double strand breaks are more serious—a complete disconnect along the chromosome.
- Cell cycle stages:
    - G_1: Cell is not dividing.
    - G_2: Cell is preparing for meitosis, chromosomes have divided.
    - S: Cell is undergoing meitosis (DNA synthesis).
- Main problem is in G_1. In G_2 there are two copies of the chromosome. In G_1 only one copy.

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
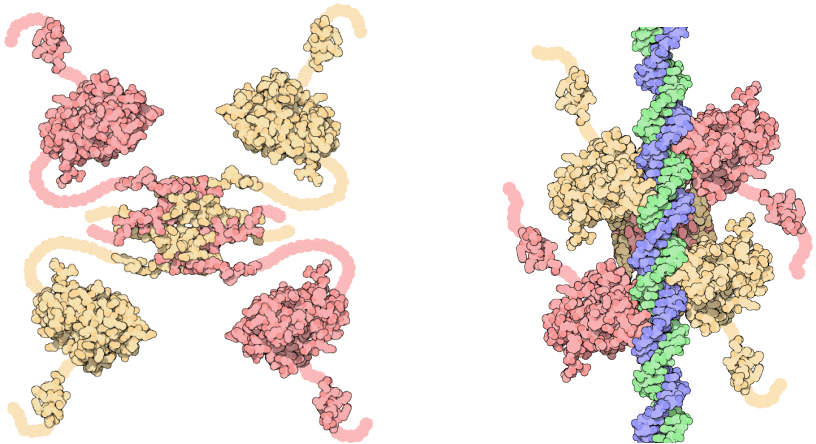
Figure: p53. *Left* unbound, *Right* bound to DNA. Images by David S. Goodsell from `http://www.rcsb.org/` (see the "Molecule of the Month" feature).
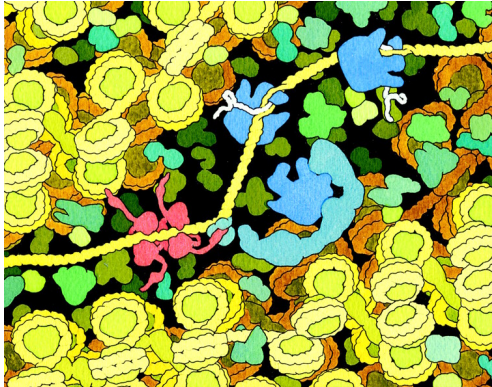
Figure: Repair of DNA damage by p53. Image from Goodsell (1999).

Some p53 Targets

DDB2 DNA Damage Specific DNA Binding Protein 2. (also governed by C/ EBP-beta, E2F1, E2F3,...).

p21 Cycline-dependent kinase inhibitor 1A (CDKN1A). A regulator of cell cycle progression. (also governed by SREBP-1a, Sp1, Sp3,...).

hPA26/SESN1 sestrin 1 Cell Cycle arrest.

BIK BCL2-interacting killer. Induces cell death (apoptosis)

TNFRSF10b tumor necrosis factor receptor superfamily, member 10b. A transducer of apoptosis signals.

Modelling Assumption

- Assume p53 affects targets as a single input module network motif (SIM).
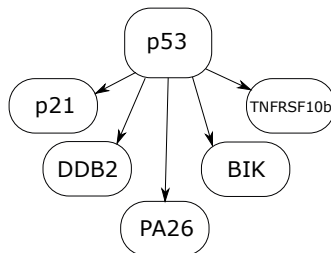
Figure: p53 SIM network motif as modelled by Barenco et al. 2006.

▶ First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

▶ Proposed by Barenco et al. (2006).

▶ $x_j(t)$ – 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?

- First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

- Proposed by Barenco et al. (2006).
- $x_j(t)$ – 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?

Ordinary Differential Equation Model

- First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

- Proposed by Barenco et al. (2006).
- $x_j(t)$ – 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?

- First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

- Proposed by Barenco et al. (2006).
- $x_j(t)$ – 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?

▶ First Order Differential Equation

$$\frac{\mathrm{d}x_j\left(t\right)}{\mathrm{d}t} = b_j + s_j f\left(t\right) - d_j x_j\left(t\right)$$

▶ Proposed by Barenco et al. (2006).

▶ $x_j(t)$ – 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?

- First Order Differential Equation

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

- Proposed by Barenco et al. (2006).
- $x_j(t)$ – 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?

- First Order Differential Equation

$$\frac{dx_j(t)}{dt} = b_j + s_j f(t) - d_j x_j(t)$$

- Proposed by Barenco et al. (2006).
- $x_j(t)$ – 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?

BIOINFORMATICS

Gaussian process modelling of latent chemical species: applications to inferring transcription factor activities

Pei Gao[1], Antti Honkela[2], Magnus Rattray[1] and Neil D. Lawrence[1],*

[1]School of Computer Science, University of Manchester, Kilburn Building, Oxford Road, Manchester, M13 9PL and
[2]Adaptive Informatics Research Centre, Helsinki University of Technology, PO Box 5400, FI-02015 TKK, Finland

ABSTRACT

Motivation: Inference of *latent chemical species* in biochemical interaction networks is a key problem in estimation of the structure

A challenging problem for parameter estimation in ODE models occurs where one or more chemical species influencing the dynamics are controlled outside of the sub-system being modelled. For

p53 Results with GP

(Gao et al., 2008)
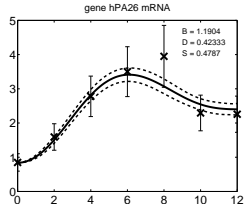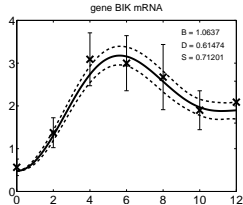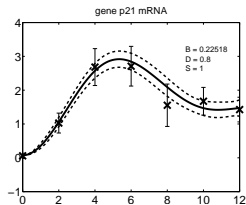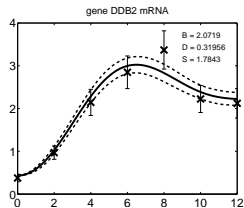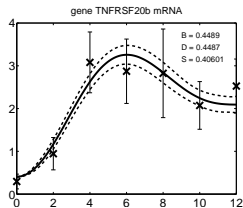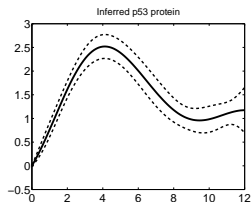
Model-based method for transcription factor target identification with limited data

Antti Honkela[a,1], Charles Girardot[b], E. Hilary Gustafson[b], Ya-Hsin Liu[b], Eileen E. M. Furlong[b], Neil D. Lawrence[c,1], and Magnus Rattray[c,1]

[a]Department of Information and Computer Science, Aalto University School of Science and Technology, Helsinki, Finland; [b]Genome Biology U European Molecular Biology Laboratory, Heidelberg, Germany; and [c]School of Computer Science, University of Manchester, Manchester, Unite

We present a computational method for identifying potential targets of a transcription factor (TF) using wild-type gene expression time series data. For each putative target gene we fit a simple differential equation model of transcriptional regulation, and the model likelihood ... used for genome-wide scoring of putative target gen is required to apply our method is wild-type time serie lected over a period where TF activity is changing. Ou allows for complementary evidence from expression

(Honkela et al., 2010)

- ▶ 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

Collaboration with Furlong Lab in EMBL Heidelberg.

- Mesoderm development in Drosophila melanogaster (fruit fly).

- Mesoderm forms in triplobastic animals (along with ectoderm and endoderm). Mesoderm develops into muscles, and circulatory system.

- The transcription factor Twist initiates Drosophila mesoderm development, resulting in the formation of heart, somatic muscle, and other cell types.

- Wildtype microarray experiments publicly available.

- Can we use the cascade model to predict viable targets of Twist?

(Honkela et al., 2010)

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

$$\frac{\mathrm{d}f(t)}{\mathrm{d}t} = \sigma y(t) - \delta f(t)$$

$$\frac{\mathrm{d}x_j(t)}{\mathrm{d}t} = b_j + s_j f(t) - d_j x_j(t)$$

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

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

RBF covariance function for $y(t)$

$$f(t) = \sigma \exp(-\delta t) \int_0^t y(u) \exp(\delta u) \, du$$

$$x_i(t) = \frac{b_i}{d_i} + s_i \exp(-d_i t) \int_0^t f(u) \exp(d_i u) \, du.$$

▶ Joint distribution for $x_1(t)$, $x_2(t)$, $f(t)$ and $y(t)$.

▶ Here:

δ	d_1	s_1	d_2	s_2
1	5	5	0.5	0.5

- `disimSample`

Figure: Joint samples from the ODE covariance, *blue*: $y(t)$ (mRNA of TF), *black*: $f(t)$ (TF concentration), *red*: $x_1(t)$ (high decay target) and *green*: $x_2(t)$ (low decay target)

.

▶ disimSample

Figure: Joint samples from the ODE covariance, *blue*: $y(t)$ (mRNA of TF), *black*: $f(t)$ (TF concentration), *red*: $x_1(t)$ (high decay target) and *green*: $x_2(t)$ (low decay target)

.

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

- disimSample

Figure: Joint samples from the ODE covariance, *blue*: $y(t)$ (mRNA of TF), *black*: $f(t)$ (TF concentration), *red*: $x_1(t)$ (high decay target) and *green*: $x_2(t)$ (low decay target)

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

- `disimSample`

Figure: Joint samples from the ODE covariance, *blue*: $y(t)$ (mRNA of TF), *black*: $f(t)$ (TF concentration), *red*: $x_1(t)$ (high decay target) and *green*: $x_2(t)$ (low decay target)

.

- ▶ Use mRNA of Twist as driving input.
- ▶ For each gene build a cascade model that forces Twist to be the only TF.
- ▶ Compare fit of this model to a baseline (*e.g.* similar model but sensitivity zero).
- ▶ Rank according to the likelihood above the baseline.
- ▶ Compare with correlation, knockouts and time series network identification (TSNI) (Della Gatta et al., 2008).

Figure: Model for flybase gene identity FBgn0002526.

Figure: Model for flybase gene identity FBgn0003486.

Figure: Model for flybase gene identity FBgn0011206.

Figure: Model for flybase gene identity FBgn00309055.

Figure: Model for flybase gene identity FBgn0031907.

Results for Twi using the Cascade model

Figure: Model for flybase gene identity FBgn0035257.
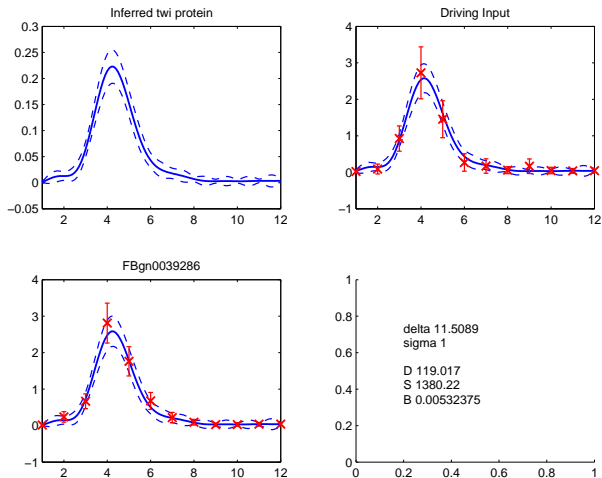
Figure: Model for flybase gene identity FBgn0039286.

- Evaluate the ranking methods by taking a number of top-ranked targets and record the number of "positives" (Zinzen et al., 2009):
  - targets with ChIP-chip binding sites within 2 kb of gene
  - (targets differentially expressed in TF knock-outs)
- Compare against
  - Ranking by correlation of expression profiles
  - Ranking by q-value of differential expression in knock-outs
- Optionally focus on genes with annotated expression in tissues of interest

Results
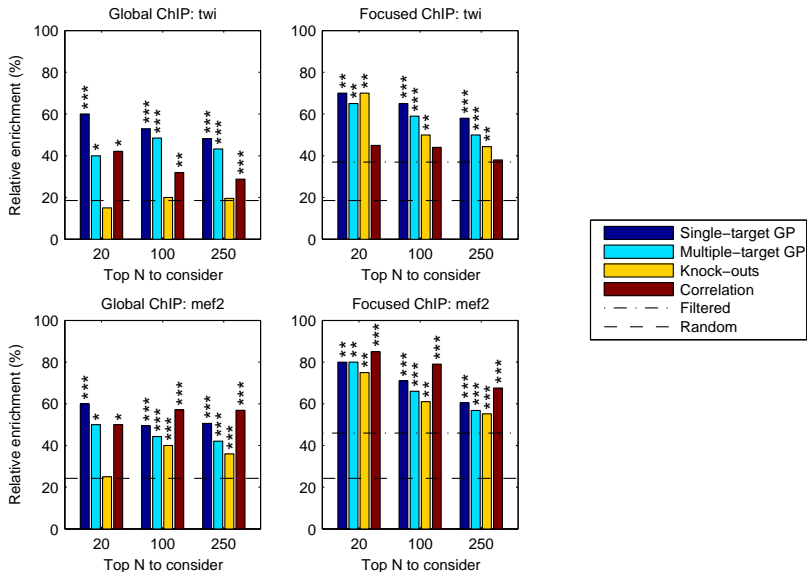
'***': $p < 0.001$, '**': $p < 0.01$, '*': $p < 0.05$

Summary

- Cascade models allow genomewide analysis of potential targets given only expression data.
- Once a set of potential candidate targets have been identified, they can be modelled in a more complex manner.
- We don't have ground truth, but evidence indicates that the approach *can* perform as well as knockouts.

Discussion and Future Work

- Integration of probabilistic inference with mechanistic models.
- Ongoing/other work:
  - Non linear response and non linear differential equations.
  - Scaling up to larger systems Álvarez et al. (2010); Álvarez and Lawrence (2009).
  - Discontinuities through Switched Gaussian Processes Álvarez et al. (2011)
  - Robotics applications.
  - Applications to other types of system, *e.g.* spatial systems.
  - Stochastic differential equations Álvarez et al. (2010).

Acknowledgements

M. Álvarez and N. D. Lawrence. Sparse convolved Gaussian processes for multi-output regression. In D. Koller, D. Schuurmans, Y. Bengio, and L. Bottou, editors, *Advances in Neural Information Processing Systems*, volume 21, pages 57–64, Cambridge, MA, 2009. MIT Press. [PDF].

M. Álvarez, D. Luengo, and N. D. Lawrence. Latent force models. In van Dyk and Welling (2009), pages 9–16. [PDF].

M. A. Álvarez, D. Luengo, M. K. Titsias, and N. D. Lawrence. Efficient multioutput Gaussian processes through variational inducing kernels. In Y. W. Teh and D. M. Titterington, editors, *Proceedings of the Thirteenth International Workshop on Artificial Intelligence and Statistics*, volume 9, pages 25–32, Chia Laguna Resort, Sardinia, Italy, 13-16 May 2010. JMLR W&CP 9. [PDF].

M. A. Álvarez, J. Peters, B. Schölkopf, and N. D. Lawrence. Switched latent force models for movement segmentation. In J. Shawe-Taylor, R. Zemel, C. Williams, and J. Lafferty, editors, *Advances in Neural Information Processing Systems*, volume 23, Cambridge, MA, 2011. MIT Press. To appear.

M. Barenco, D. Tomescu, D. Brewer, R. Callard, J. Stark, and M. Hubank. Ranked prediction of p53 targets using hidden variable dynamic modeling. *Genome Biology*, 7(3):R25, 2006.

P. Boyle and M. Frean. Dependent Gaussian processes. In L. Saul, Y. Weiss, and L. Bouttou, editors, *Advances in Neural Information Processing Systems*, volume 17, pages 217–224, Cambridge, MA, 2005. MIT Press.

G. Della Gatta, M. Bansal, A. Ambesi-Impiombato, D. Antonini, C. Missero, and D. di Bernardo. Direct targets of the trp63 transcription factor revealed by a combination of gene expression profiling and reverse engineering. *Genome Research*, 18(6):939–948, Jun 2008. [URL]. [DOI].

P. Gao, A. Honkela, M. Rattray, and N. D. Lawrence. Gaussian process modelling of latent chemical species: Applications to inferring transcription factor activities. *Bioinformatics*, 24:i70–i75, 2008. [PDF]. [DOI].

D. S. Goodsell. The molecular perspective: p53 tumor suppressor. *The Oncologist, Vol. 4, No. 2, 138-139, April 1999*, 4(2):138–139, 1999.

P. Goovaerts. *Geostatistics For Natural Resources Evaluation*. Oxford University Press, 1997. [Google Books] .

D. M. Higdon. Space and space-time modelling using process convolutions. In C. Anderson, V. Barnett, P. Chatwin, and A. El-Shaarawi, editors, *Quantitative methods for current environmental issues*, pages 37–56. Springer-Verlag, 2002.

References II

A. Honkela, C. Girardot, E. H. Gustafson, Y.-H. Liu, E. E. M. Furlong, N. D. Lawrence, and M. Rattray. Model-based method for transcription factor target identification with limited data. *Proc. Natl. Acad. Sci. USA*, 107(17):7793–7798, Apr 2010. [DOI].

M. A. Osborne, A. Rogers, S. D. Ramchurn, S. J. Roberts, and N. R. Jennings. Towards real-time information processing of sensor network data using computationally efficient multi-output Gaussian processes. In *Proceedings of the International Conference on Information Processing in Sensor Networks (IPSN 2008)*, 2008.

A. D. Polyanin. *Handbook of Linear Partial Differential Equations for Engineers and Scientists*. Chapman & Hall/CRC, 1 edition, 2002.

J. Quiñonero Candela and C. E. Rasmussen. A unifying view of sparse approximate Gaussian process regression. *Journal of Machine Learning Research*, 6:1939–1959, 2005.

S. T. Roweis. EM algorithms for PCA and SPCA. In M. I. Jordan, M. J. Kearns, and S. A. Solla, editors, *Advances in Neural Information Processing Systems*, volume 10, pages 626–632, Cambridge, MA, 1998. MIT Press.

E. Snelson and Z. Ghahramani. Sparse Gaussian processes using pseudo-inputs. In Y. Weiss, B. Schölkopf, and J. C. Platt, editors, *Advances in Neural Information Processing Systems*, volume 18, Cambridge, MA, 2006. MIT Press.

Y. W. Teh, M. Seeger, and M. I. Jordan. Semiparametric latent factor models. In R. G. Cowell and Z. Ghahramani, editors, *Proceedings of the Tenth International Workshop on Artificial Intelligence and Statistics*, pages 333–340, Barbados, 6-8 January 2005. Society for Artificial Intelligence and Statistics.

M. E. Tipping and C. M. Bishop. Probabilistic principal component analysis. *Journal of the Royal Statistical Society, B*, 6(3):611–622, 1999. [PDF]. [DOI].

M. K. Titsias. Variational learning of inducing variables in sparse Gaussian processes. In van Dyk and Welling (2009), pages 567–574.

D. van Dyk and M. Welling, editors. *Artificial Intelligence and Statistics*, volume 5, Clearwater Beach, FL, 16-18 April 2009. JMLR W&CP 5.

R. P. Zinzen, C. Girardot, J. Gagneur, M. Braun, and E. E. M. Furlong. Combinatorial binding predicts spatio-temporal cis-regulatory activity. *Nature*, 462(7269):65–70, Nov 2009. [URL]. [DOI].

Partial Differential Equations and Latent Forces

Mauricio Alvarez

- ▶ Can extend the concept to latent functions in PDEs.
- ▶ Jura data: concentrations of heavy metal pollutants from the Swiss Jura.
- ▶ Consider a latent function that represents how the pollutants were originally laid down (initial condition).
- ▶ Assume pollutants diffuse at different rates resulting in the concentrations observed in the data set.

$$\frac{\partial x_q(\mathbf{x}, t)}{\partial t} = \sum_{j=1}^{d} \kappa_q \frac{\partial^2 x_q(\mathbf{x}, t)}{\partial x_j^2},$$

- ▶ Latent function $f_r(\mathbf{x})$ represents the concentration of pollutants at time zero (i.e. the system's initial condition).

Solution to the PDE

Mauricio Alvarez

- The solution to the system (Polyanin, 2002) is then given by

$$x_q(\mathbf{x}, t) = \sum_{r=1}^{R} S_{rq} \int_{\mathbb{R}^d} f_r(\mathbf{x}') G_q(\mathbf{x}, \mathbf{x}', t) \mathrm{d}\mathbf{x}'$$

where $G_q(\mathbf{x}, \mathbf{x}', t)$ is the Green's function given as

$$G_q(\mathbf{x}, \mathbf{x}', t) = \frac{1}{2^d \pi^{d/2} T_q^{d/2}} \exp\left[-\sum_{j=1}^{d} \frac{(x_j - x_j')^2}{4 T_q}\right],$$

with $T_q = \kappa_q t$.

Covariance Function

Mauricio Alvarez

- For latent function given by a GP with the RBF covariance function this is tractable.

$$k_{x_p x_q}(\mathbf{x}, \mathbf{x}', t) = \sum_{r=1}^{R} \frac{S_{rp} S_{rq} |\mathbf{L}_r|^{1/2}}{|\mathbf{L}_{rp} + \mathbf{L}_{rq} + \mathbf{L}_r|^{1/2}}$$

$$\times \exp\left[-\frac{1}{2}\left(\mathbf{x} - \mathbf{x}'\right)^{\top}\left(\mathbf{L}_{rp} + \mathbf{L}_{rq} + \mathbf{L}_r\right)^{-1}\left(\mathbf{x} - \mathbf{x}'\right)\right],$$

where $\mathbf{L}_{rp}$, $\mathbf{L}_{rq}$ and $\mathbf{L}_r$ are diagonal isotropic matrices with entries $2\kappa_p t$, $2\kappa_q t$ and $1/\ell_r^2$ respectively. The covariance function between the output and latent functions is given by

$$k_{x_q f_r}(\mathbf{x}, \mathbf{x}', t) = \frac{S_{rq} |\mathbf{L}_r|^{1/2}}{|\mathbf{L}_{rq} + \mathbf{L}_r|^{1/2}}$$

$$\times \exp\left[-\frac{1}{2}\left(\mathbf{x} - \mathbf{x}'\right)^{\top}\left(\mathbf{L}_{rq} + \mathbf{L}_r\right)^{-1}\left(\mathbf{x} - \mathbf{x}'\right)\right].$$

Prediction of Metal Concentrations

Mauricio Alvarez

- ▶ Replicate experiments in (Goovaerts, 1997, pp. 248,249):
  - ▶ *Primary variable* (Cd, Cu, Pb, Co) predicted in conjunction with *secondary variables* (Ni and Zn for Cd; Pb, Ni, and Zn for Cu; Cu, Ni, and Zn for Pb; Ni and Zn for Co).[1]
- ▶ Condition on the secondary variables to improve prediction for primary variables.
- ▶ Compare results for the diffusion kernel with independent GPs and "ordinary co-kriging" (Goovaerts, 1997, pp. 248,249).

---

[1]Data available at `http://www.ai-geostats.org/`.

Mauricio Alvarez

Table: Mean absolute error and standard deviation for ten repetitions of the experiment for the Jura dataset. IGPs stands for independent GPs, GPDK stands for GP diffusion kernel, OCK for ordinary co-kriging. For the Gaussian process with diffusion kernel, we learn the diffusion coefficients and the length-scale of the covariance of the latent function.

Metals	IGPs	GPDK	OCK
Cd	0.5823 ± 0.0133	0.4505 ± 0.0126	0.5
Cu	15.9357 ± 0.0907	7.1677 ± 0.2266	7.8
Pb	22.9141 ± 0.6076	10.1097 ± 0.2842	10.7
Co	2.0735 ± 0.1070	1.7546 ± 0.0895	1.5

Convolutions and Computational Complexity

Mauricio Alvarez

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

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

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

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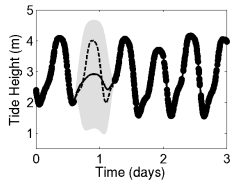
Mauricio Alvarez

- 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 $O\left(N^3 d k^2\right)$ complexity, $O\left(N^2 d k\right)$ storage.
  - Can also do a FITC style approximation (Snelson and Ghahramani, 2006).
  - Reduces to $O\left(N d k^2\right)$ complexity, $O\left(N d k\right)$ 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.
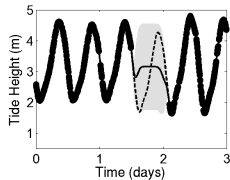- Take $k = 100$.

Tide Height Results
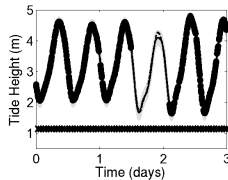
Mauricio Alvarez

(a) Bramblemet Independent
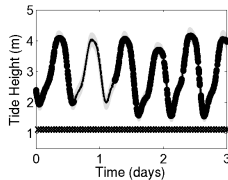
(b) Bramblemet PITC

(c) Cambermet Independent

(d) Cambermet PITC

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).

Mauricio Alvarez
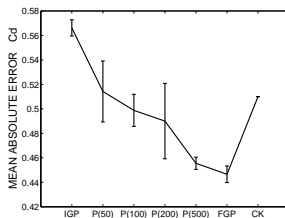
(a) Cadmium
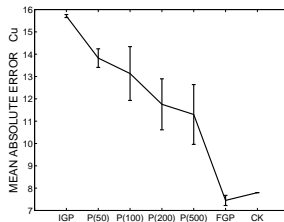
(b) Copper

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.