Capturing the impact of climate on Dengue using stochastic dynamical systems

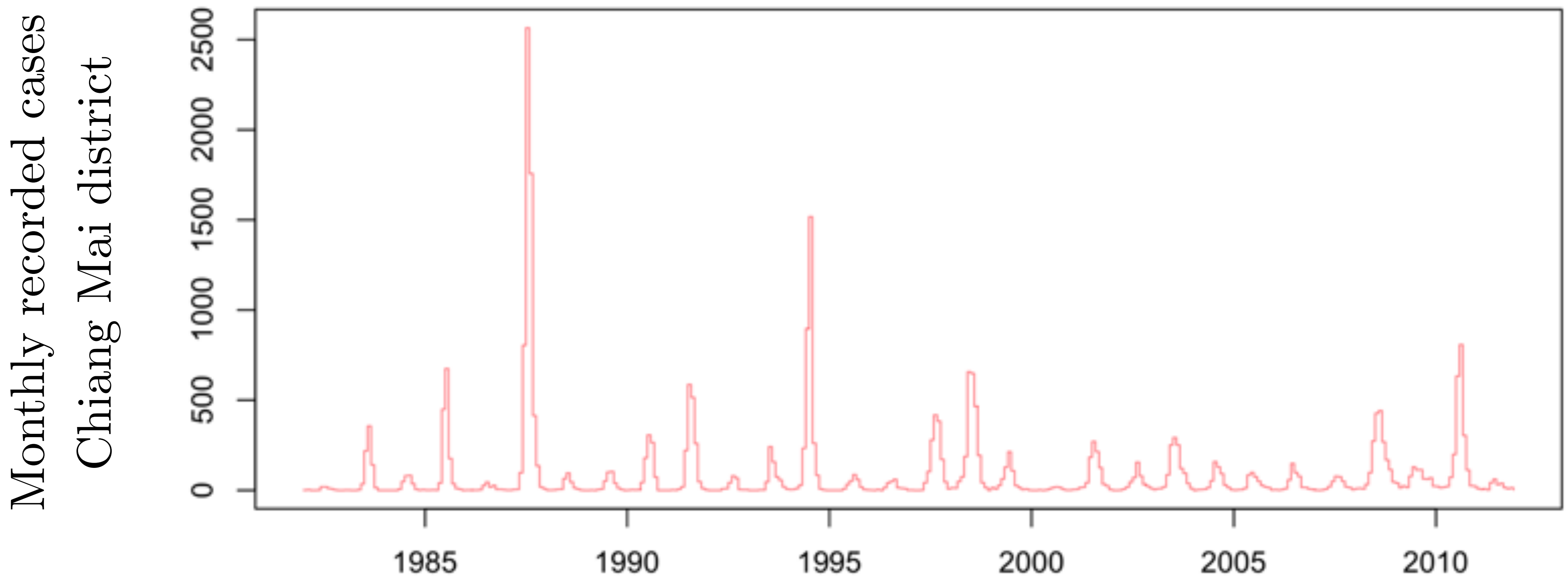
Joseph Dureau
Ecole Normale Supérieure
PhD student at London School of Economics,
Statistics Department

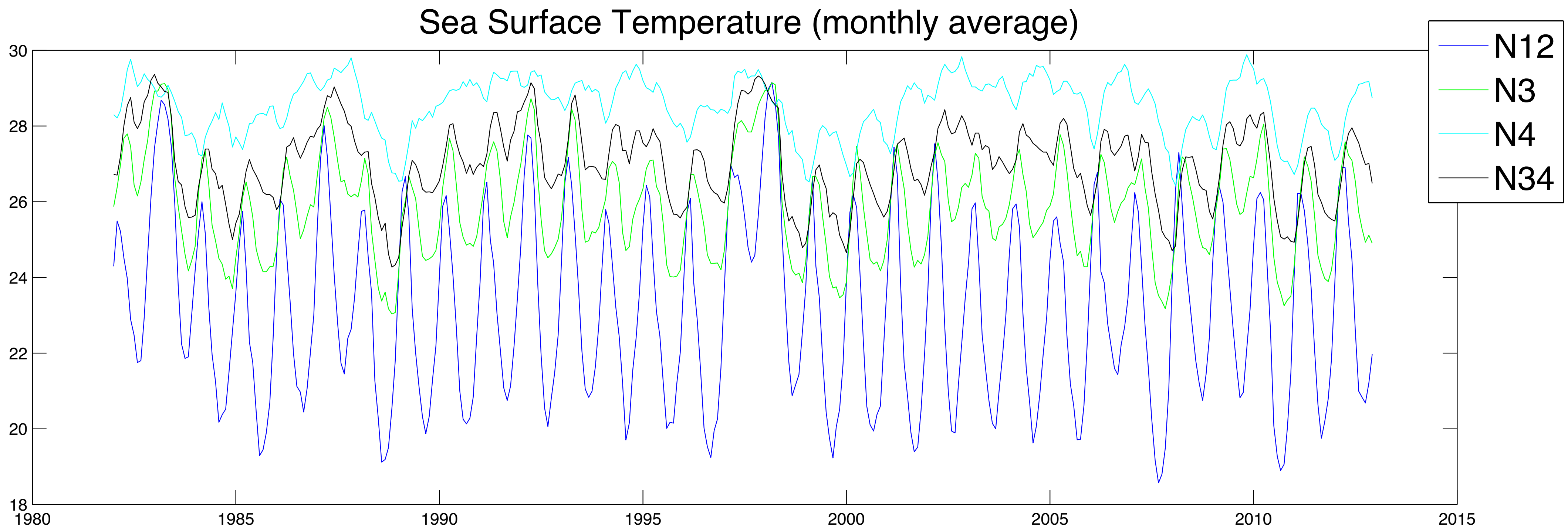
Joint work with Bernard Cazelles
as part of the DENFREE project

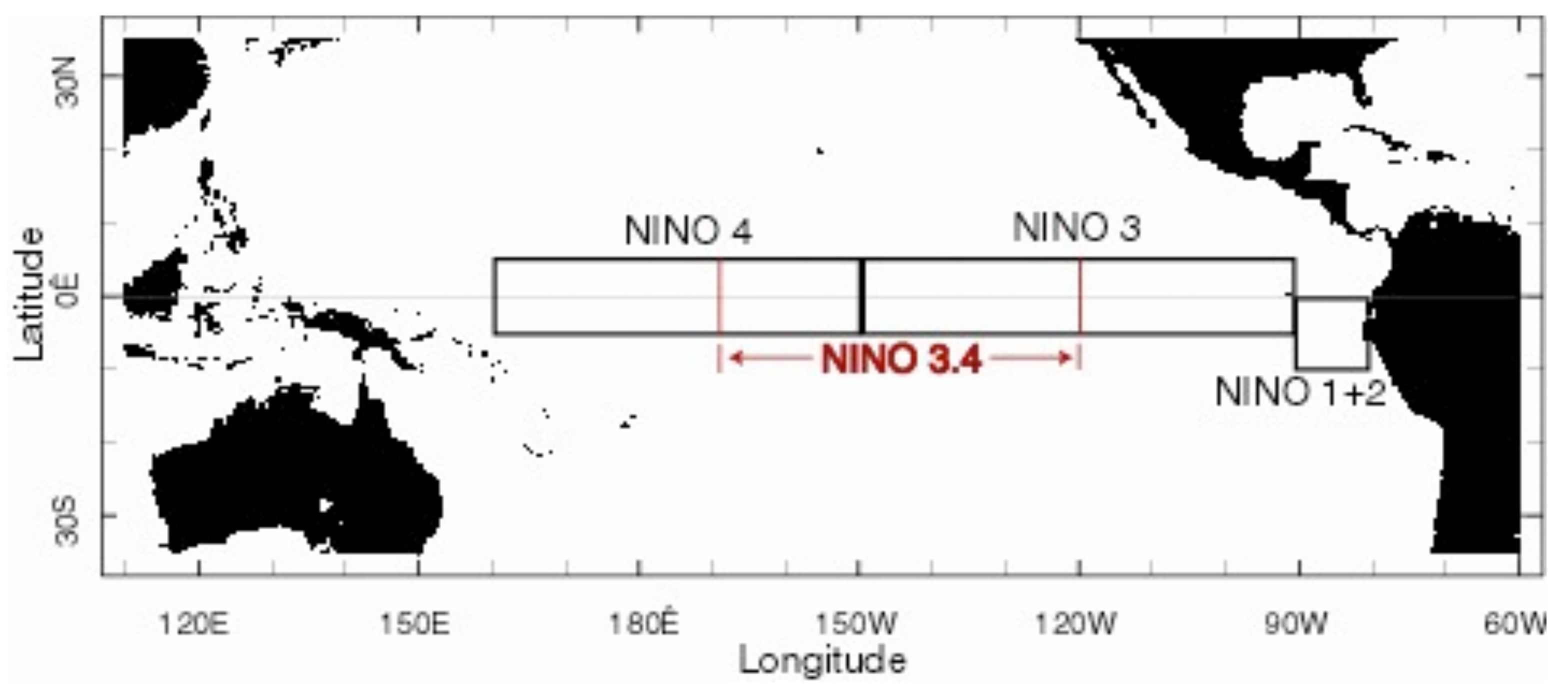
Outline

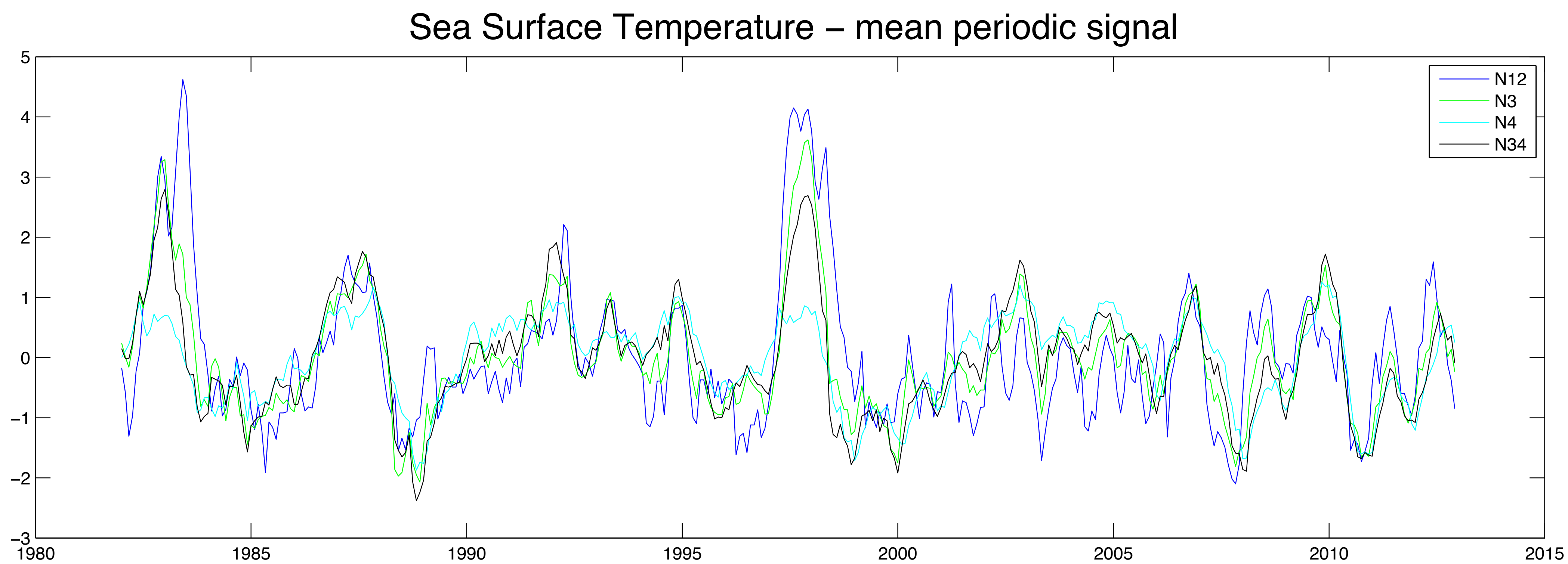
1. At first sight
2. A mechanistic modeling approach
3. Computationally intensive inference
4. Results
5. Conclusions

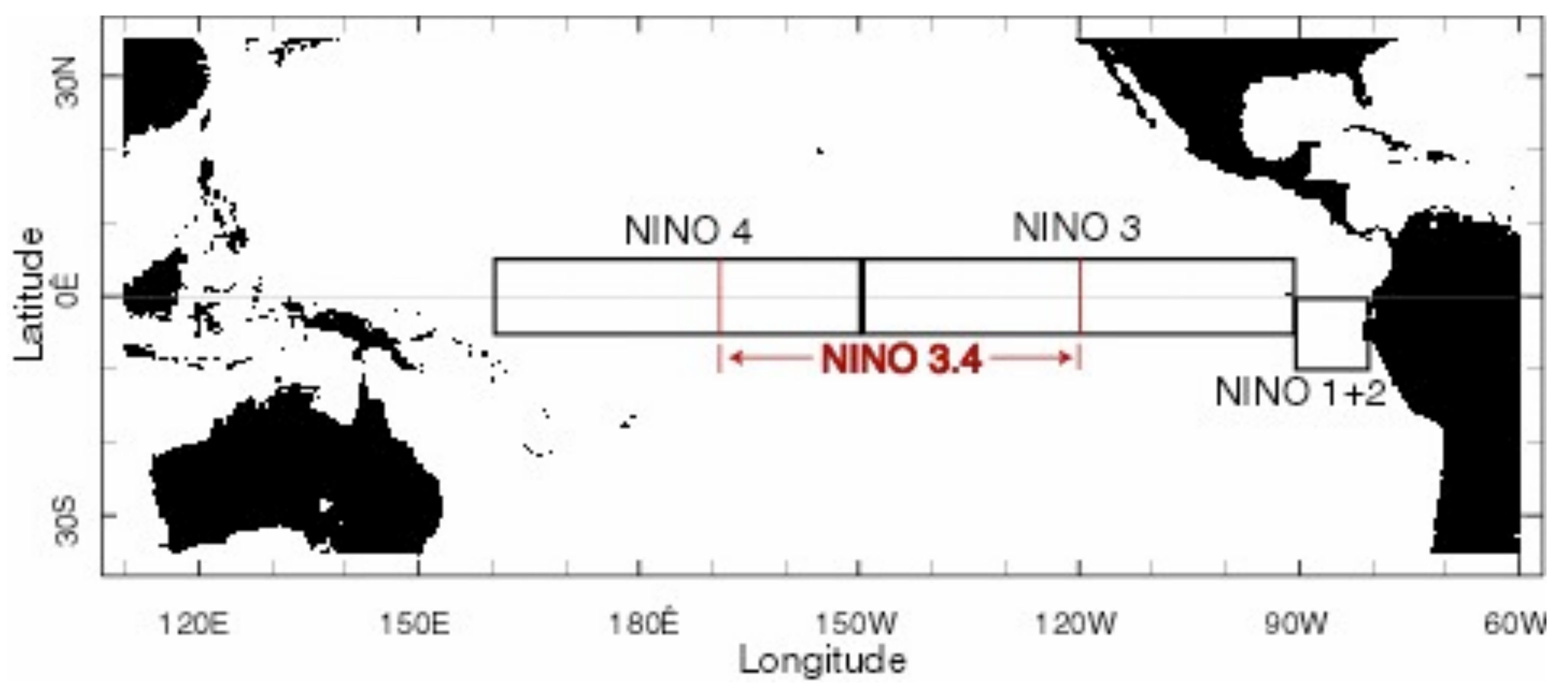
1. At first sight


Monthly recorded cases
Chiang Mai district
0
500
1000
1500
2000
2500
1985
1990
1995
2000
2005
2010


Sea Surface Temperature (monthly average)
N12
N3
N4
N34
30
28
26
24
22
20
18
1980
1985
1990
1995
2000
2005
2010
2015


30N
0E
30S
Latitude
NINO 4
NINO 3
NINO 3.4
NINO 1+2
120E
150E
180E
150W
120W
90W
60W
Longitude


Sea Surface Temperature – mean periodic signal
N12
N3
N4
N34
1980
1985
1990
1995
2000
2005
2010
2015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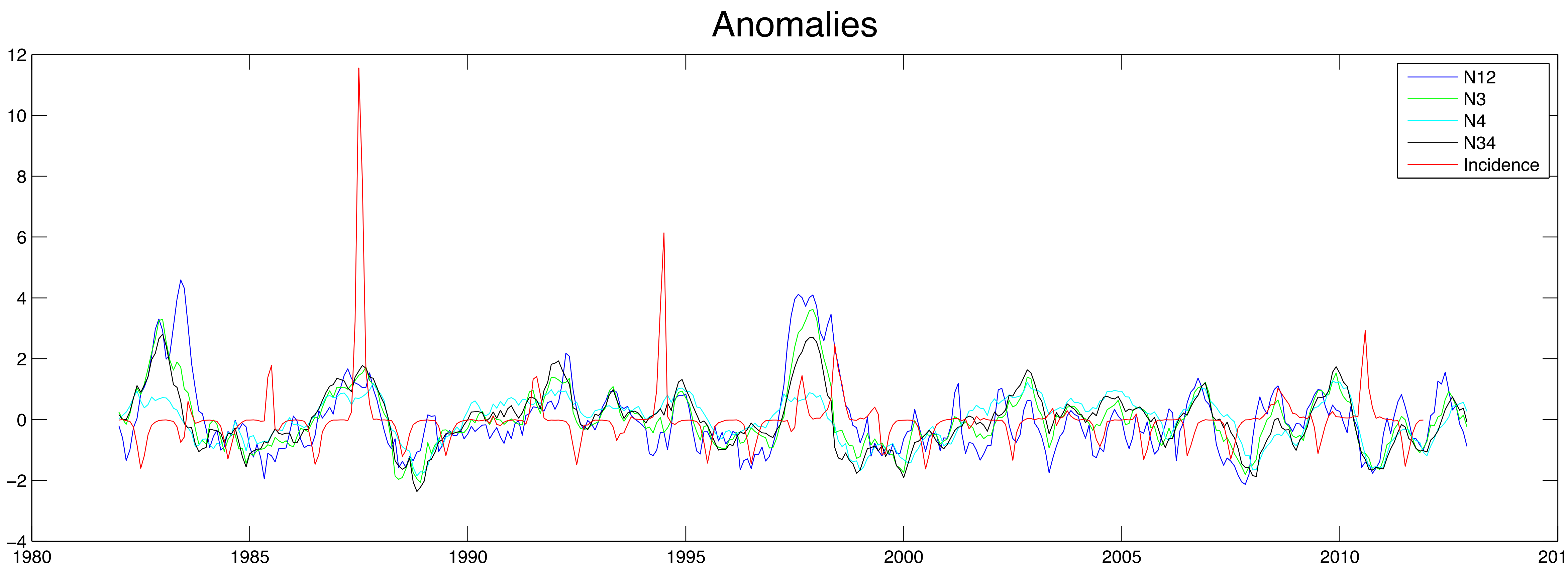
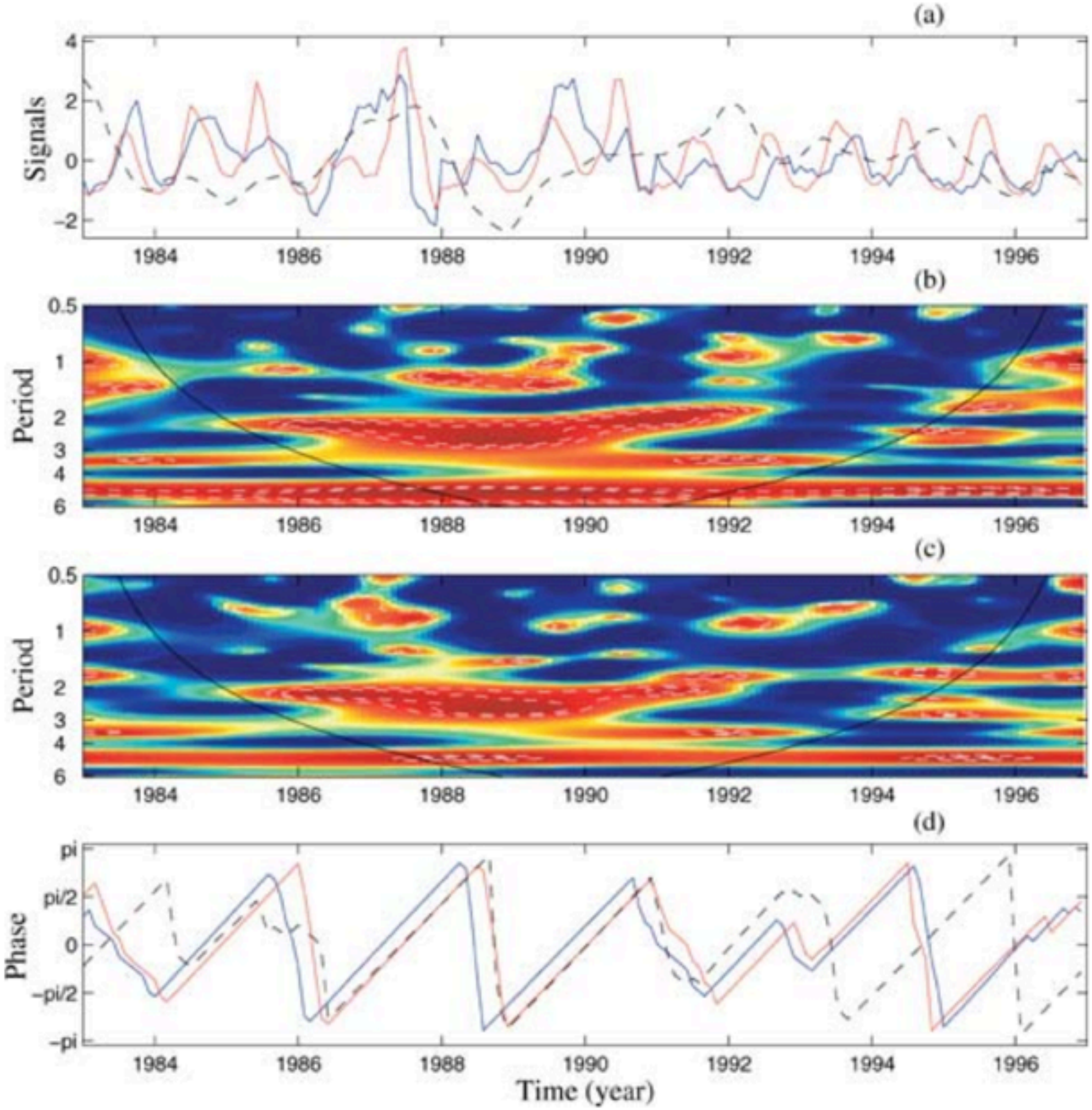


	Lag (months)	Correlation	p-value
N12	-6	0.17	0.001
N3	-6	0.17	0.001
N4	-6	0.16	0.002
N34	-6	0.19	0.0002



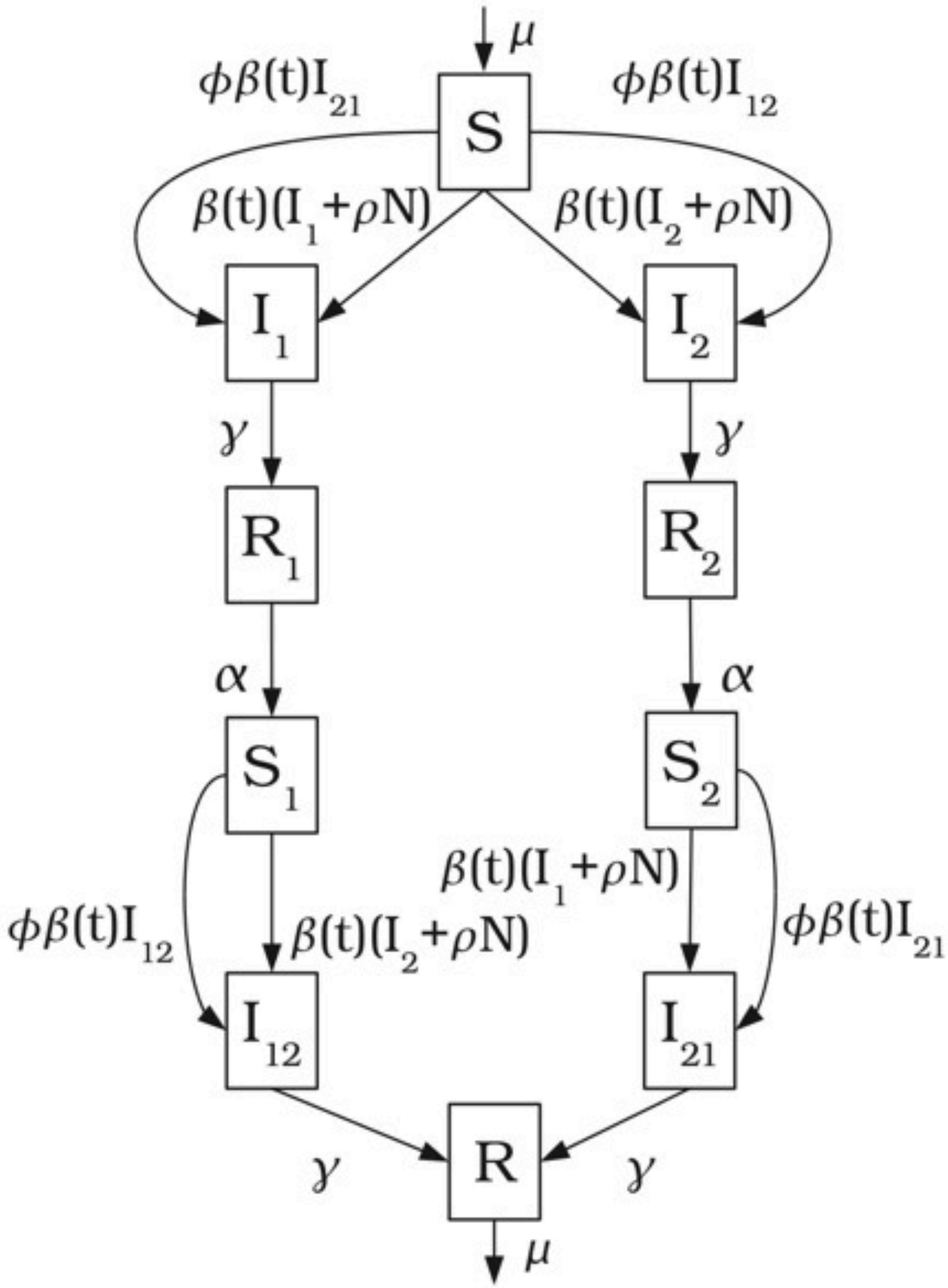
"(...) significant association between El Niño, climate variables, and DHF incidence for Bangkok and for the rest of Thailand.'

"Dengue in Bangkok seems to precede the oscillations of the Nino 3 index."

"These findings do not exclude an important role for other factors, such as intrinsic disease dynamics, in explaining patterns of dengue incidence in Thailand."

Cazelles, B., Chavez, M., McMichael, A. J., & Hales, S. (2005). Nonstationary influence of El Nino on the synchronous dengue epidemics in Thailand. *PLoS medicine*, *2*(4), e106.

2. A mechanistic modeling approach

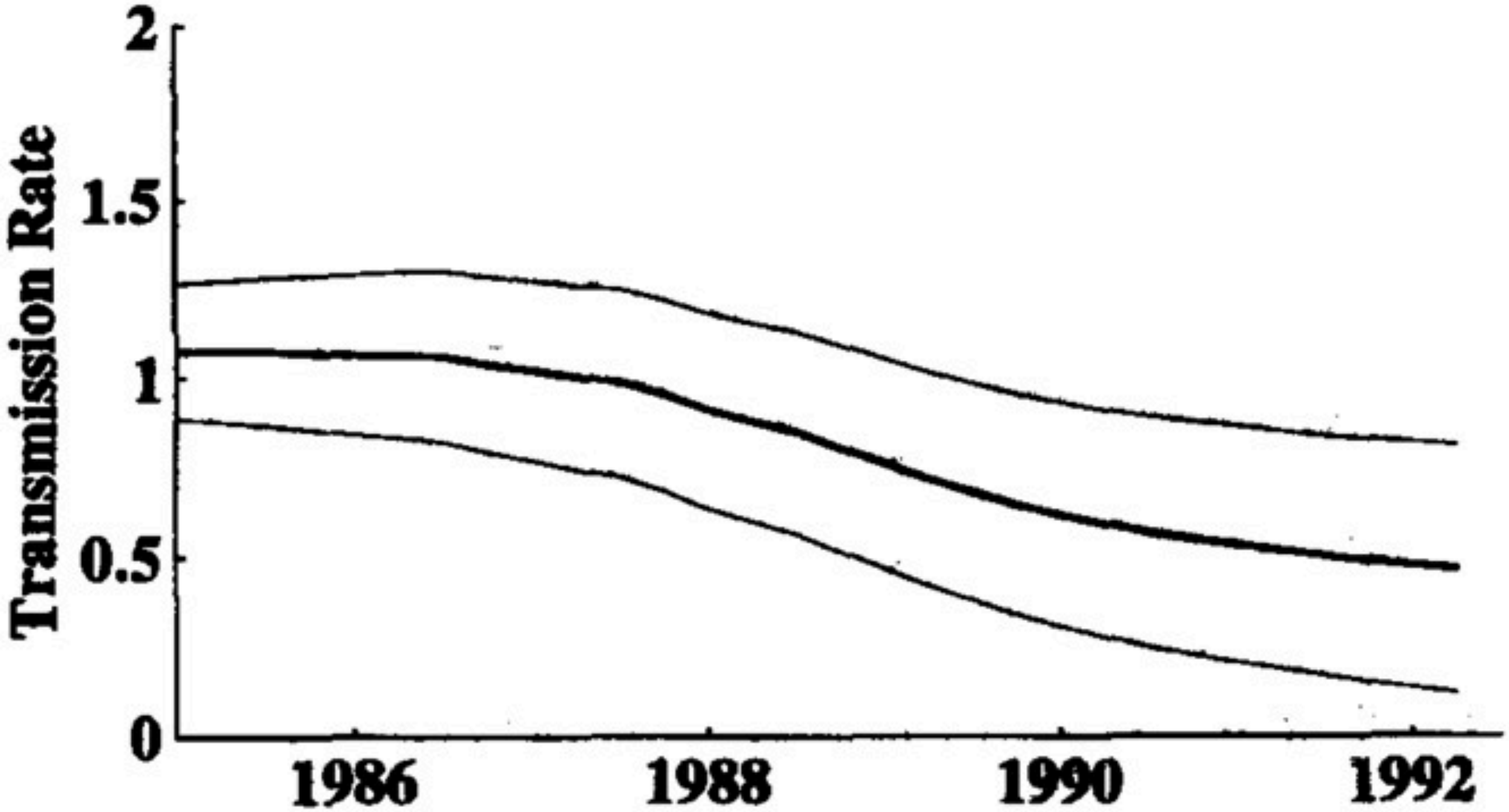


$$\beta_t = \beta_0 * (1 + e * cos(\omega(t + \phi)) + \tilde{\beta}_t)$$

Aguiar, M., Ballesteros, S., Kooi, B. W., & Stollenwerk, N. (2011). The role of seasonality and import in a minimalistic multi-strain dengue model capturing differences between primary and secondary infections: complex dynamics and its implications for data analysis. *Journal of Theoretical Biology*, *289*, 181-196.

Capturing unknown variations of a key parameter

HIV transmission rate among the Parisian gay community



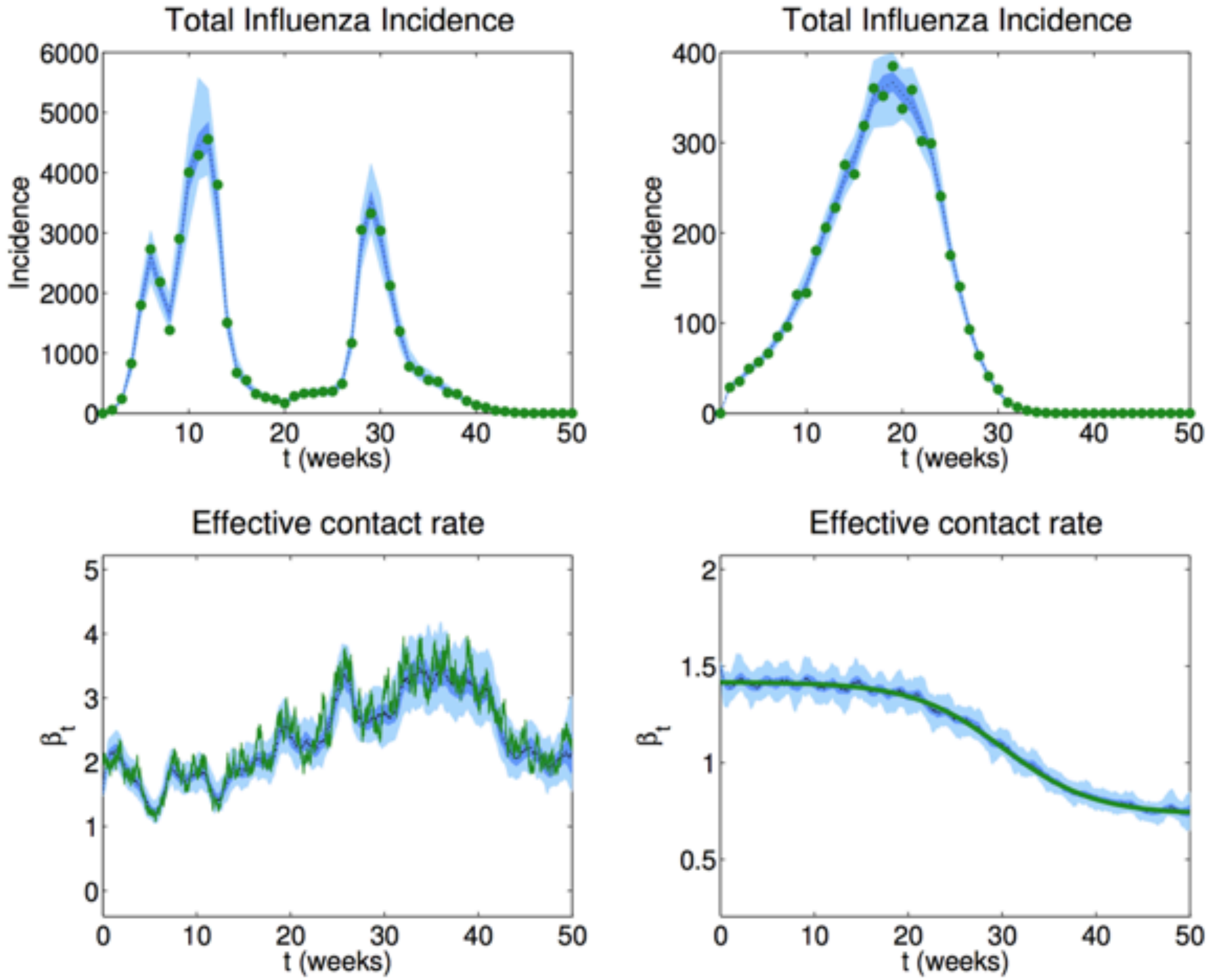
$$\beta_t = \sigma dB_t$$

Cazelles, B., & Chau, N. P. (1997). Using the Kalman filter and dynamic models to assess the changing HIV/AIDS epidemic. *Mathematical biosciences*, *140*(2), 131-154.

Capturing unknown variations of a key parameter

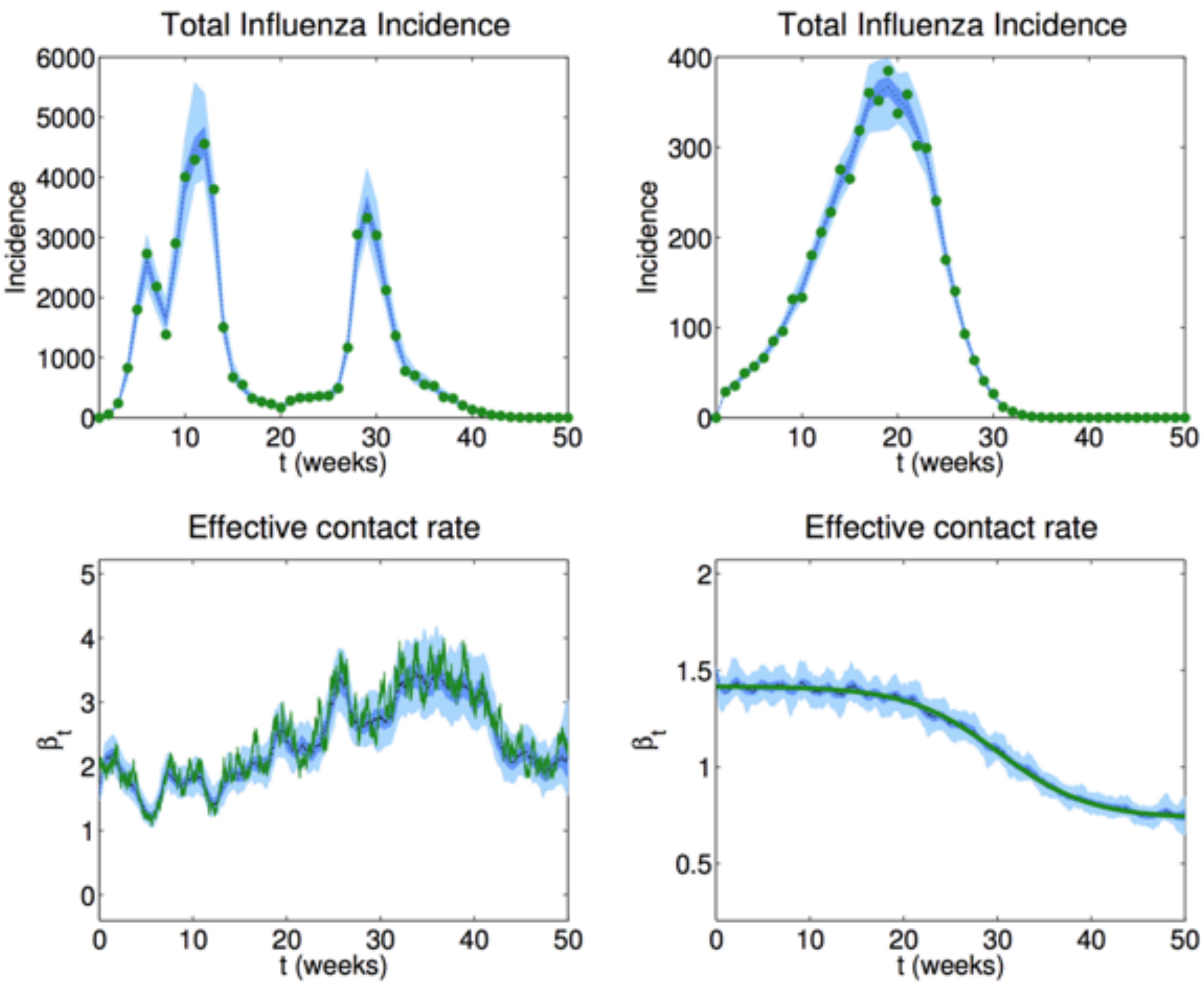
$$
\begin{cases}
\dfrac{dS_t}{dt} = -\beta_t S_t \dfrac{I_t}{N} \\
\dfrac{dE_t}{dt} = \beta_t S_t \dfrac{I_t}{N} - kE_t \\
\dfrac{dI_t}{dt} = kE_t - \gamma I_t \\
\dfrac{dR_t}{dt} = \gamma I_t \\
d\log(\beta_t) = \sigma dB_t
\end{cases}
$$

Capturing unknown variations of a key parameter



- Simulated incidence observations
- Simulated unobserved path of β_t
- 95% credible interval
- 50% credible interval

Capturing unknown variations of a key parameter



- Simulated incidence observations
- Simulated unobserved path of β_t
- 95% credible interval
- 50% credible interval

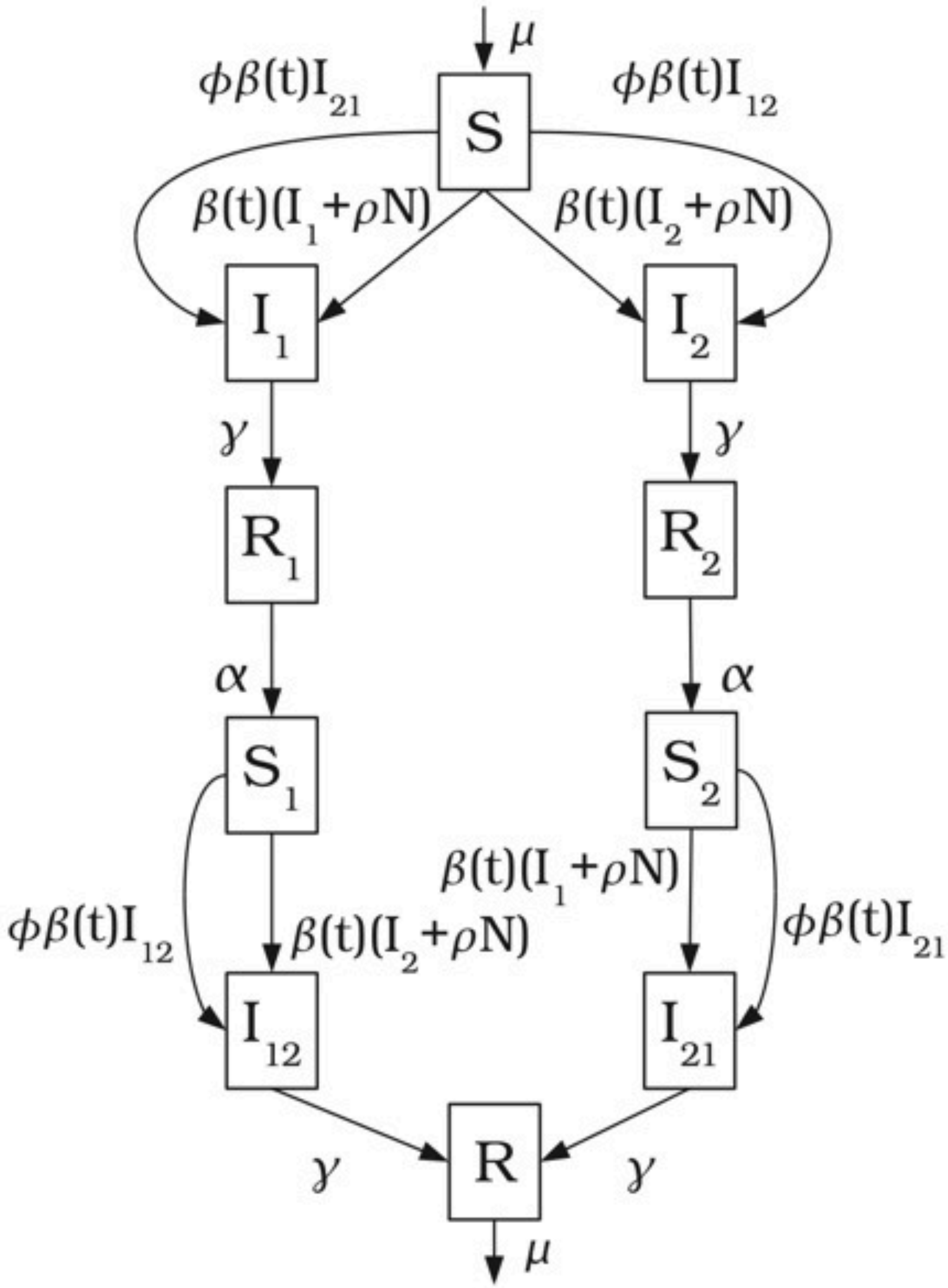
Generic framework:

$$dh(\beta_t) = \mu(\beta_t, \theta)dt + \sigma(\beta_t, \theta)dB_t$$

Exact exploration of $p_\delta(\beta_t|\theta^*, y_{1:n})$
or $p_\delta(\beta_t|y_{1:n})$

Robust algorithm when $\delta \to 0$

Dureau, J., Kalogeropoulos, K., & Baguelin, M. (2012). Capturing the time-varying drivers of an epidemic using stochastic dynamical systems. *arXiv preprint arXiv: 1203.5950.*



$$\beta_t = \beta_0 * (1 + e * cos(\omega(t+\phi)) + \tilde{\beta}_t)$$

$$d\, logit_{[-0.3;0.3]}(\tilde{\beta}_t) = \sigma dB_t$$

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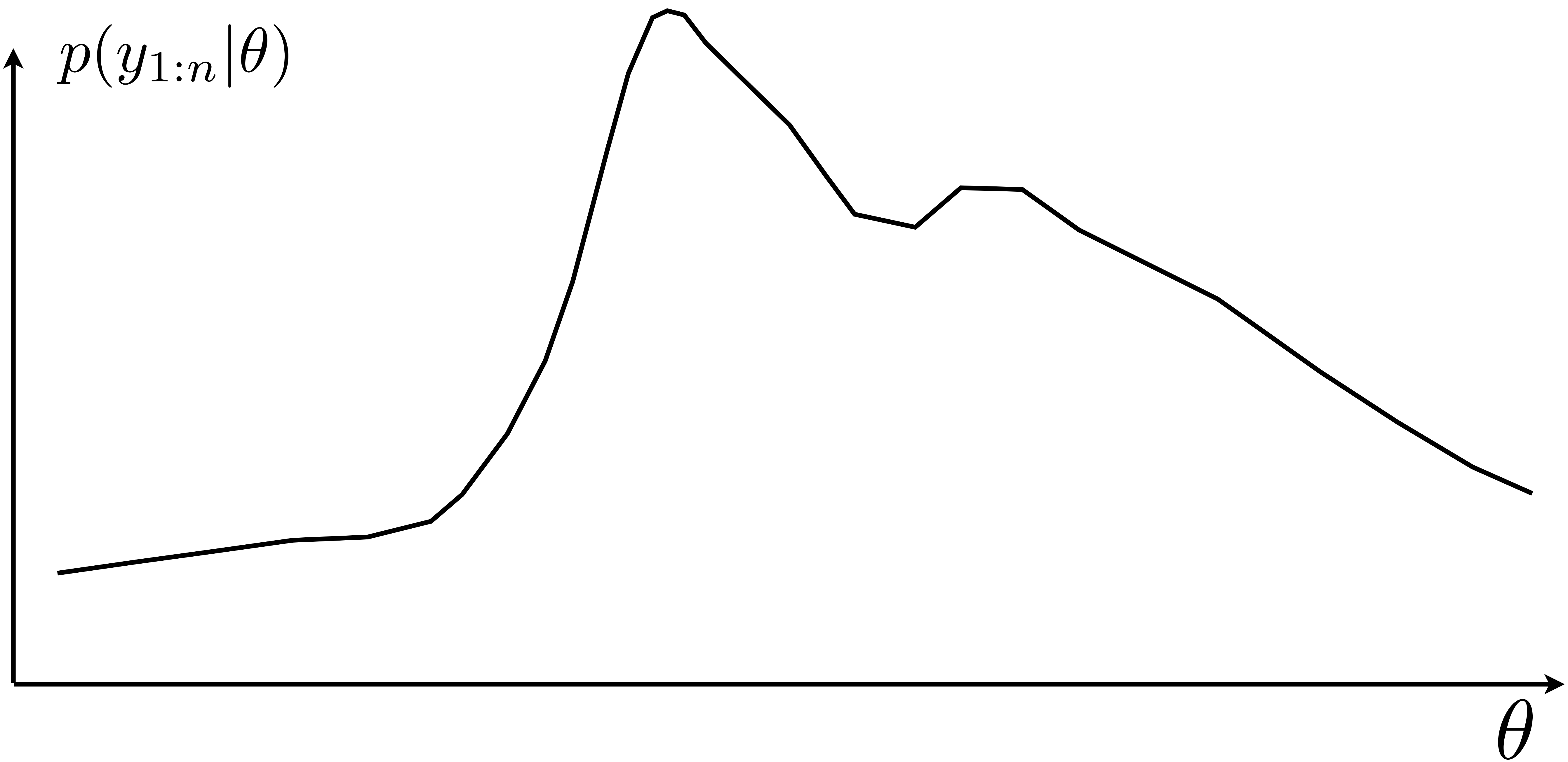
3. Computationally intensive inference

Iterated Filtering

a simplified view

Ionides, E. L., Bretó, C., & King, A. A. (2006). Inference for nonlinear dynamical systems. *Proceedings of the National Academy of Sciences*, *103*(49), 18438-18443.



Iterated Filtering

a simplified view

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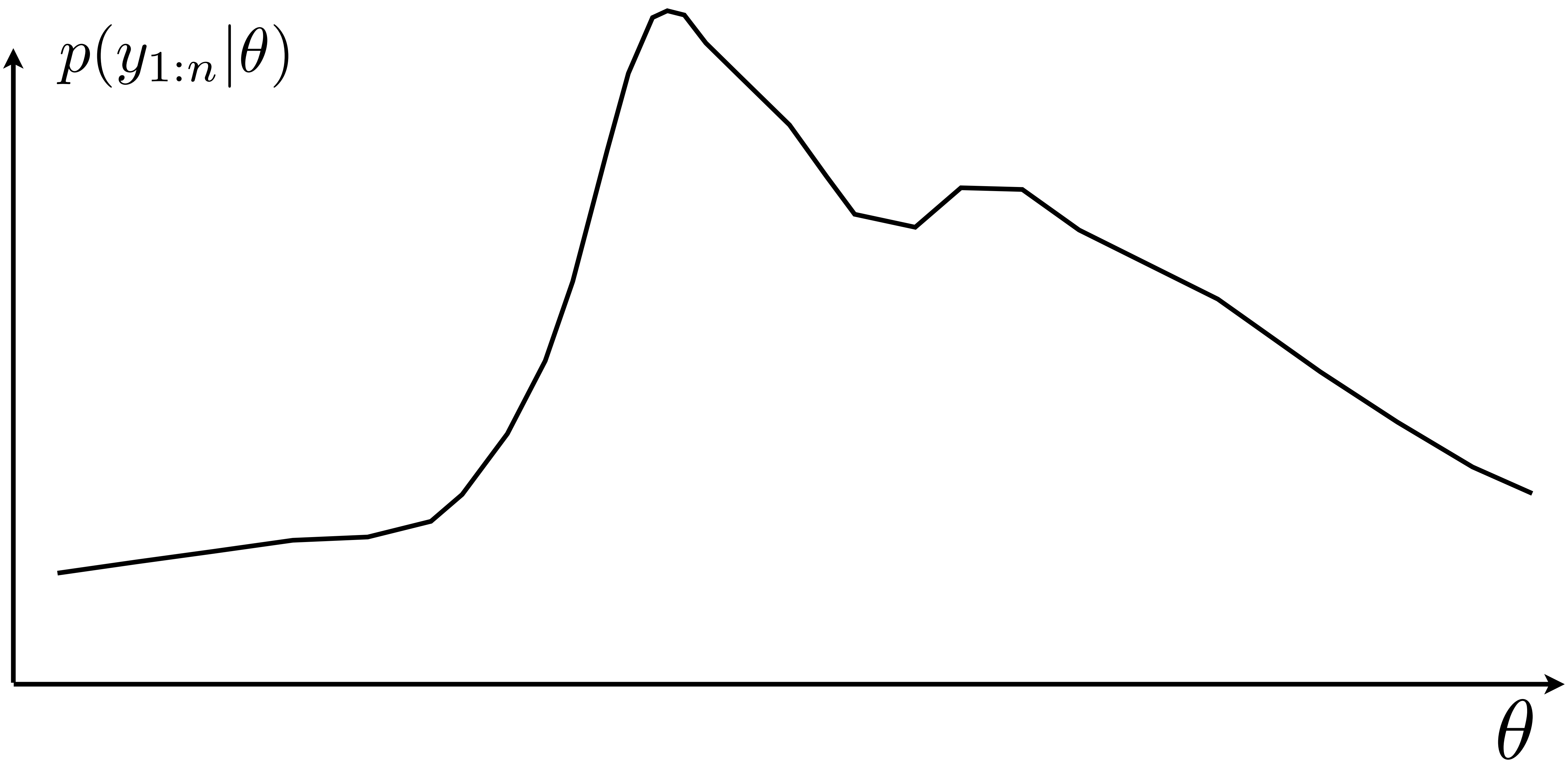

here, $\dim(\theta)=19$

Iterated Filtering

a simplified view

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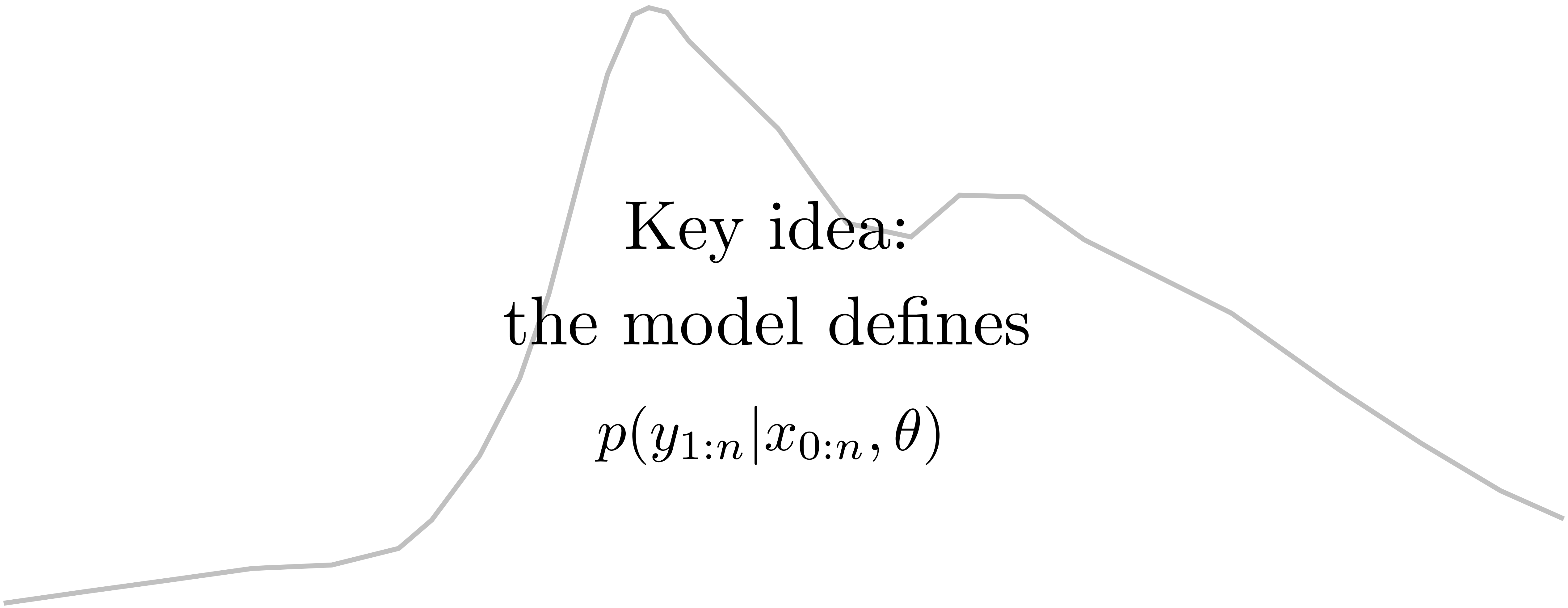


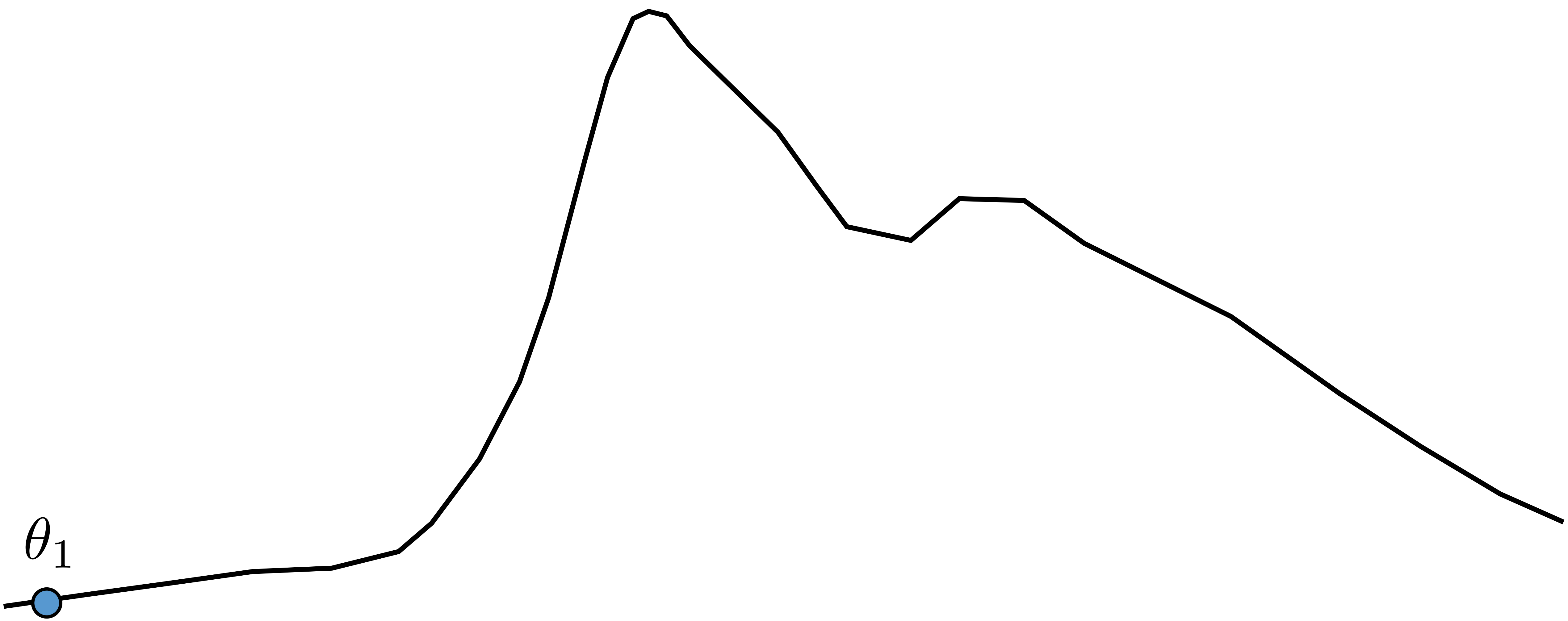
Key idea:

the model defines

$$p(y_{1:n}|x_{0:n},\theta)$$

Iterated Filtering

a simplified view



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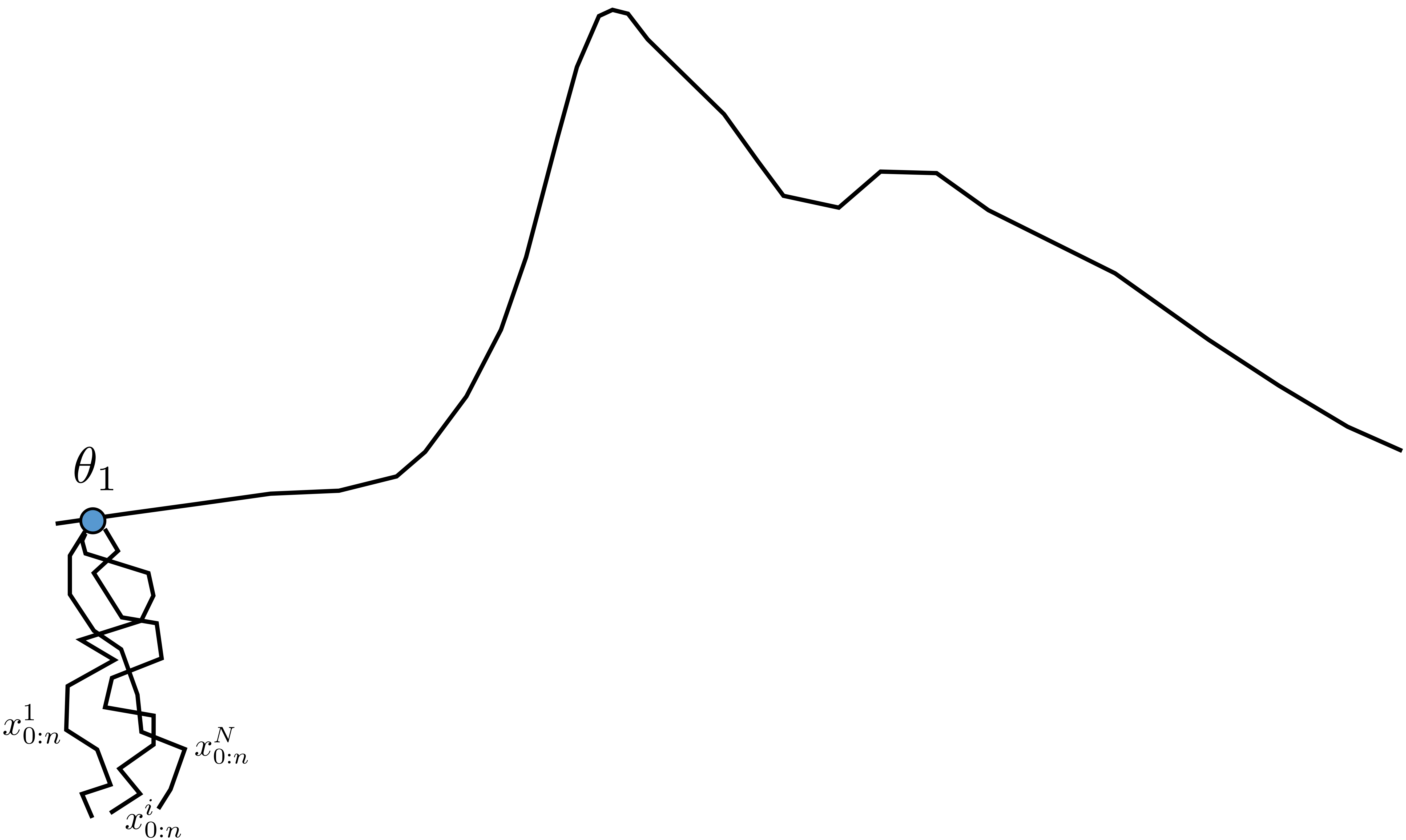

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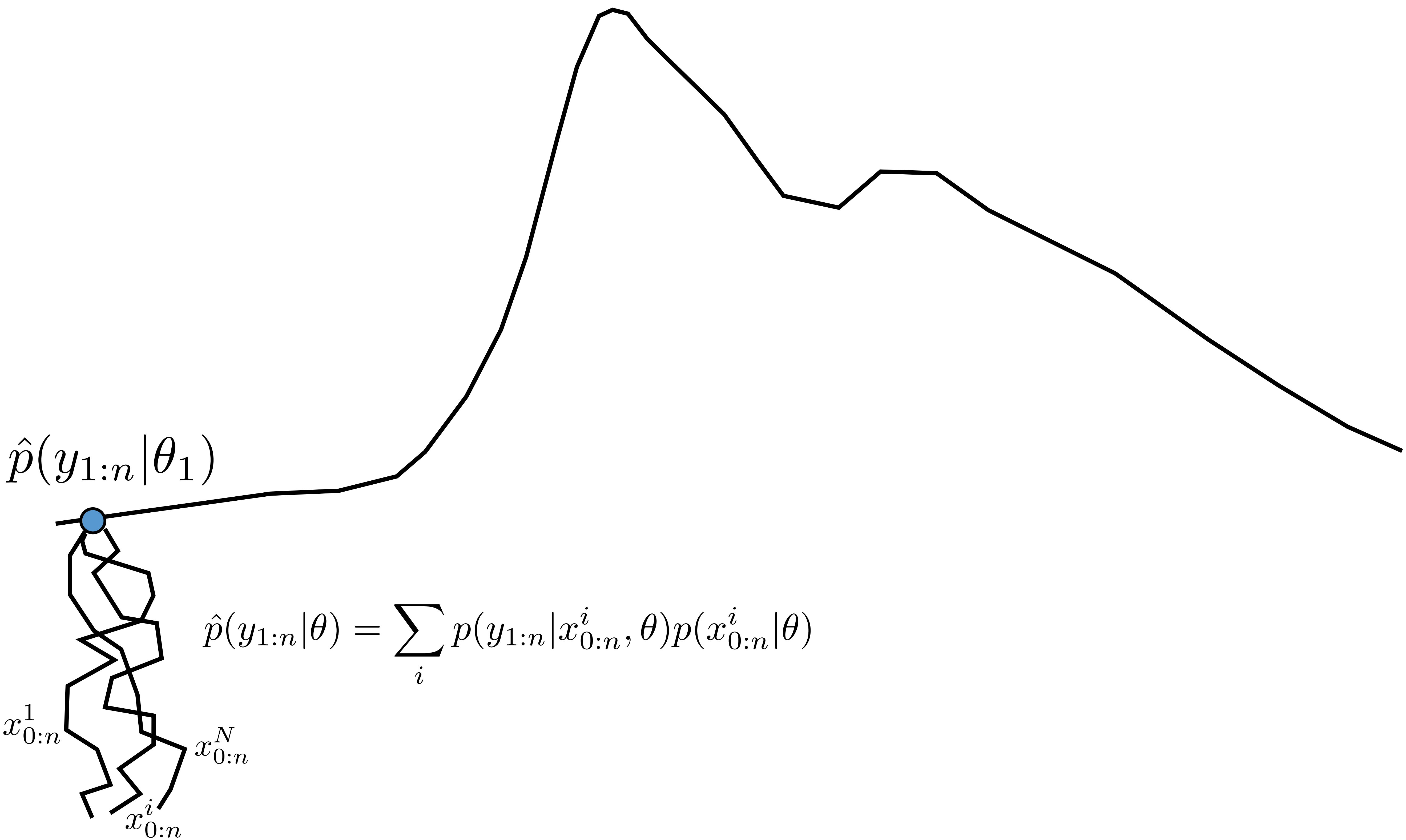
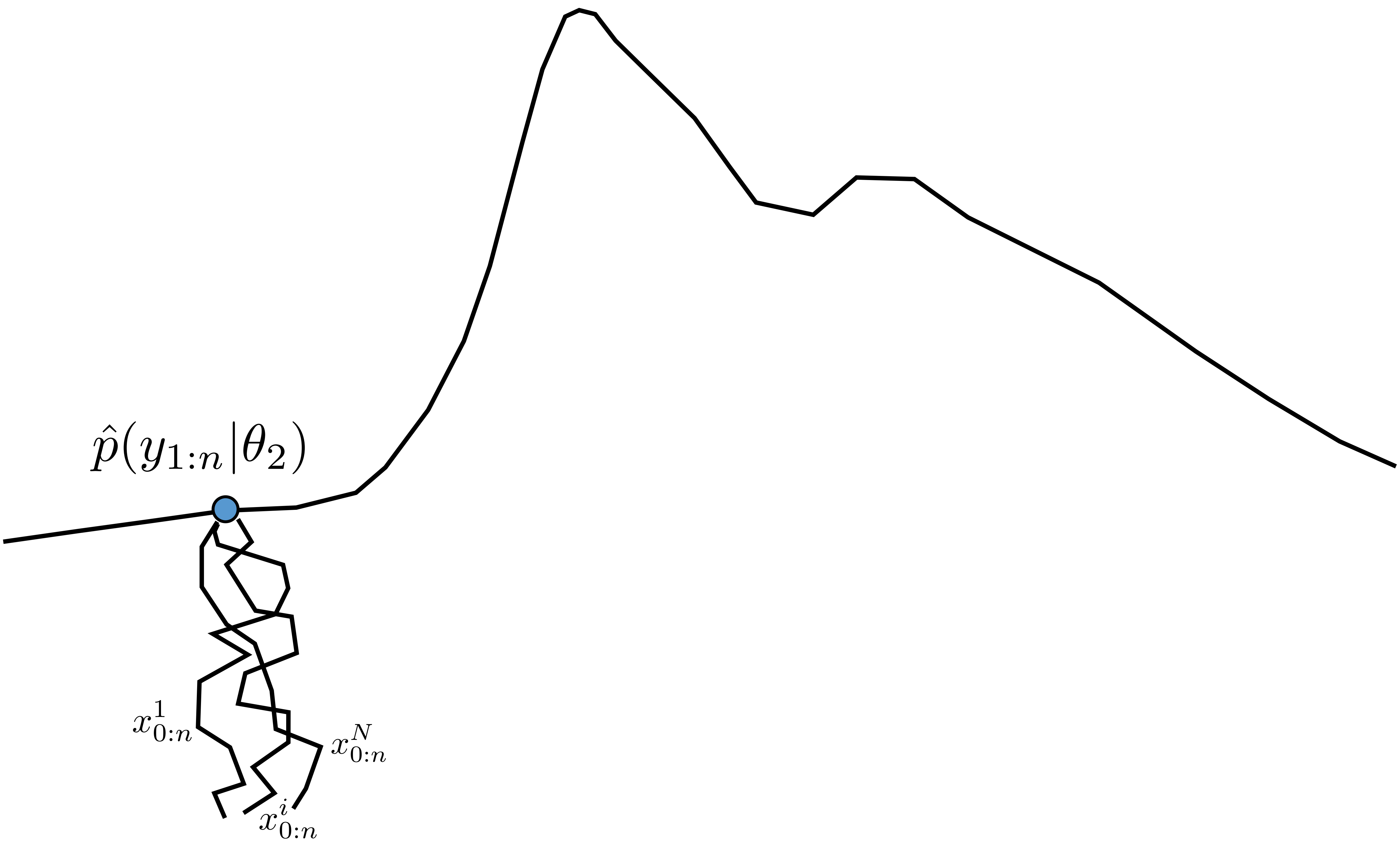


$$\hat{p}(y_{1:n}|\theta) = \sum_i p(y_{1:n}|x^i_{0:n}, \theta)p(x^i_{0:n}|\theta)$$

Iterated Filtering

a simplified view



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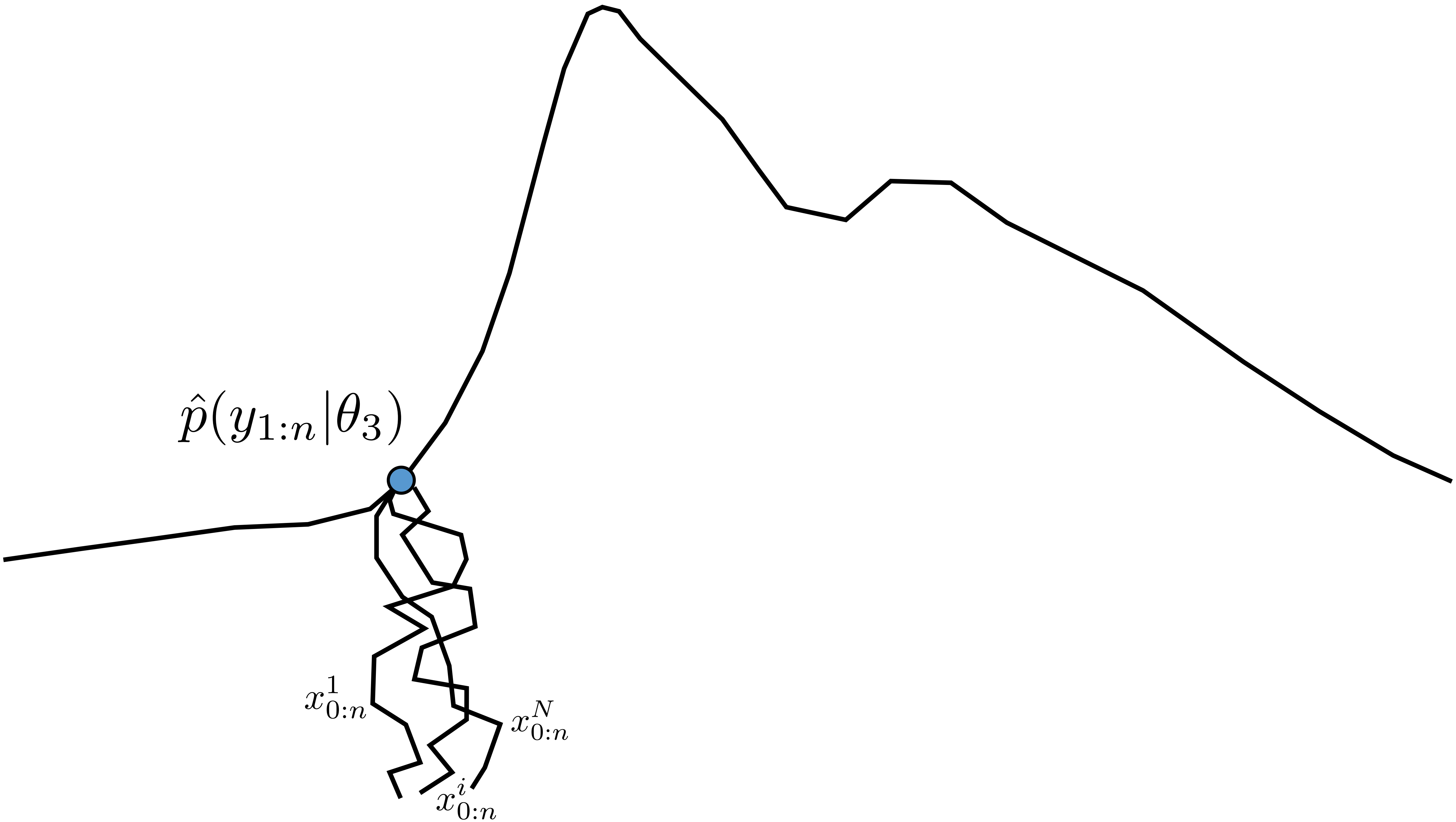

Iterated Filtering

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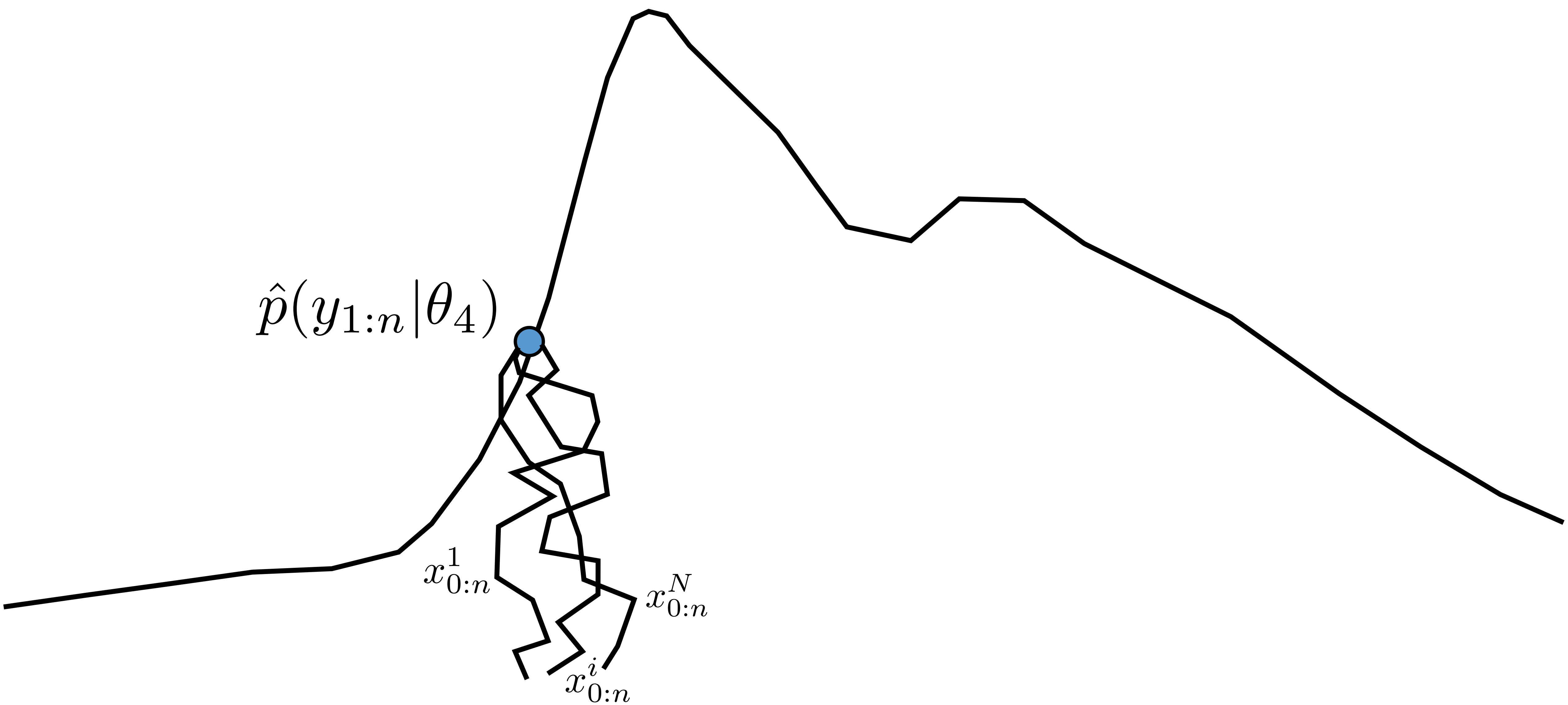

Iterated Filtering

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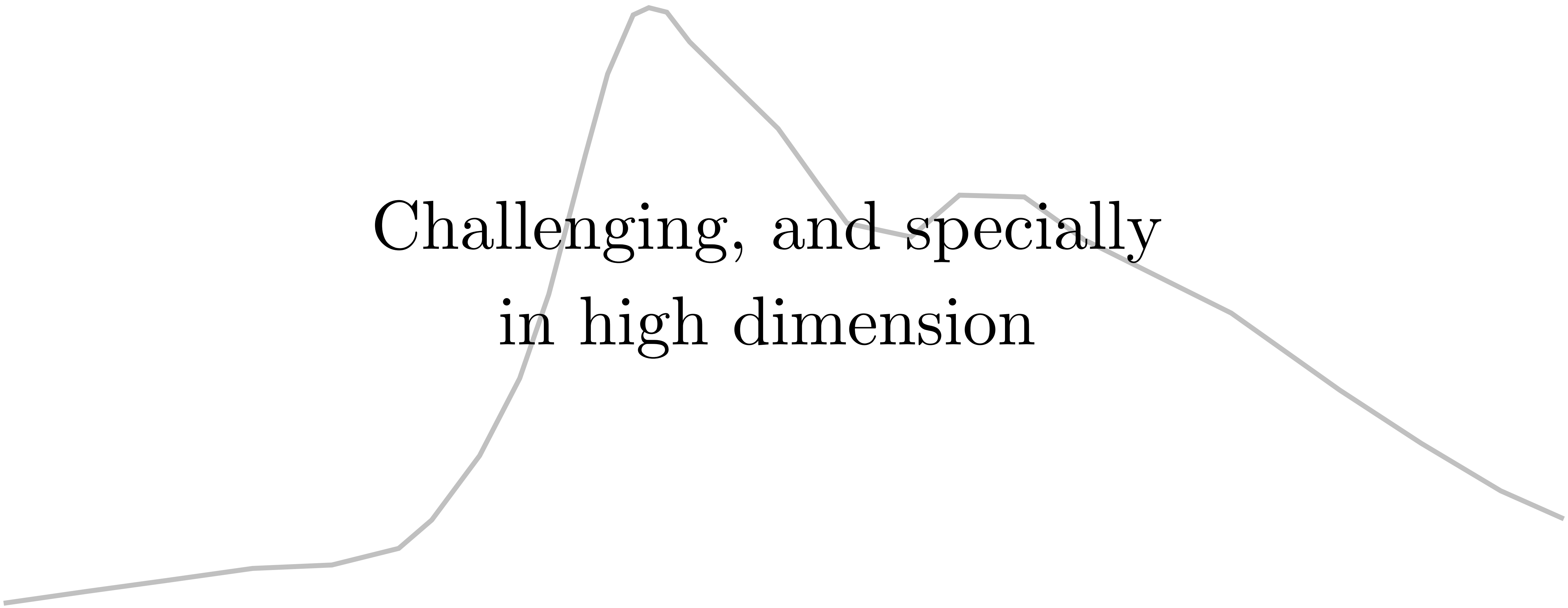
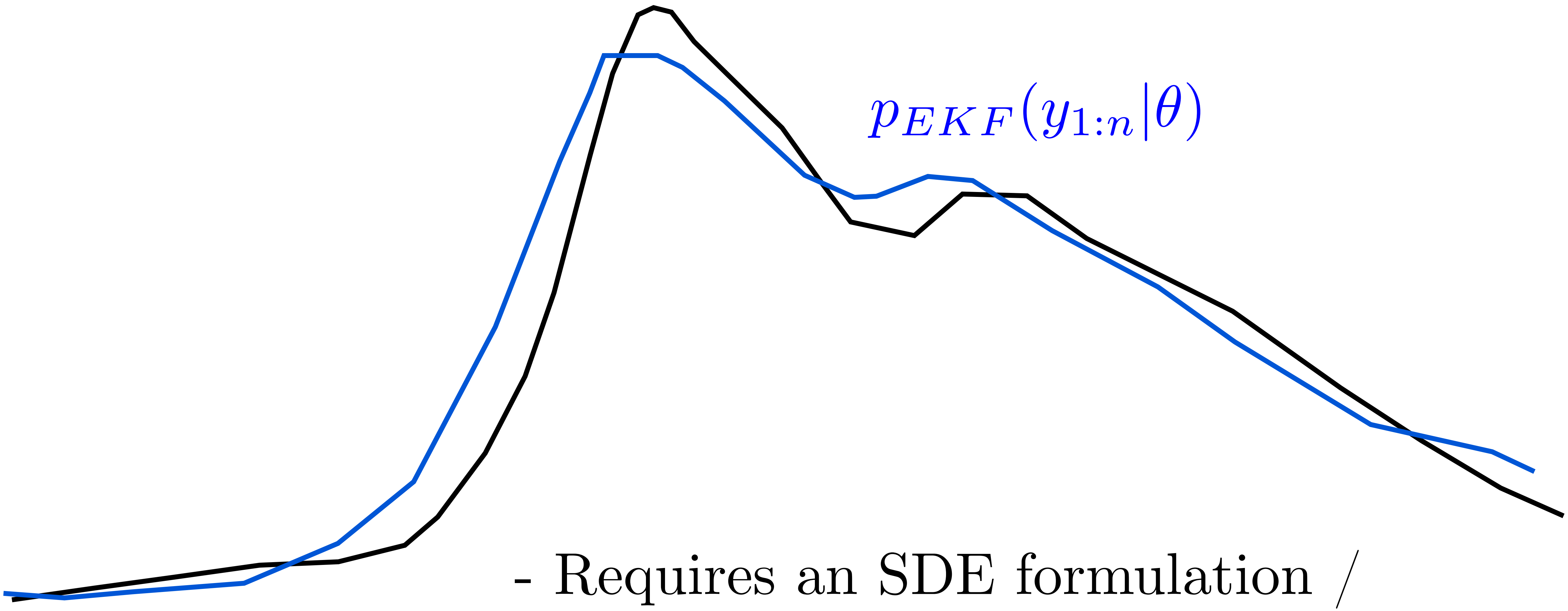


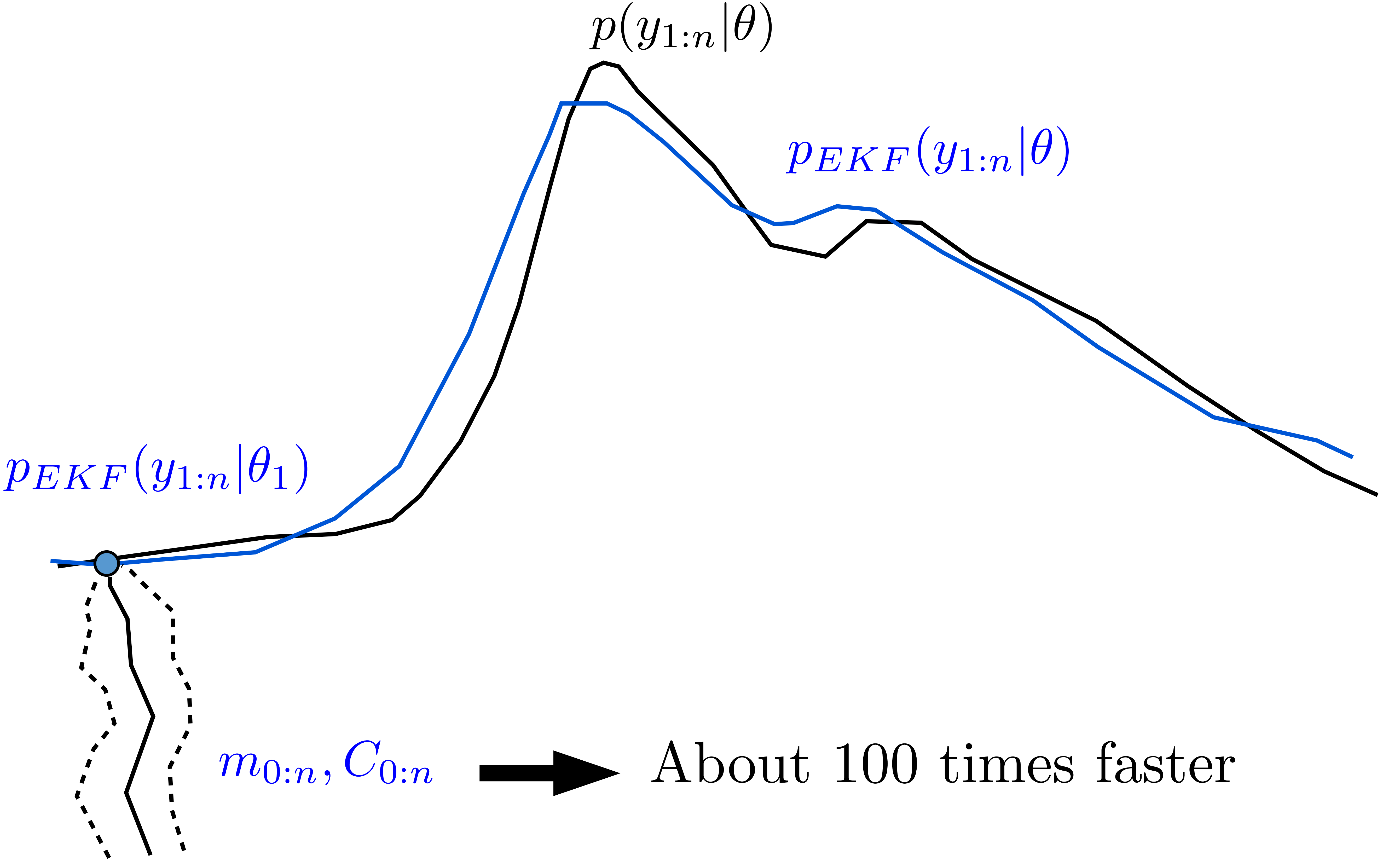
Challenging, and specially in high dimension

Relying on the Extended Kalman Filter



- Requires an SDE formulation / approximation of the model
- Relies on a Gaussian approximation of $p(x_t|y_{1:n},\theta)$ and $p(y_{1:n}|x_t,\theta)$

Relying on the Extended Kalman Filter



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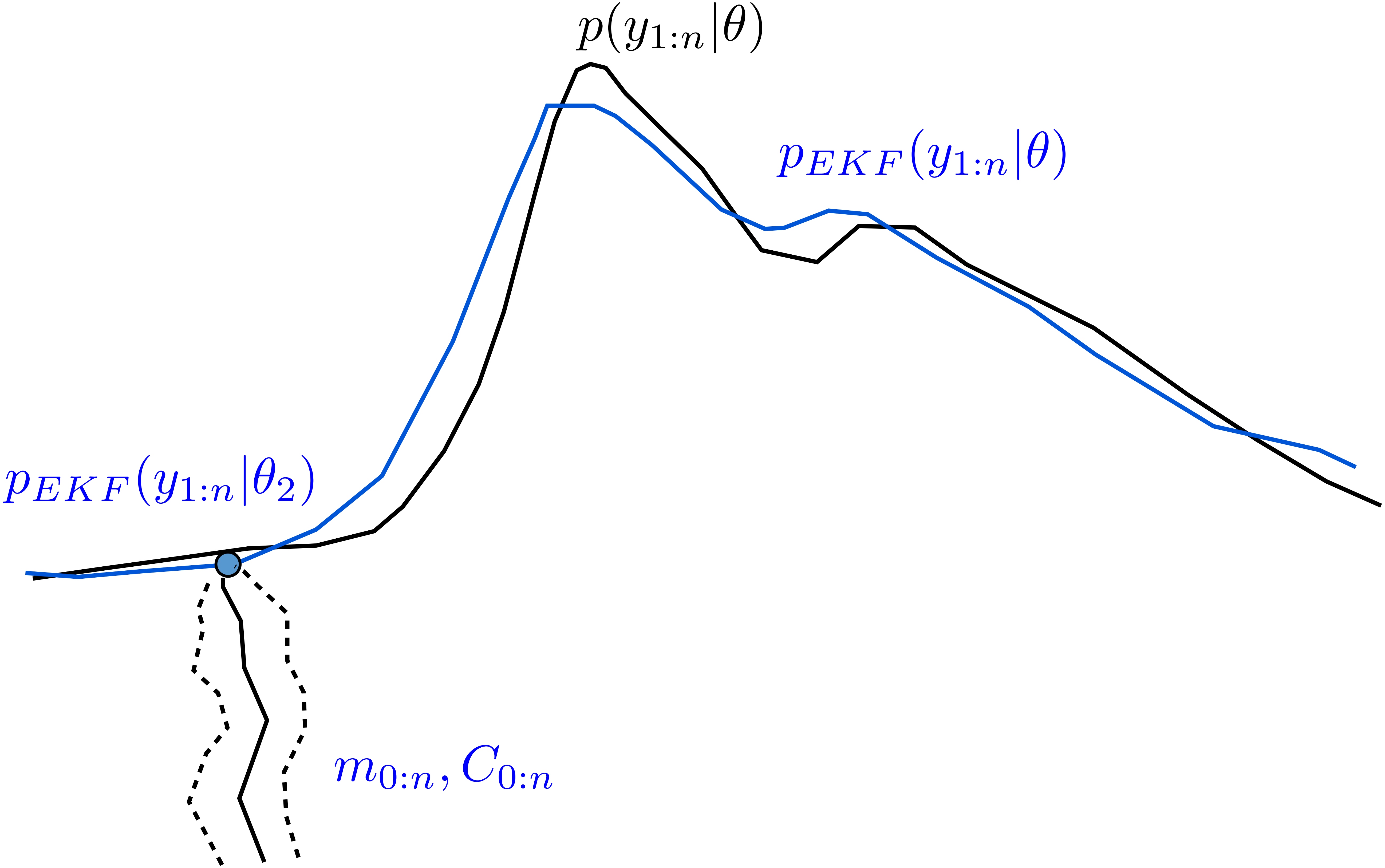

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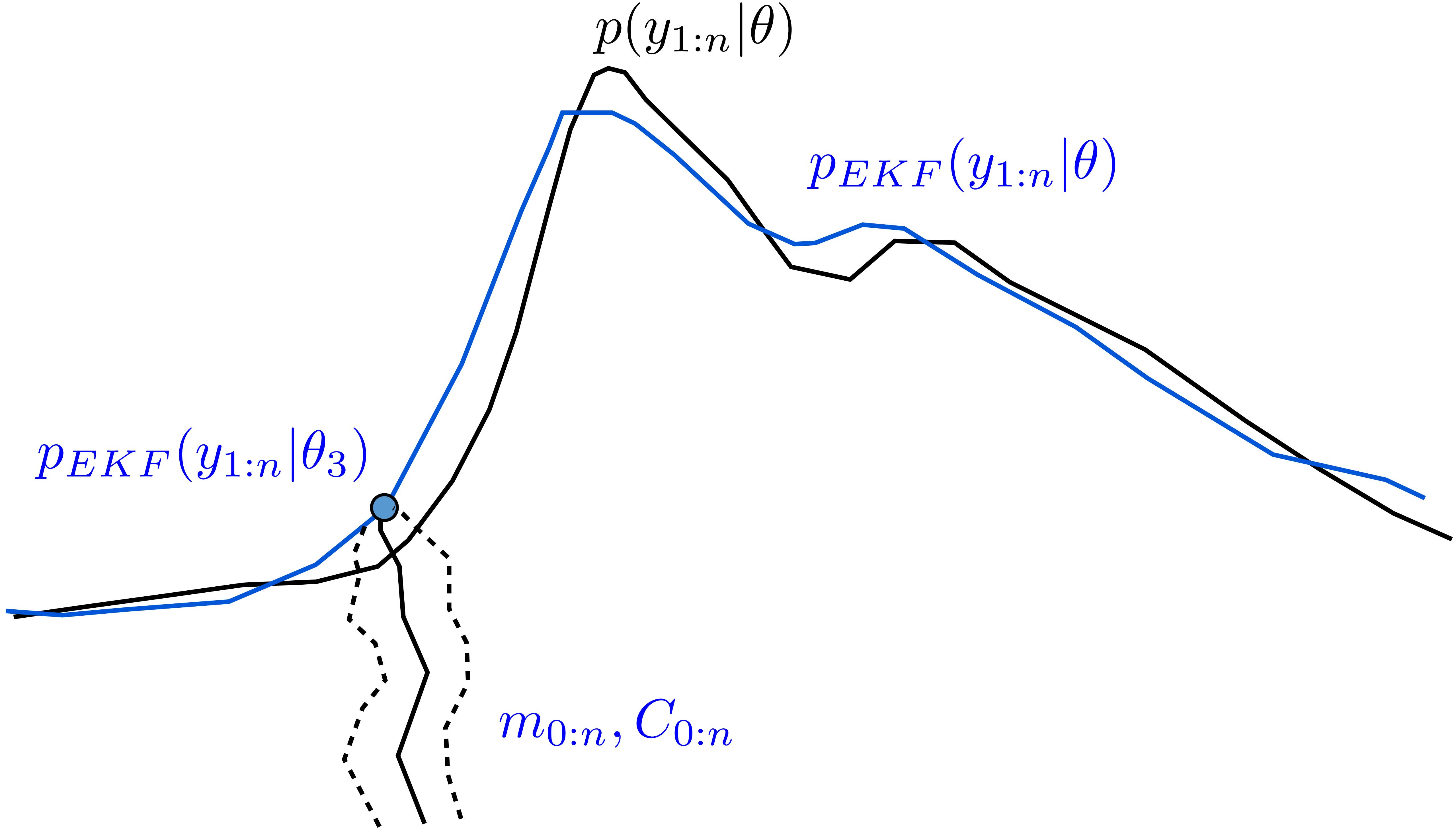

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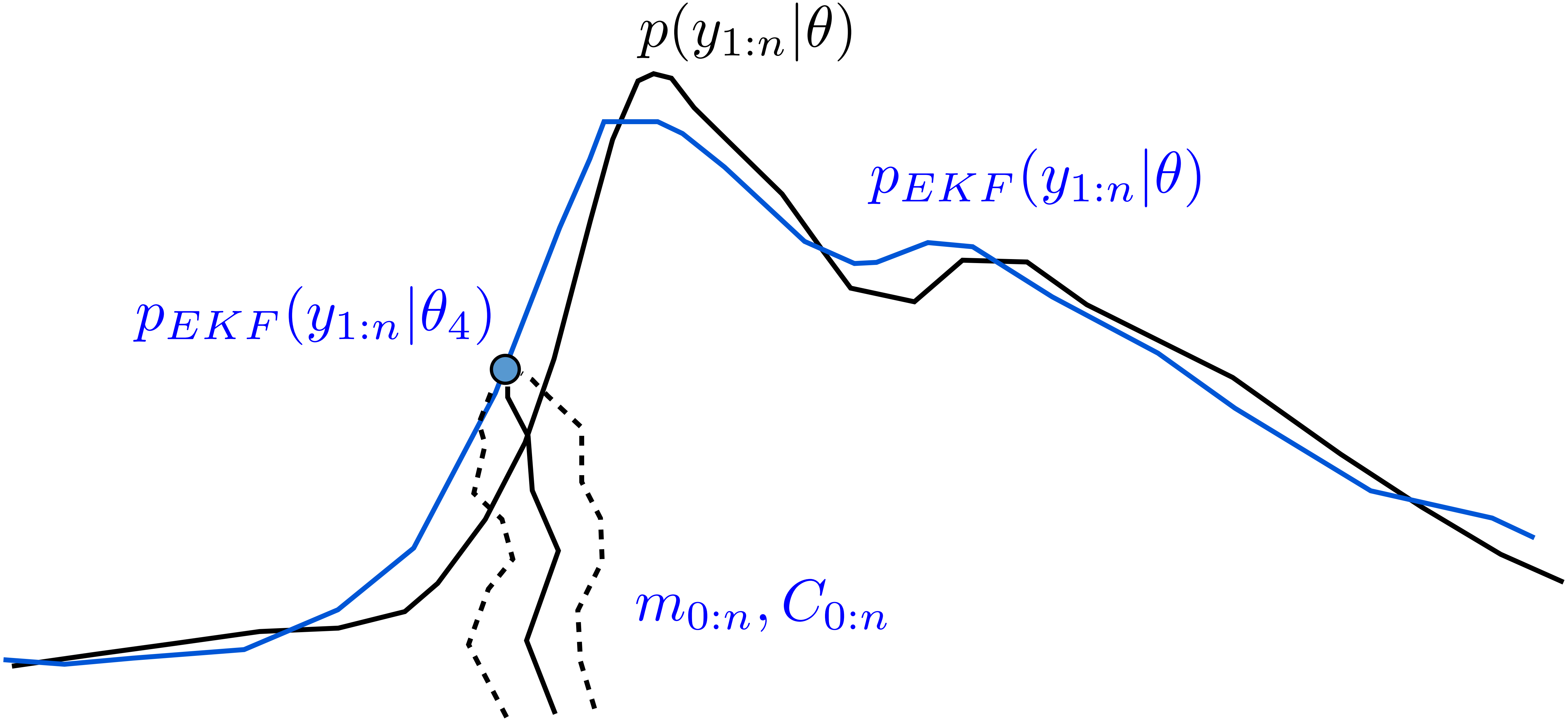

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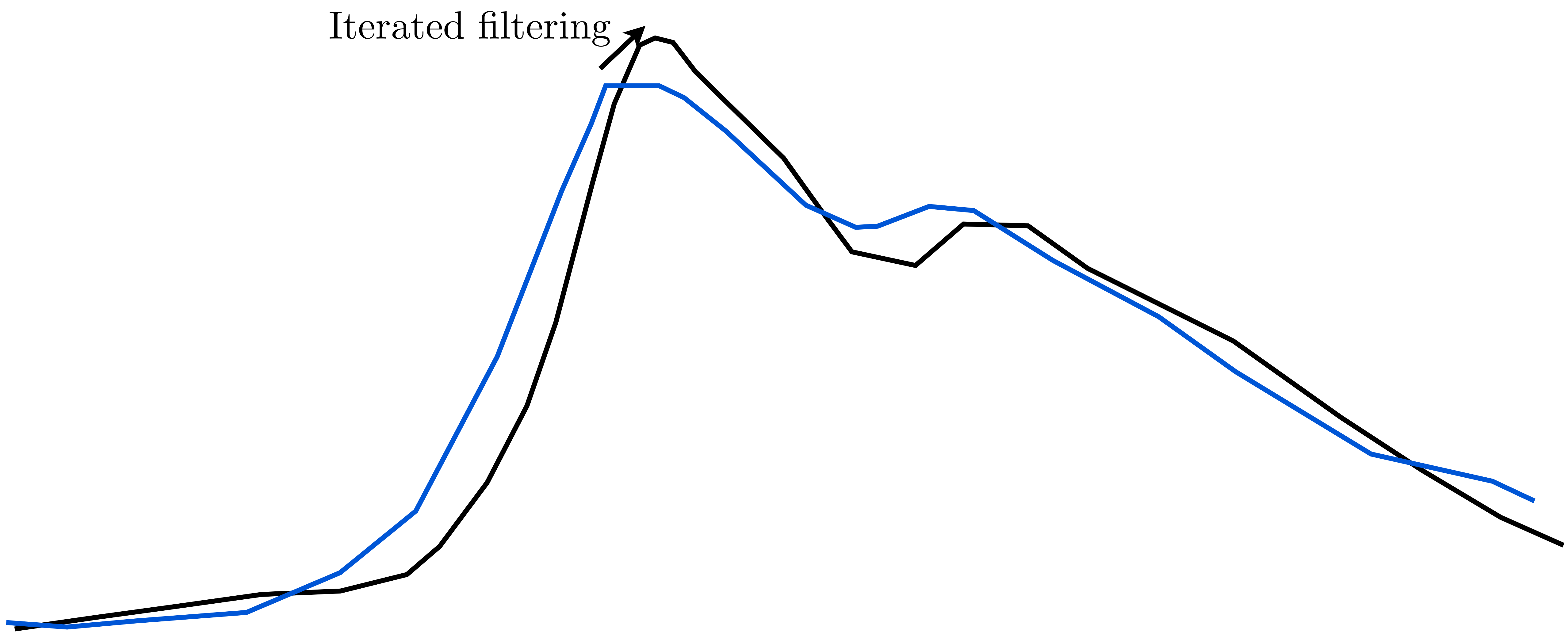


Combining quick approximate methods to "exact" inference algorithms

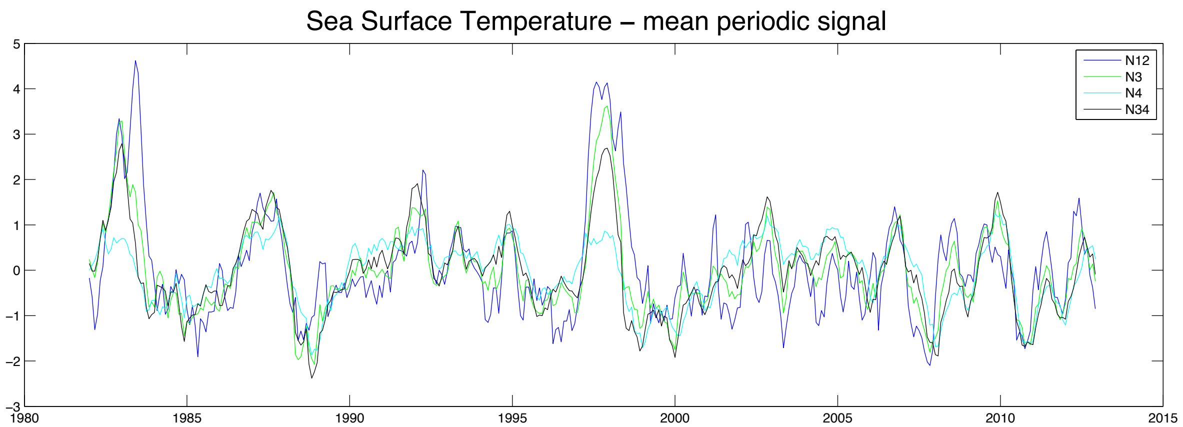
Plug-and-play versions of
MIF, pMCMC, ksimplex, kMCMC
available soon on www.plom.io

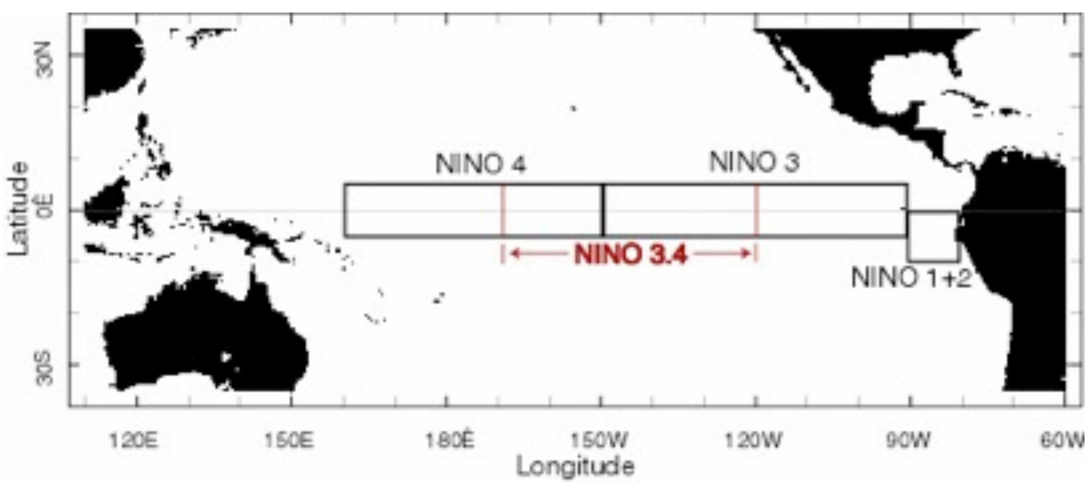
PLoM.io

Public Library of Models (starting with epidemiology)

Developped by S. Ballesteros, T. Bogich and J. Dureau
with the support of B. Grenfell and B. Cazelles

4. Results





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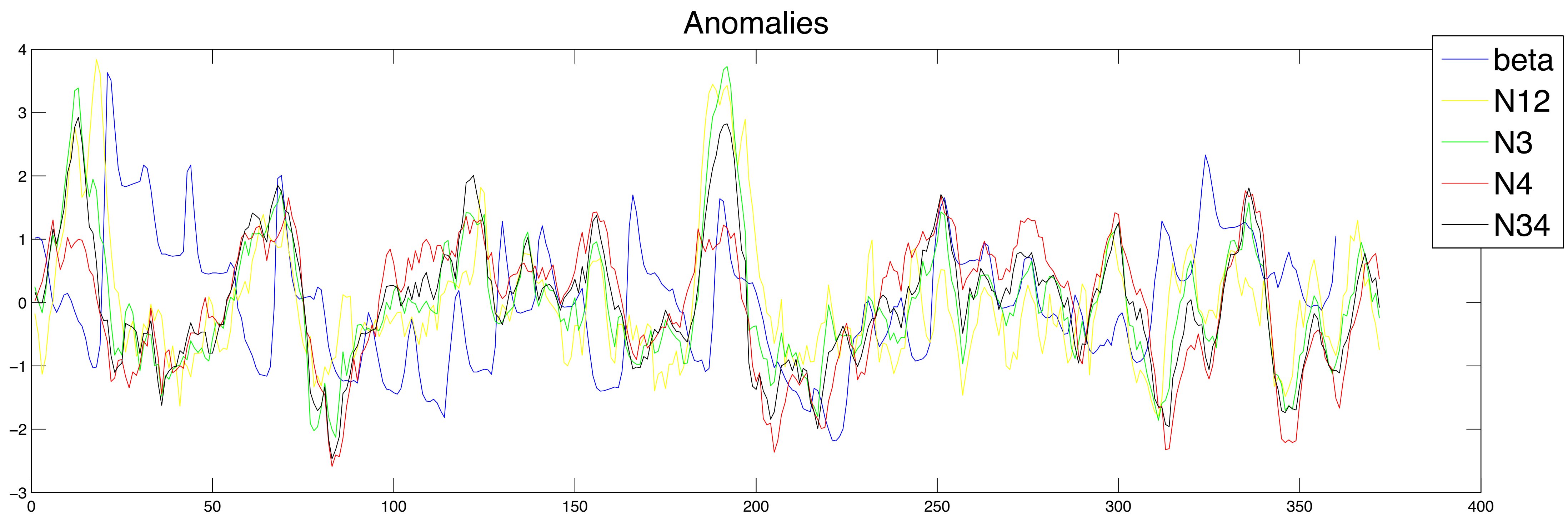
$$d\, logit_{[-0.3;0.3]}(\tilde{\beta}_t) = \sigma dB_t$$

Chiang Mai



	Lag (months)	Correlation	p-value
N12	-9 (-6)	0.28 (0.17)	1e-8 (0.001)
N3	-9 (-6)	0.24 (0.17)	1e-6 (0.001)
N4	-9 (-6)	0.13 (0.16)	0.01 (0.002)
N34	-9 (-6)	0.21 (0.19)	1e-5 (0.0002)

5. Conclusions

Take-home message:

This approach may allow to disentangle the role of extrinsic and intrinsic determinants.

It is a work in progress.

Further work:

- Further exploration of likelihood function

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- Critical analysis of fit and model

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- Other districts (in particular rural/urban)

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- Further exploration of likelihood function
- Critical analysis of fit and model
- Other districts (in particular rural/urban)
- Confront to climate data from Thailand

Questions:

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- Should we also explore non-chaotic states?
- Can we build an explicit coupling of climate and dengue through the transmission rate?
- Can the predictibility horizon be extended?

Thanks!