

Managing heterogeneity in the study of neural oscillator dynamics

Carlo R. Laing and Ben Smith
Massey University, Auckland, New Zealand

Yu Zou and Yannis G. Kevrekidis
Department of Chemical Engineering, Princeton University, USA



MARSDEN FUND
TE PŪTEA RANGAHAU
A MARSDEN

- Consider a network of Hodgkin-Huxley type neurons, thought to describe dynamics of pre-Bötzinger complex:

$$\begin{aligned} C \frac{dV_i}{dt} &= -g_{Na}m(V_i)h_i(V_i - V_{Na}) - g_L(V_i - V_L) + I_{\text{syn}}^i + I_{\text{app}}^i \\ \frac{dh_i}{dt} &= \frac{h_\infty(V_i) - h_i}{\tau(V_i)} \end{aligned}$$

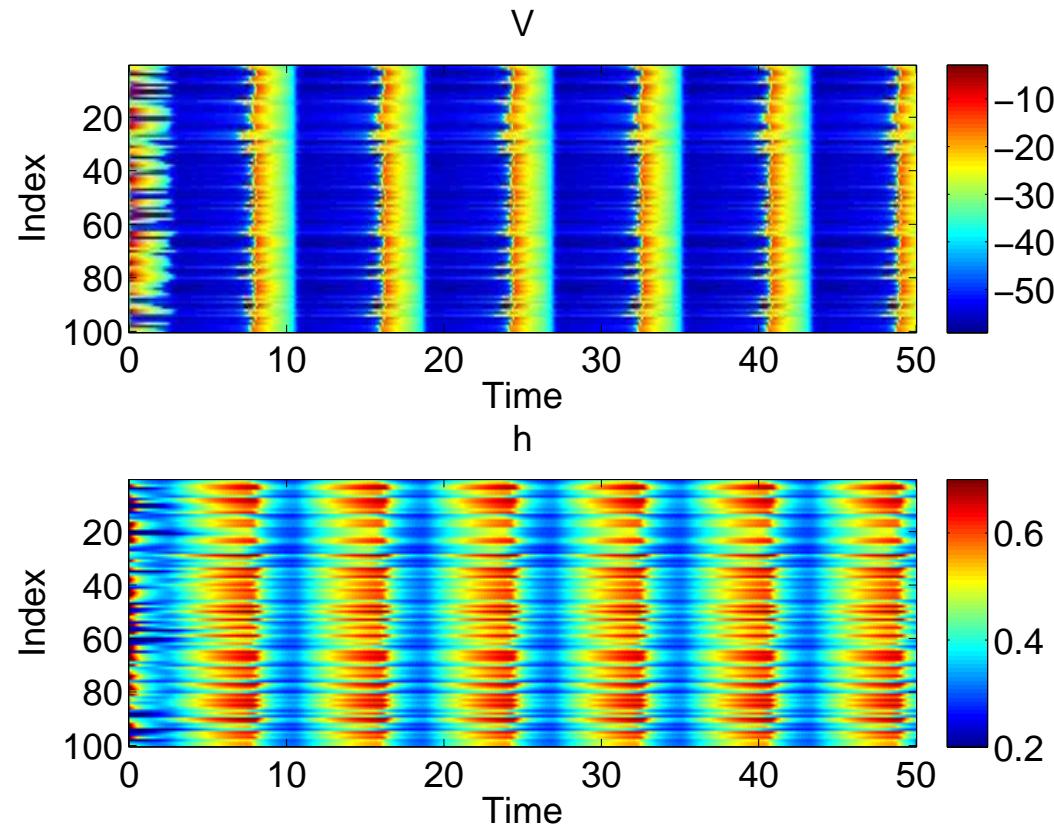
for $i = 1 \dots N$, where

$$I_{\text{syn}}^i = \frac{g_{\text{syn}}(V_{\text{syn}} - V_i)}{N} \sum_{j=1}^N s(V_j),$$

- Excitatory, instantaneous synaptic coupling, all-to-all.
- Spiking currents removed.
- Studied by Rubin and Terman, 2002.

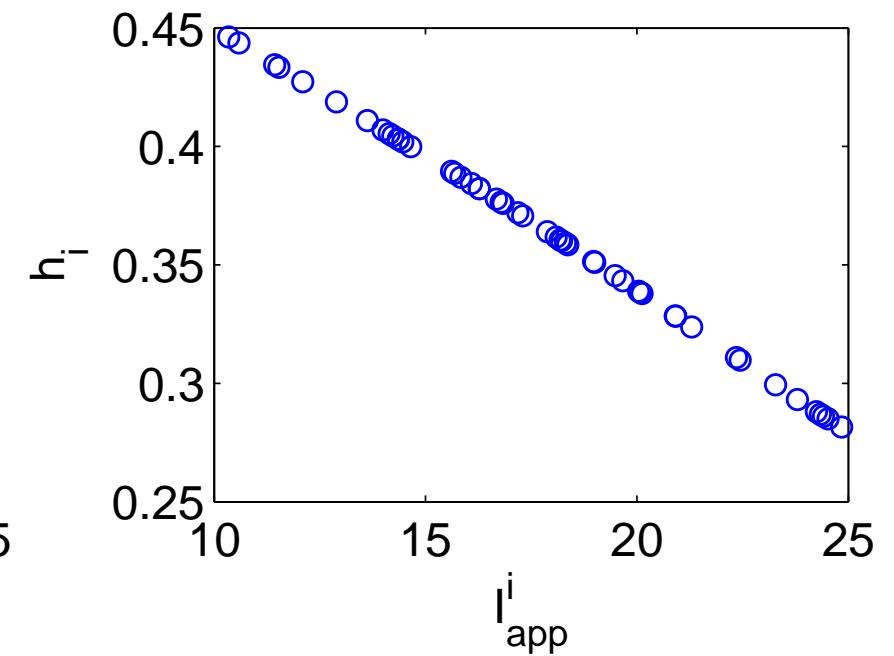
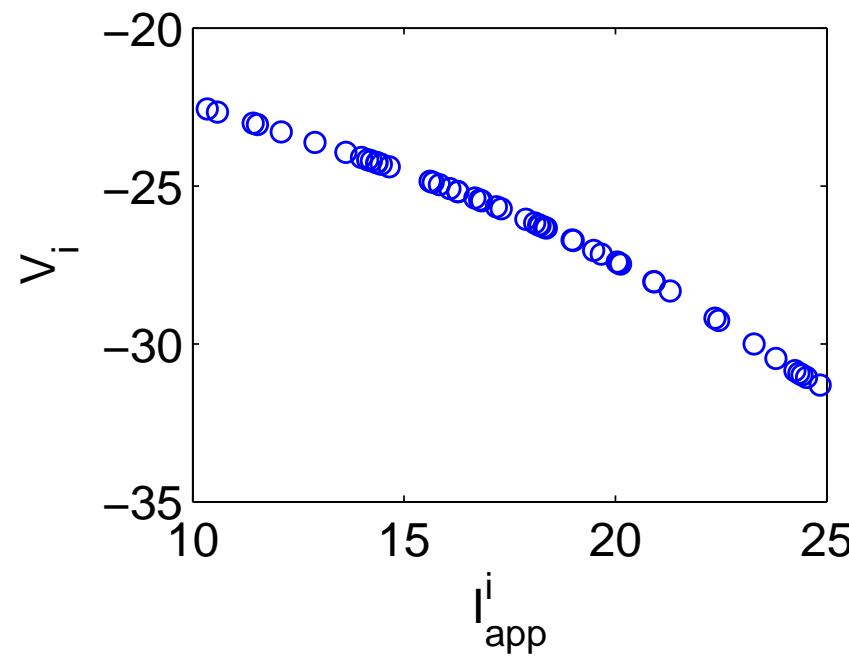
- The population is heterogeneous, as all I_{app}^i are different.
- Take the I_{app}^i to be uniformly distributed on [10, 25].
- Assume that the actual number of neurons is much bigger than the number we want to simulate — essentially infinite.
 1. What values of I_{app}^i should we take to best approximate the behaviour of the infinite network?
 2. What is the effect of this heterogeneity?

- Try randomly sampling from distribution:



- For parameters of interest, we have stable synchronous oscillation.

- But each realisation gives a different period (and values of parameters at which bifurcations occur).
- Key point: after transients, correlations develop between state of neuron i and value of heterogeneous parameter I_{app}^i : Movie



- So in the limit $N \rightarrow \infty$, the system is described by

$$\begin{aligned} C \frac{\partial V(\mu, t)}{\partial t} &= -g_{Na} m(V(\mu, t)) h(\mu, t) [V(\mu, t) - V_{Na}] \\ &\quad - g_L [V(\mu, t) - V_L] + I_{syn}(\mu, t) + 17.5 + 7.5\mu \\ \frac{\partial h(\mu, t)}{\partial t} &= \frac{h_\infty(V(\mu, t)) - h(\mu, t)}{\tau(V(\mu, t))} \end{aligned}$$

where

$$I_{syn}(\mu, t) = g_{syn}(V_{syn} - V(\mu, t)) \int_{-1}^1 s(V(\mu, t)) p(\mu) d\mu.$$

and the probability density function for the random variable μ is

$$p(\mu) = \begin{cases} 1/2, & -1 \leq \mu \leq 1 \\ 0, & \text{otherwise} \end{cases}$$

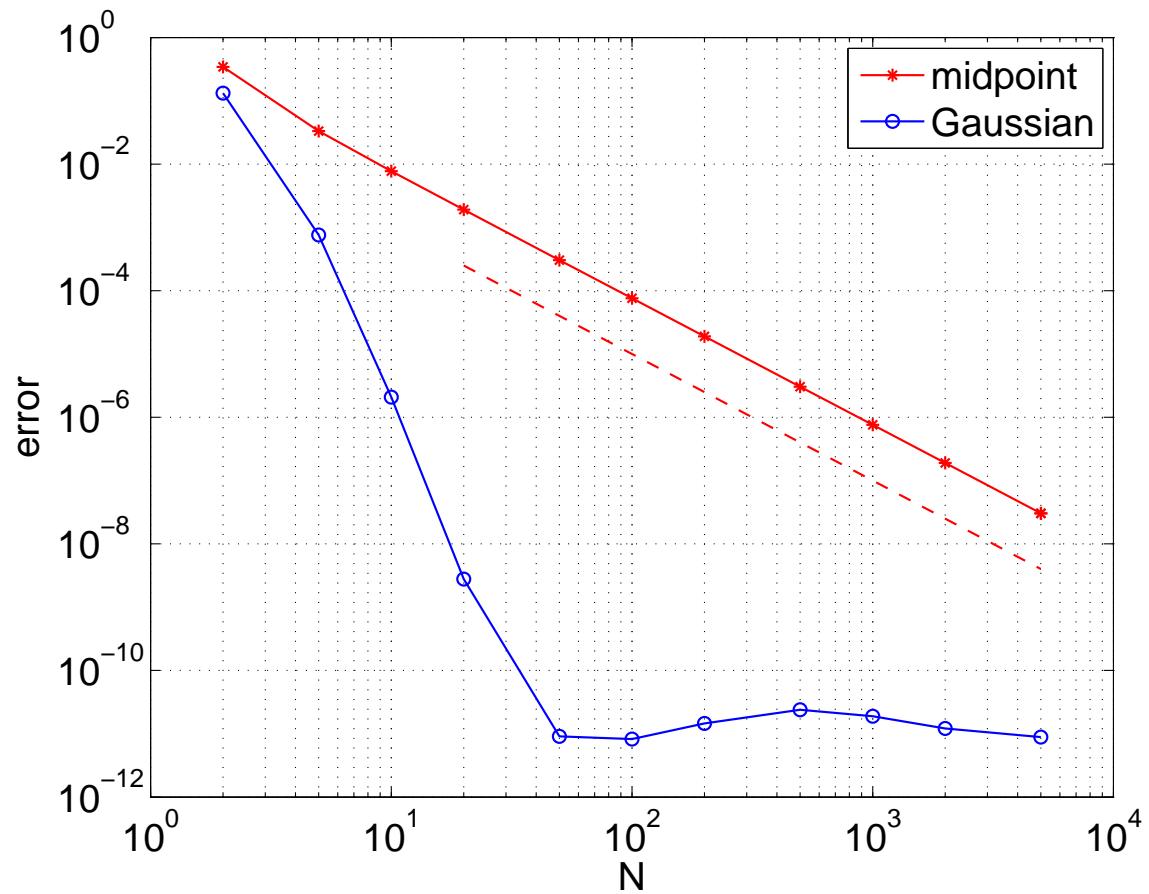
1. How to represent the μ -dependence of $V(\mu, t)$ and $h(\mu, t)$?
2. How to best calculate the integral

$$\int_{-1}^1 s(V(\mu, t))p(\mu) d\mu?$$

- Discretise in the μ direction.
- μ is uniformly distributed over $[-1, 1]$, so try $\mu_i = -1 + 2(i - 1/2)/N$ for $i = 1, 2 \dots N$.
- Then approximate the integral using the composite midpoint rule:

$$\int_{-1}^1 s(V(\mu, t))p(\mu) d\mu \approx \frac{1}{N} \sum_{i=1}^N s(V(\mu_i, t))$$

Calculation of oscillation period. Error $\sim N^{-2}$.



- But Gaussian quadrature is much more accurate:
- For a fixed N , choose μ_i to be the i th root of $P_N(\mu)$, where P_N is the N th Legendre polynomial, normalised so that $P_N(1) = 1$.
- Choose weights

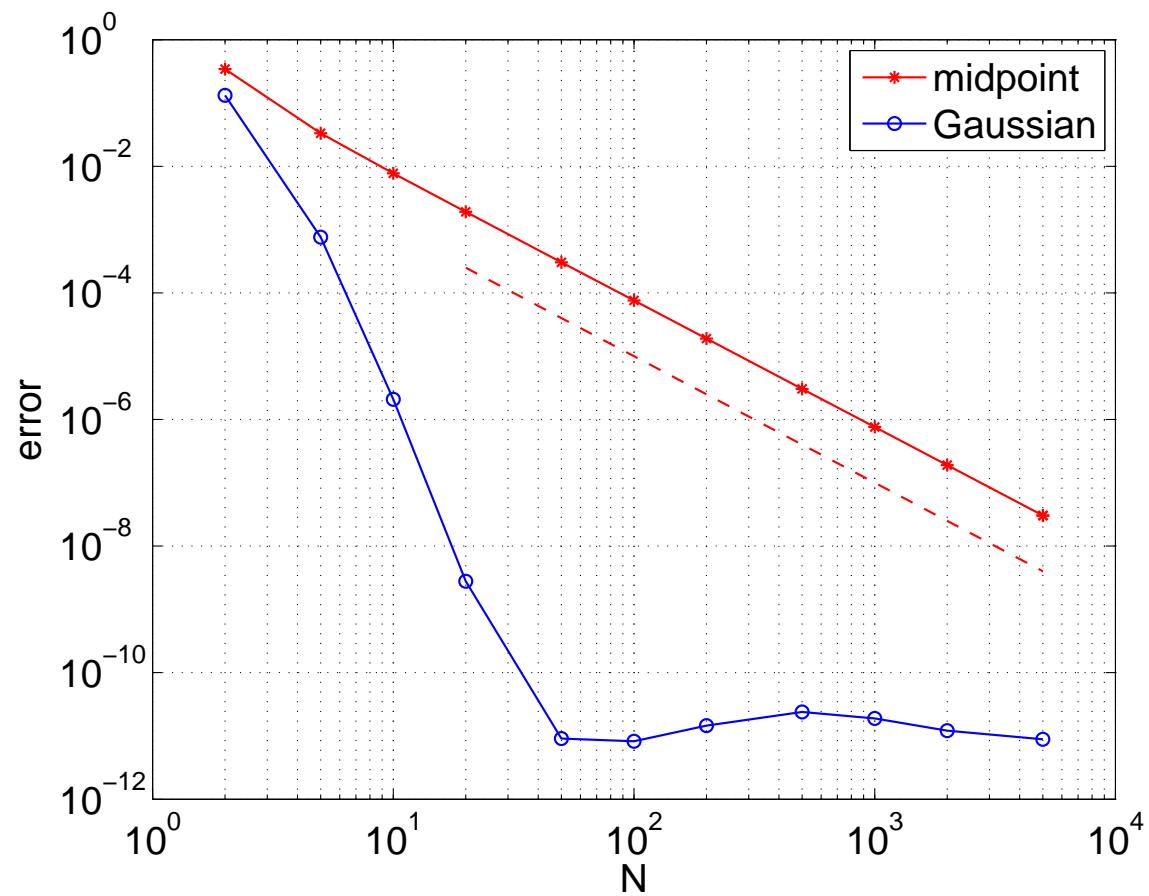
$$w_i = \frac{1}{(1 - \mu_i^2) [P'_N(\mu_i)]^2},$$

- The Gauss-Legendre quadrature rule is

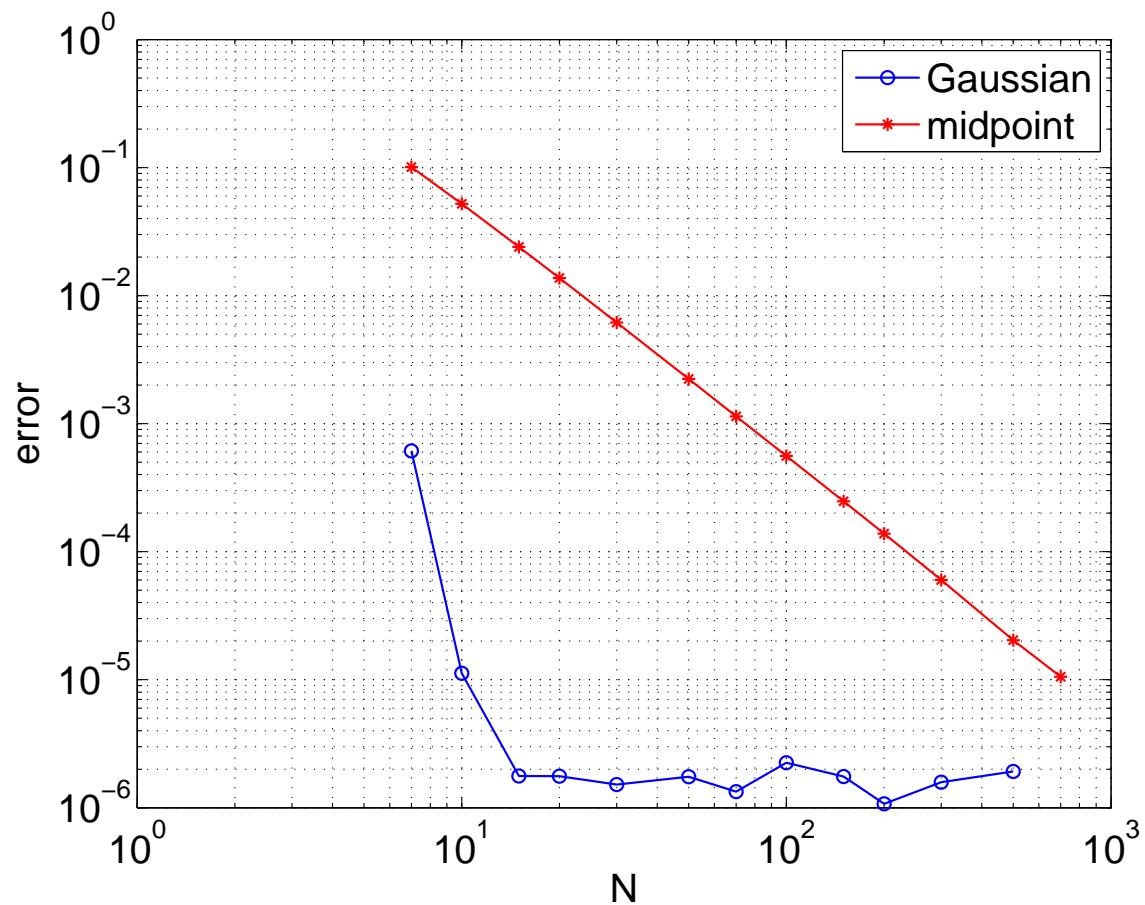
$$\int_{-1}^1 s(V(\mu, t)) p(\mu) d\mu \approx \sum_{i=1}^N w_i s(V(\mu_i, t)).$$

i.e. non-uniformly spaced μ_i , and weighted sum.

Calculation of oscillation period. “Spectral accuracy”



Calculation of Hopf bifurcation point.



- For more than one heterogeneous parameter, use tensor products.
- E.g. g_{Na} are also normally distributed with mean 2.8 and standard deviation 0.3.
- New variables are $V(\mu, \lambda, t)$ and $h(\mu, \lambda, t)$, where $g_{Na} = 2.8 + 0.3\lambda$ and PDF of λ is

$$q(\lambda) = \frac{1}{\sqrt{2\pi}} e^{-\lambda^2/2}$$

- The coupling integral is now

$$\int_{-\infty}^{\infty} \int_{-1}^1 s(V(\mu, \lambda, t)) p(\mu) q(\lambda) d\mu d\lambda$$

- For normal distribution, use Gauss-Hermite quadrature.

$$\begin{aligned} & \int_{-\infty}^{\infty} \int_{-1}^1 s(V(\mu, \lambda, t)) p(\mu) q(\lambda) d\mu d\lambda \\ & \approx \sum_{j=1}^M \sum_{i=1}^L v_j w_i s(V(\mu_i, \lambda_j, t)). \end{aligned}$$

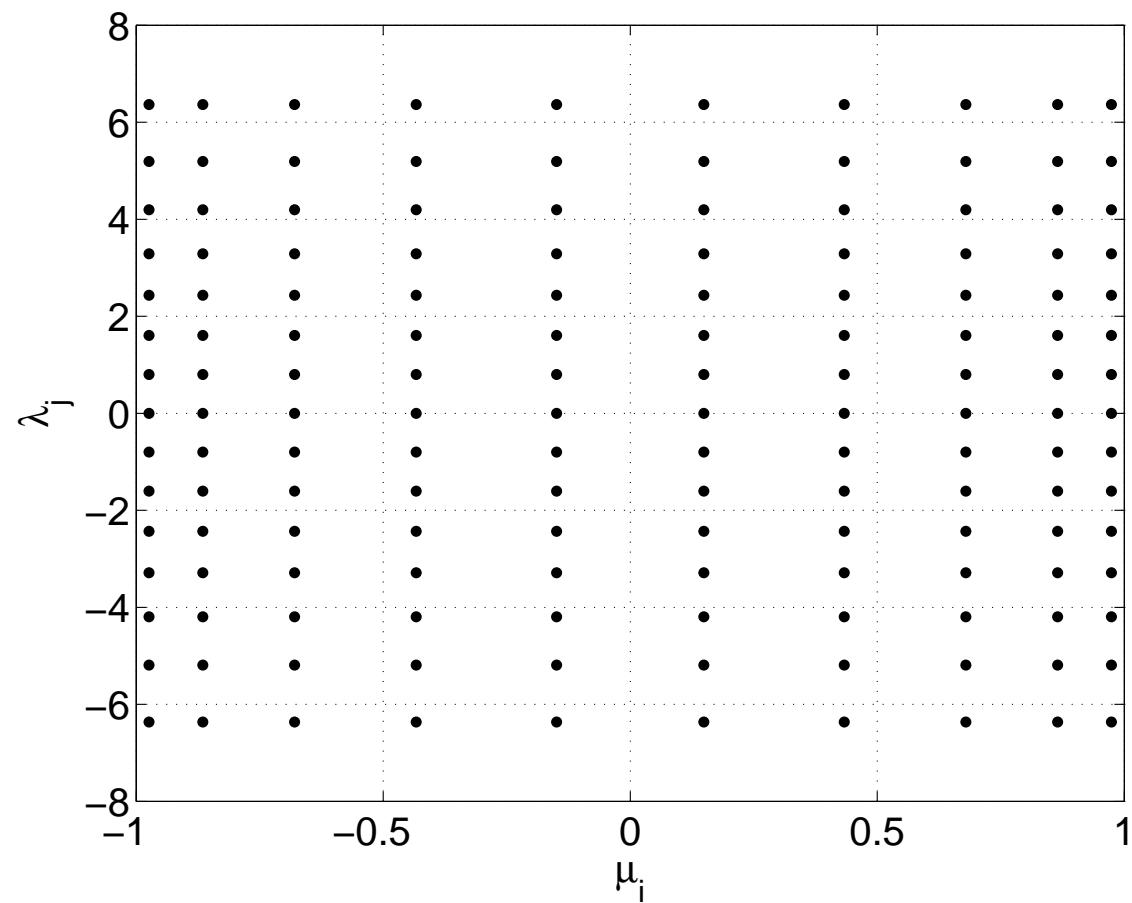
(L points in μ direction, M in λ direction).

where λ_j is the j th root of H_M , the M th probabilists' Hermite polynomial

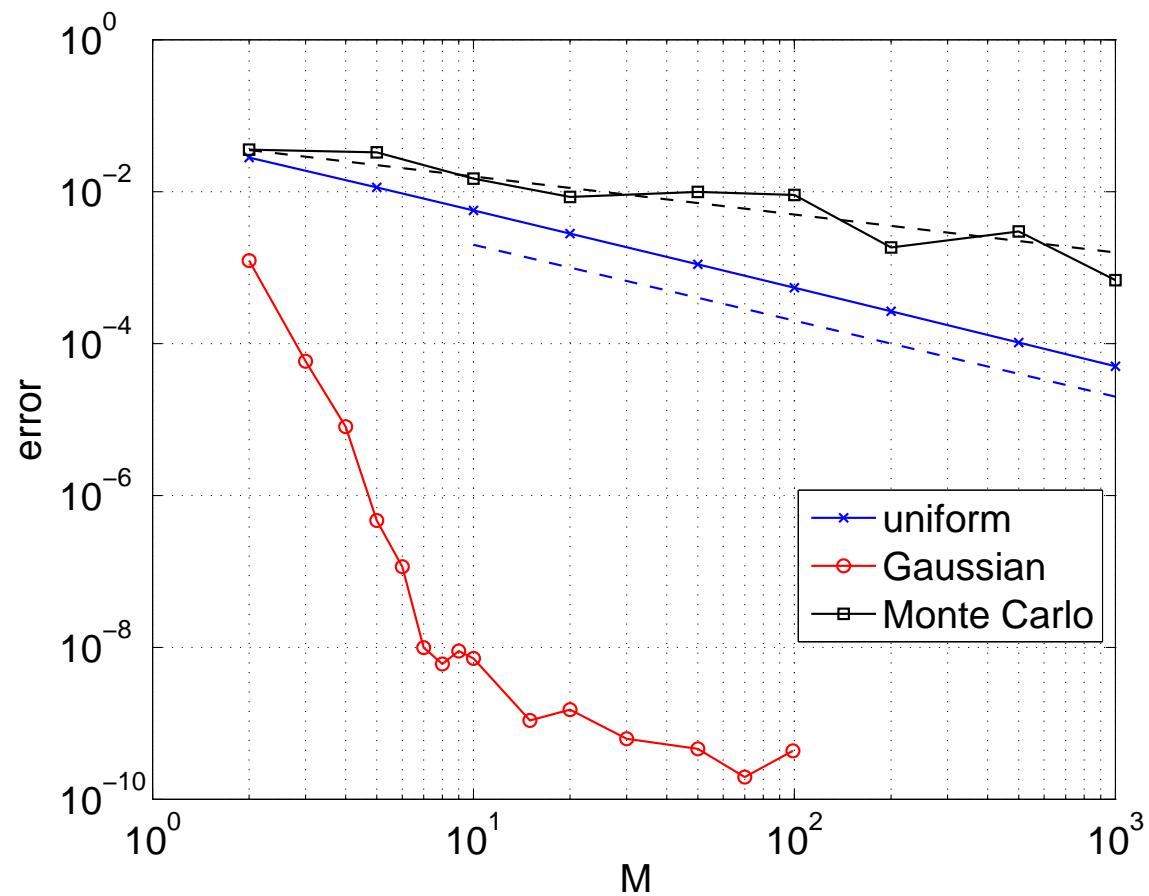
- weights v_j are given by

$$v_j = \frac{M!}{[M H_{M-1}(\lambda_j)]^2}$$

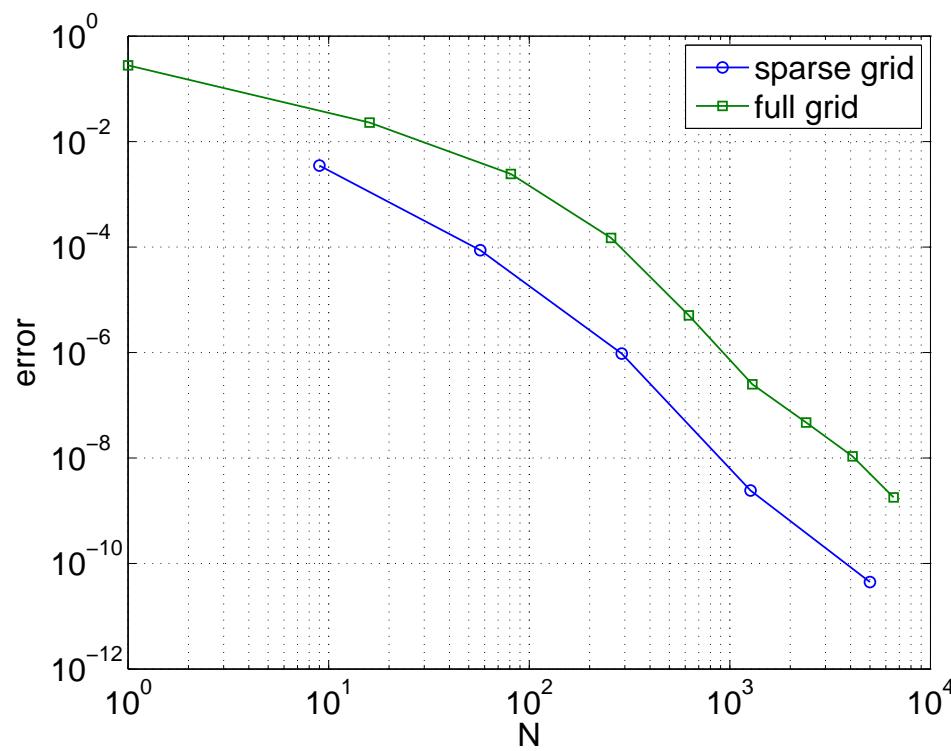
$L = 10, M = 15$:



Period calculation when $L = 10$.



- For a large number of heterogeneous parameters, curse of dimensionality kicks in — use sparse grids (Smolyak).
- Period calculation when **four** parameters are distributed:



Summary

- Heterogeneity in dynamical systems can be dealt with using techniques from uncertainty quantification.
- Distribution of random parameter determines quadrature scheme used.
- Effectively simulating a small number of neurons, but judiciously chosen (and coupled).
- Useful for systematically exploring effects of parameter heterogeneity.
- Requires smooth dependence of state on parameter(s).