Bayesian Analysis (2013) **8**, Number 1, pp. 27–32

Comment on Article by Schmidl et al.

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We thoroughly enjoyed reading this paper and are delighted to contribute to its discussion. The authors have been particularly innovative in drawing upon quite different areas of statistical inference to devise efficient Markov transition kernels for complex posterior distributions. Landmark papers provoke discussion and raise many open questions leading to potentially fruitful new avenues of investigation and this paper is no exception.

1 Statistical inference for dynamic systems

The authors have arguably chosen one of the most challenging problems for Bayesian inference: sampling from the induced posterior of the parameters of a deterministic nonlinear dynamic system. To illustrate the problem, consider the simple dynamic system[1] below

$$\frac{dx}{dt} = \frac{72}{36+y} - k_3 \qquad \frac{dy}{dt} = k_4 x - 1. \tag{1}$$

Setting initial conditions of $x(0) = 7$, $y(0) = -10$ and parameters to values of $k_3 = 2$ and $k_4 = 1$, the system is forward simulated in time steps of 0.5 from $t = 0$ to $t = 60$. An additive zero mean Gaussian observation error with covariance $0.5\mathbf{I}_2$ then generates the 120 observations of the system dynamics $\mathcal{D}$. The induced posterior under flat priors $p(k_3, k_4|\mathcal{D})$ is shown in Figure 1. The multiple elongated ridges show strong nonlinear correlation separated by regions of low density. This simple low dimensional model presents challenges due to the near isolated ridges and their long correlated structure, making them challenging to traverse and move between.

Statistical inference for systems described by nonlinear ordinary differential equations is a relatively recent area of interest. The non-Bayesian tradition has had major contributions from the likes of Ramsay et al. (2007); Maiwald and Timmer (2008). Bayesian approaches have been spearheaded by, for example, Wilkinson (2009); Toni et al. (2009); Raue et al. (2013). Recent work by Gutenkunst et al. (2007) has described the posterior distributions of dynamic system parameters as *sloppy*, a catchy term describing the effects of the lack of identifiability and complexity of the underlying models. The authors of this paper under discussion therefore have made an important contribution to an area of research that is much in need of innovation and new insight.

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[1]Mark Girolami is grateful to Simon Byrne, Anne-Marie Lyne and Ben Calderhead for producing the two figures in this contribution.

 DOI:10.1214/13-BA801B