Supplementary material for our Bioinformatics paper: 'Improvements in the reconstruction of time-varying gene regulatory networks: dynamic programming and regularization by information sharing among genes'

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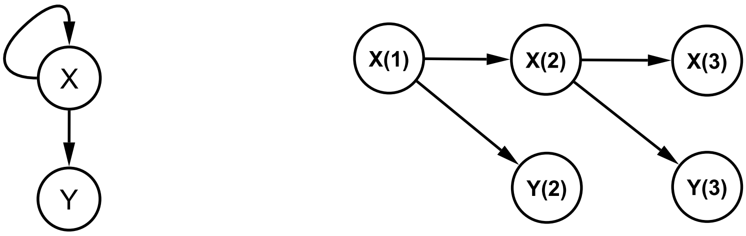
Abstract: *This paper is a supplement to our Bioinformatics paper 'Improvements in the reconstruction of time-varying gene regulatory networks: dynamic programming and regularization by information sharing among genes' (Grzegorczyk and Husmeier, 2011a). It contains the algorithmic details of the proposed model improvements and provides further results obtained for the circadian genes in Arabidopsis thaliana data. Section 1 gives a comprehensive description of the dynamic programming schemes, the cpBGe model, and the novel regularized cpBGe model. Please note that Sections 1.1-1.6 are preliminary versions of a methodological paper published (Grzegorczyk and Husmeier, 2011b). In Section 2 the inferred network topology and the inferred changepoint locations for circadian genes in* Arabidopsis thaliana *are presented and discussed.*

1 Methodology

1.1 The homogeneous dynamic BGe network

DBNs are flexible models for representing probabilistic relationships between interacting variables (nodes) $X_1, \dots, X_N$ via a directed graph $\mathcal{G}$. In most applications first-order DBNs are considered so that all interactions are subject to a time delay $\tau = 1$. An edge pointing from X_j to X_n, symbolically $\mathcal{G}(j,n) = 1$, in a DBN with $\tau = 1$ indicates that the realization of X_n at time point t, symbolically: $X_n(t)$, is conditionally dependent on the realization of X_j at time point $t-1$, symbolically: $X_j(t-1)$. See Figure 1 for an example of a DBN consisting of two nodes X and Y. The parent node set of node X_n in $\mathcal{G}$, $\pi_n = \pi_n(\mathcal{G})$, is the set of all nodes from which an edge points to node X_n in $\mathcal{G}$. Note that there is a one-to-one mapping between the graph $\mathcal{G}$ and the N parent node sets π_n; i.e. $\mathcal{G}(j,n) = 1$ if and only if $X_j \in \pi_n$; and vice-versa $\mathcal{G}(j,n) = 0$ if and



(a) recurrent network

(b) unfolded dynamic network

Figure 1: **State space graph and corresponding dynamic Bayesian network of order $\tau = 1$.** Panel (a) shows a recurrent state space graph containing two nodes. Node X has a recurrent feedback loop and acts as a regulator of node Y. Panel (b) shows the same graph unfolded in time.

only if $X_j \notin \pi_n$. Given a data set $\mathcal{D}$, where $\mathcal{D}_{n,t}$ and $\mathcal{D}_{(\pi_n,t)}$ are the tth realizations $X_n(t)$ and $\pi_n(t)$ of X_n and π_n, respectively, and $1 \leq t \leq m$ represents time, DBNs are based on the following homogeneous Markov chain expansion:

$$P(\mathcal{D}|\mathcal{G},\boldsymbol{\theta}) = \prod_{n=1}^{N}\prod_{t=2}^{m} P\Big(X_n(t) = \mathcal{D}_{n,t}|\pi_n(t-1) = \mathcal{D}_{(\pi_n,t-1)}, \boldsymbol{\theta}_n\Big) \tag{1}$$

where $\boldsymbol{\theta}$ is the total parameter vector, composed of node-specific subvectors $\boldsymbol{\theta}_n$, which specify the local conditional distributions in the factorization. From Eq. (1) and under the assumption of parameter independence, $P(\boldsymbol{\theta}|\mathcal{G}) = \prod_n P(\boldsymbol{\theta}_n|\pi_n)$, the marginal likelihood is given by

$$P(\mathcal{D}|\mathcal{G}) \;=\; \int P(\mathcal{D}|\mathcal{G},\boldsymbol{\theta})P(\boldsymbol{\theta}|\mathcal{G})d\boldsymbol{\theta} \;=\; \prod_{n=1}^{N} \Psi(\mathcal{D}_n^{\pi_n}) \tag{2}$$

$$\Psi(\mathcal{D}_n^{\pi_n}) \;=\; \int \prod_{t=2}^{m} P\Big(X_n(t) = \mathcal{D}_{n,t}|\pi_n(t-1) = \mathcal{D}_{(\pi_n,t-1)}, \boldsymbol{\theta}_n\Big) P(\boldsymbol{\theta}_n|\pi_n)d\boldsymbol{\theta}_n \tag{3}$$

where $\mathcal{D}_n^{\pi_n} := \{(\mathcal{D}_{n,t}, \mathcal{D}_{\pi_n,t-1}) : 2 \leq t \leq m\}$ is the subset of data pertaining to node X_n and parent set π_n. We will refer to $\Psi(\mathcal{D}_n^{\pi_n})$ as *local score* of X_n. For the local scores $\Psi(\mathcal{D}_n^{\pi_n})$ various modelling frameworks, such as sparse Bayesian regression models (e.g. see Rogers and Girolami (2005)), have been proposed and applied in the literature. In this study we focus on the BGe model, which was proposed by Geiger and Heckerman (1994). That is, a linear Gaussian distribution is chosen for the local conditional distribution $P(X_n|\pi_n, \boldsymbol{\theta}_n)$ in Eq.(3), and the conjugate normal-Wishart distribution is assigned to the local prior distributions $P(\boldsymbol{\theta}_n|\pi_n)$. Under fairly weak regularity conditions discussed in Geiger and Heckerman (1994) (parameter modularity), the integral in Eq. (3) has a closed form solution, given by Eq. (24) in Geiger and Heckerman (1994). The resulting expression is called the (local) BGe score.

1.2 The inhomogeneous dynamic changepoint BGe model (cpBGe)

To obtain a inhomogeneous DBN, we generalize Eq. (1) with a node-specific mixture model:

$$P(\mathcal{D}|\mathcal{G},\mathbf{V},\mathbf{K},\boldsymbol{\theta}) = \prod_{n=1}^{N}\prod_{t=2}^{m}\prod_{k=1}^{\mathcal{K}_n} P\Big(X_n(t) = \mathcal{D}_{n,t}|\pi_n(t-1) = \mathcal{D}_{(\pi_n,t-1)}, \boldsymbol{\theta}_n^k\Big)^{\delta_{\mathbf{V}_n(t),k}} \tag{4}$$

where $\delta_{\mathbf{V}_n(t),k}$ is the Kronecker delta, $\mathbf{V}$ is a matrix of latent variables $\mathbf{V}_n(t)$, $\mathbf{V}_n(t) = k$ indicates that the realization of node X_n at time t, $X_n(t)$, has been generated by the kth component of a mixture with $\mathcal{K}_n$ components, and $\mathbf{K} = (\mathcal{K}_1, \ldots, \mathcal{K}_n)$. Note that the matrix $\mathbf{V}$ divides the data into several disjoined subsets, each of which can be regarded as pertaining to a separate BGe model with parameters $\boldsymbol{\theta}_n^k$. The vectors $\mathbf{V}_n$ are node-specific, i.e. different nodes can have different changepoints so that the proposed model has a higher flexibility in modelling nonlinear relationships than the BGM model proposed in Grzegorczyk *et al.* (2008). The probability model defined in Eq. (4) is effectively a mixture model with local probability distributions $P(X_n|\pi_n, \boldsymbol{\theta}_n^k)$ and it can hence, under a free allocation of the latent variables, approximate any probability distribution arbitrarily closely. But different from the free allocation of latent variables in Grzegorczyk *et al.* (2008), in the present work, we change the assignment of data points to mixture components from a free allocation to a changepoint process. This allocation scheme provides the approximation of a nonlinear regulation process by a piecewise linear process under the assumption that the temporal processes are sufficiently smooth. Employing a changepoint process effectively reduces the complexity of the latent variable space and incorporates our prior belief that, in a time series, adjacent time points are likely to be assigned to the same component. From Eq. (4), the marginal likelihood conditional on the latent variables $\mathbf{V}$ is given by

$$\begin{aligned} P(\mathcal{D}|\mathcal{G}, \mathbf{V}, \mathbf{K}) &= \int P(\mathcal{D}|\mathcal{G}, \mathbf{V}, \mathbf{K}, \boldsymbol{\theta}) P(\boldsymbol{\theta}) d\boldsymbol{\theta} = \prod_{n=1}^{N} \Psi^\dagger(\mathcal{D}_n^{\pi_n}[\mathcal{K}_n, \mathbf{V}_n]) && (5) \\ \Psi^\dagger(\mathcal{D}_n^{\pi_n}[\mathcal{K}_n, \mathbf{V}_n]) &= \prod_{k=1}^{\mathcal{K}_n} \Psi(\mathcal{D}_n^{\pi_n}[k, \mathbf{V}_n]) && (6) \end{aligned}$$

where the factors in Eq. (6) are given by:

$$\Psi(\mathcal{D}_n^{\pi_n}[k, \mathbf{V}_n]) = \int \prod_{t=2}^{m} P\Big(X_n(t) = \mathcal{D}_{n,t}|\pi_n(t-1) = \mathcal{D}_{(\pi_n, t-1)}, \boldsymbol{\theta}_n^k\Big)^{\delta_{\mathbf{V}_n(t),k}} P(\boldsymbol{\theta}_n^k|\pi_n) d\boldsymbol{\theta}_n^k \qquad (7)$$

Eq. (7) is similar to Eq. (3), and can be interpreted as a local BGe score restricted to the data subset $\mathcal{D}_n^{\pi_n}[k, \mathbf{V}_n] := \{(\mathcal{D}_{n,t}, \mathcal{D}_{\pi_n,t-1}) : \mathbf{V}_n(t) = k, 2 \leq t \leq m\}$. The product $\Psi^\dagger(\mathcal{D}_n^{\pi_n}[\mathcal{K}_n, \mathbf{V}_n])$ in Eq. (6) is the *local cpBGe score* of X_n. Note that there is a factor for each mixture component k and that each factor $\Psi(\mathcal{D}_n^{\pi_n}[k, \mathbf{V}_n])$ can be interpreted as a local BGe score for the data subset $\mathcal{D}_n^{\pi_n}[k, \mathbf{V}_n]$.

When the regularity conditions defined in Geiger and Heckerman (1994) are satisfied, then the expression in Eq. (7) has a closed-form solution: it is given by Eq. (24) in Geiger and Heckerman (1994) restricted to the subset of the data pertaining to node X_n and its parents π_n that has been assigned to the kth mixture component (or kth segment).

The joint probability distribution of the proposed cpBGe model is given by:

$$P(\mathcal{G}, \mathbf{V}, \mathbf{K}, \mathcal{D}) = P(\mathcal{G}) P(\mathbf{V}|\mathbf{K}) P(\mathbf{K}) P(\mathcal{D}|\mathcal{G}, \mathbf{V}, \mathbf{K}) \qquad (8)$$

We restrict on graph prior distributions that can be factorized into node-specific factors, symbolically: $P(\mathcal{G}) = \prod_{n=1}^{N} P(\pi_n)$ and in the absence of genuine prior knowledge about the regulatory network structure, we assume for $P(\pi_n)$ a uniform distribution. As done in our earlier work (Grzegorczyk and Husmeier, 2009) and in other Bayesian network studies (e.g. Friedman and Koller (2003) or Grzegorczyk and Husmeier (2008)) we impose a fan-in restriction on the cardinality of the parent node sets, symbolically: $|\pi_n| \leq 3$, to ensure sparsity of the inferred graph structures. Moreover, we assume that the distributions of the node-specific numbers of mixture components and allocation vectors $P(\mathbf{V}_n|\mathcal{K}_n)P(\mathcal{K}_n)$ are independent $(n = 1, \ldots, N)$ so that the joint probability distribution in Eq. (8) can be factorized:

$$P(\mathcal{G}, \mathbf{V}, \mathbf{K}, \mathcal{D}) = \prod_{n=1}^{N} P(\pi_n) P(\mathbf{V}_n|\mathcal{K}_n) P(\mathcal{K}_n) \Psi^\dagger(\mathcal{D}_n^{\pi_n}[\mathcal{K}_n, \mathbf{V}_n]) \qquad (9)$$

Accordingly, the posterior distribution $P(\mathcal{G}, \mathbf{V}, \mathbf{K}|\mathcal{D})$ can be factorized into independent node-specific posterior distributions:

$$P(\mathcal{G}, \mathbf{V}, \mathbf{K}|\mathcal{D}) = \prod_{n=1}^{N} P(\pi_n, \mathbf{V}_n, \mathcal{K}_n|\mathcal{D}_n^{1:N}) \tag{10}$$

where $\mathcal{D}_n^{1:N} := \{(\mathcal{D}_{n,t}, \mathcal{D}_{1,t-1}, \dots, \mathcal{D}_{N,t-1}) : 2 \leq t \leq m\}$ contains the last $m-1$ observations $\mathcal{D}_{n,2}, \dots, \mathcal{D}_{n,m}$ of X_n and the first $m-1$ observations $\mathcal{D}_{j,1}, \dots, \mathcal{D}_{j,m-1}$ of all potential parent nodes X_j $(j = 1, \dots, N)$ of X_n. We note that each factor $P(\pi_n, \mathbf{V}_n, \mathcal{K}_n|\mathcal{D}_n^{1:N})$ in Eq. (10) can be infered independently.
As prior probability distributions on the node-specific numbers of mixture components $\mathcal{K}_n$, $P(\mathcal{K}_n)$, we take iid truncated Poisson distributions with shape parameter $\lambda = 1$, restricted to $1 \leq \mathcal{K}_n \leq \mathcal{K}_{MAX}$ (we set $\mathcal{K}_{MAX} = 10$ in our simulations). The prior distribution on the node-specific latent variable vectors, $P(\mathbf{V}_n|\mathcal{K}_n)$, is implicitly defined via a changepoint process. We identify $\mathcal{K}_n$ components with $\mathcal{K}_n - 1$ changepoints $\mathbf{b}_n = (b_{n,1}, \dots, b_{n,\mathcal{K}_n-1})$ on the *discrete* set $\{2, \dots, m-1\}$. For node X_n the observation at time point t is assigned to the kth component, symbolically $\mathbf{V}_n(t) = k$, if and only if $b_{n,k-1} < t \leq b_{n,k}$, where $b_{n,k}$ is the kth changepoint implied by $\mathbf{V}_n$, and $b_{n,0} = 1$ and $b_{n,\mathcal{K}_n} = m$ are two pseudo changepoints. There is a one-to-one mapping between allocation vectors and changepoints: For $t = 2, \dots, m$ and $k = 1, \dots, \mathcal{K}_n$: $b_{n,k-1} < t \leq b_{n,k} \Leftrightarrow \mathbf{V}_n(t) = k$. To make that more specific, we henceforth use the notation $\mathbf{b}_{\mathbf{V}_n} = (b_{\mathbf{V}_n,1}, \dots, b_{\mathbf{V}_n,\mathcal{K}_n-1})$ for the changepoint vector implied by $\mathbf{V}_n$. Following Green (1995) we assume that the changepoints are distributed as the even-numbered order statistics of $\mathcal{L} := 2(\mathcal{K}_n - 1) + 1$ points $u_1, \dots, u_{\mathcal{L}}$ uniformly and independently distributed on the set $\{2, \dots, m-1\}$. The even-numbered order statistics prior on the discrete changepoint locations induces the following prior distribution on the node-specific allocation vectors $P(\mathbf{V}_n|\mathcal{K}_n)$:

$$P(\mathbf{V}_n|\mathcal{K}_n) = \frac{1}{\begin{pmatrix} m-2 \\ 2(\mathcal{K}_n - 1) + 1 \end{pmatrix}} \prod_{k=0}^{\mathcal{K}_n-1} (b_{\mathbf{V}_n,k+1} - b_{\mathbf{V}_n,k} - 1) \tag{11}$$

where $b_{\mathbf{V}_n,0} = 1$ and $b_{\mathbf{V}_n,\mathcal{K}_n} = m$. We note that the even-numbered order statistics prior avoids changepoints at neighbouring time points t and $t+1$, and we have: $|b_{\mathbf{V}_n,k+1} - b_{\mathbf{V}_n,k}| > 1$ for $k = 0, \dots, \mathcal{K}_n - 1$.

In the following sections we discuss Metropolis-Hastings and Gibbs MCMC sampling schemes for sampling from the local posterior distributions $P(\pi_n, \mathbf{V}_n, \mathcal{K}_n|\mathcal{D}_n^{1:N})$ $(n = 1, \dots, N)$. The Metropolis-Hastings samplers employ local changepoint birth, death and reallocation moves on $(\mathcal{K}_n, \mathbf{V}_n)$, and the acceptance probabilities depend on $P(\mathcal{K}_n)P(\mathbf{V}_n|\mathcal{K}_n)$ ratios, which are straightforward to compute. For the Gibbs samplers, which include dynamic programming schemes to sample the changepoints from the correct posterior distribution, closed-form expressions for $P(\mathcal{K}_n)P(\mathbf{V}_n|\mathcal{K}_n)$ are crucial.

1.3 MCMC based model inference

1.3.1 Metropolis-Hastings sampling schemes

We now describe a Metropolis-Hastings (MH) MCMC algorithm to obtain a sample $\{\mathcal{G}^i, \mathbf{V}^i, \mathbf{K}^i\}_{i=1,\dots,I}$ from the posterior distribution $P(\mathcal{G}, \mathbf{V}, \mathbf{K}|\mathcal{D}) \propto P(\mathcal{G}, \mathbf{V}, \mathbf{K}, \mathcal{D})$ of Eq. (10). Our MH samplers combine the structure MCMC algorithm for Bayesian networks (Giudici and Castelo, 2003; Madigan and York, 1995) with the reversible jump MCMC sampling scheme for changepoints presented in Green (1995). This can be done straightforwardly, since conditional on the node-specific allocation vectors $\mathbf{V}_n$ the model parameters can be integrated out to obtain the local cpBGe scores $\Psi^{\dagger}(\mathcal{D}_n^{\pi_n}[\mathcal{K}_n, \mathbf{V}_n])$ in closed form, as shown in the previous Section 1.2. The resulting algorithm is effectively an RJMCMC scheme (Green, 1995) in the discrete space of network structures and latent allocation vectors, where the Jacobian in the acceptance criterion is always 1 and can be omitted. With probability $p_G = 0.5$ we perform a single edge move on the current graph $\mathcal{G}^i$ and leave the latent variable matrix and the numbers of mixture components unchanged, symbolically: $\mathbf{V}^{i+1} = \mathbf{V}^i$ and $\mathbf{K}^{i+1} = \mathbf{K}^i$. The new candidate graph is obtained by randomly selecting one of the domain nodes X_n and changing its parent set π_n^i by either adding or removing a parent node. There are $|\pi_n^i|$ nodes that can be removed from π_n^i and there are $N - |\pi_n^i|$ nodes that can be added to π_n^i, unless the maximal fan-in $\mathcal{F}$ is reached; for $|\pi_n^i| = \mathcal{F}$ no more edges can be added. This gives a set $\mathcal{N}(\pi_n^i)$ of new candidate parent sets with $|\mathcal{N}(\pi_n^i)| \in \{\mathcal{F}, N\}$ from which we randomly select a new candidate parent set π_n^{i+1}. The MH sampler proposes the new candidate graph $\mathcal{G}^{i+1}$ which results from $\mathcal{G}^i$ by replacing π_n^i by π_n^{i+1}, and the new graph is accepted with probability:

$$A(\mathcal{G}^{i+1}|\mathcal{G}^i) = min\left\{1, \frac{\Psi^{\dagger}(\mathcal{D}_n^{\pi_n^{i+1}}[\mathcal{K}_n^i, \mathbf{V}_n^i])}{\Psi^{\dagger}(\mathcal{D}_n^{\pi_n^i}[\mathcal{K}_n^i, \mathbf{V}_n^i])} \frac{P(\pi_n^{i+1})}{P(\pi_n^i)} \frac{|\mathcal{N}(\pi_n^i)|}{|\mathcal{N}(\pi_n^{i+1})|}\right\} \tag{12}$$

where $|.|$ is the cardinality, and the local $\Psi^{\dagger}(.)$ scores have been specified in Eq. (6). The graph is left unchanged, symbolically $\mathcal{G}^{i+1} := \mathcal{G}^i$, if the move is not accepted.

With the complementary probability $1 - p_G$ we leave the graph $\mathcal{G}^i$ unchanged and perform a move on $(\mathbf{V}^i, \mathbf{K}^i)$, where $\mathbf{V}_n^i$ is the latent variable vector of X_n in $\mathbf{V}^i$, and $\mathbf{K}^i = (\mathcal{K}_1^i, \dots, \mathcal{K}_N^i)$. We randomly select a node X_n and change its current number of components $\mathcal{K}_n^i$ and its allocation vector $\mathbf{V}_n^i$ via a changepoint birth or death move, or we keep $\mathcal{K}_n^i$ and change its latent variable vector $\mathbf{V}_n^i$ by a changepoint re-allocation move along the lines of the RJMCMC algorithm of Green (1995).
The changepoint birth (death) move increases (decreases) $\mathcal{K}_n^i$ by 1 and changes $\mathbf{V}_n^i$ correspondingly. The changepoint reallocation move leaves $\mathcal{K}_n^i$ unchanged and modifies $\mathbf{V}_n^i$ only. If with probability $(1 - p_G)/N$ a changepoint move on $(\mathcal{K}_n^i, \mathbf{V}_n^i)$ is performed, we randomly draw the move type. Under fairly mild regularity conditions (ergodicity), the MH MCMC sampling scheme converges to the desired posterior distribution (Green, 1995) if the acceptance probabilities for the three changepoint moves $(\mathcal{K}_n^i, \mathbf{V}_n^i) \to (\mathcal{K}_n^{i+1}, \mathbf{V}_n^{i+1})$ are chosen of the form $min(1, R)$, with

$$R = \frac{\Psi^{\dagger}(\mathcal{D}_n^{\pi_n}[\mathcal{K}_n^{i+1}, \mathbf{V}_n^{i+1}])}{\Psi^{\dagger}(\mathcal{D}_n^{\pi_n}[\mathcal{K}_n^i, \mathbf{V}_n^i])} \times A \times B = \frac{\prod_{k=1}^{\mathcal{K}_n^{i+1}} \Psi(\mathcal{D}_n^{\pi_n}[k, \mathbf{V}_n^{i+1}])}{\prod_{k=1}^{\mathcal{K}_n^i} \Psi(\mathcal{D}_n^{\pi_n}[k, \mathbf{V}_n^i])} \times A \times B \tag{13}$$

where $A = P(\mathbf{V}_n^{i+1}|\mathcal{K}_n^{i+1})P(\mathcal{K}_n^{i+1})/P(\mathbf{V}_n^i|\mathcal{K}_n^i)P(\mathcal{K}_n^i)$ is the prior probability ratio, B is the inverse proposal probability ratio, and the $\Psi(.)^{\dagger}$- and $\Psi(.)$-terms have been specified in Eqn. (6) and (7).

In our implementation we choose $\mathcal{K}_n^i$-dependent proposal probabilities $b_{\mathcal{K}_n^i}$, $d_{\mathcal{K}_n^i}$, and $r_{\mathcal{K}_n^i}$ for birth (b), death (d) and re-allocation (r) moves. Like Green (1995) we set: $b_{\mathcal{K}_n^i} = c\ min\{1, \frac{P(\mathcal{K}_n^i+1)}{P(\mathcal{K}_n^i)}\}$ and $d_{\mathcal{K}_n^i} = c\ min\{1, \frac{P(\mathcal{K}_n^i-1)}{P(\mathcal{K}_n^i)}\}$ with the constant c as large as possible subject to the constraint $b_{\mathcal{K}_n^i} + d_{\mathcal{K}_n^i} \leq 0.9$ for all i so that the ratio of the proposal probabilities for birth versus death moves $d_{(\mathcal{K}_n^i+1)}/b_{\mathcal{K}_n^i}$ cancels out against the prior ratio $P(\mathcal{K}_n^i + 1)/P(\mathcal{K}_n^i)$. The proposal probability for a changepoint (re-)allocation move is given by: $r_{\mathcal{K}_n^i} = 1 - b_{\mathcal{K}_n^i} - d_{\mathcal{K}_n^i}$.

(i) For a changepoint reallocation (r) we randomly select one of the existing changepoints $b_{\mathbf{V}_n^i,j}$ from the vector $(b_{\mathbf{V}_n^i,1}, \dots, b_{\mathbf{V}_n^i,\mathcal{K}_n-1})$, and the replacement value $b^{\dagger}$ is drawn from a uniform distribution on the discrete set $\left\{b_{\mathbf{V}_n^i,j-1} + 2, \dots, b_{\mathbf{V}_n^i,j+1} - 2\right\}$ where $b_{V_n^i,0} = 1$ and $b_{\mathbf{V}_n^i,\mathcal{K}_n} = m$. The proposal probability ratio is one and the prior probabilities $P(\mathcal{K}_n^{i+1}) = P(\mathcal{K}_n^i)$ cancel out, $B_r = 1$. From Eq. (11) it can be seen that the remaining prior probability ratio is $P(\mathbf{V}_n^{i+1}|\mathcal{K}_n^{i+1})/P(\mathbf{V}_n^i|\mathcal{K}_n^i)$ is given by:

$$A_r = \frac{(b_{\mathbf{V}_n^i,j+1} - b^{\dagger} - 1)(b^{\dagger} - b_{\mathbf{V}_n^i,j-1} - 1)}{(b_{\mathbf{V}_n^i,j+1} - b_{\mathbf{V}_n^i,j} - 1)(b_{\mathbf{V}_n^i,j} - b_{\mathbf{V}_n^i,j-1} - 1)}, \tag{14}$$

If there is no changepoint ($\mathcal{K}_n^i = 1$) the move is rejected and the Markov chain is left unchanged.

(ii) If a changepoint birth move (b) on $(\mathcal{K}_n^i, \mathbf{V}_n^i)$ is proposed, the location of the new changepoint $b^\dagger$ is randomly drawn from a uniform distribution on the set of all valid new changepoint locations:

$$B^\dagger(\mathbf{V}_n^i) := \big\{b : 2 \leq b \leq m-1 \wedge \forall j \in \{1, \dots, \mathcal{K}_n - 1\} : |b - b_{\mathbf{V}_n^i,j}| > 1\big\} \tag{15}$$

The new candidate changepoint $b^\dagger$ with $b_{\mathbf{V}_n^i,j} < b^\dagger < b_{\mathbf{V}_n^i,j+1}$ yields $\mathcal{K}_n^{i+1} = \mathcal{K}_n^i + 1$ mixture components and a new candidate allocation vector $\mathbf{V}_n^{i+1}$ in which one segment has been subdivided into 2 segments. The proposal probability for this move is $b_{\mathcal{K}_n^i}/|B^\dagger(\mathbf{V}_n^i)|$, where $|B^\dagger(\mathbf{V}_n^i)|$ is the number of valid changepoint locations for $b^\dagger$. The reverse death move, which is selected with probability $d_{(\mathcal{K}_n^i+1)}$, consists in discarding randomly one of the $(\mathcal{K}_n^i + 1) - 1 = \mathcal{K}_n^i$ changepoints from $(\mathcal{K}_n^{i+1}, \mathbf{V}_n^{i+1})$. The prior probability ratio A_b can be computed with Eq. (11):

$$A_b = \frac{P(\mathcal{K}_n^i + 1)}{P(\mathcal{K}_n^i)} \frac{(2\mathcal{K}_n^i + 1)(2\mathcal{K}_n^i)}{(m - 2\mathcal{K}_n^i - 1)(m - 2\mathcal{K}_n^i - 2)} \frac{(b_{\mathbf{V}_n^i,j+1} - b^\dagger - 1)(b^\dagger - b_{\mathbf{V}_n^i,j} - 1)}{(b_{\mathbf{V}_n^i,j+1} - b_{\mathbf{V}_n^i,j} - 1)}, \tag{16}$$

and the inverse proposal probability ratio is $B_b = \frac{d_{(\mathcal{K}_n^i+1)}|B^\dagger(\mathbf{V}_n^i)|}{(b_{\mathcal{K}_n^i}\mathcal{K}_n^i)}$. This can be simplified to:

$$A_b B_b = \frac{(2\mathcal{K}_n^i + 1)(2\mathcal{K}_n^i)}{(m - 2\mathcal{K}_n^i - 1)(m - 2\mathcal{K}_n^i - 2)} \frac{(b_{\mathbf{V}_n^i,j+1} - b^\dagger - 1)(b^\dagger - b_{\mathbf{V}_n^i,j} - 1)}{(b_{\mathbf{V}_n^i,j+1} - b_{\mathbf{V}_n^i,j} - 1)} \frac{|B^\dagger(\mathbf{V}_n^i)|}{\mathcal{K}_n^i} \tag{17}$$

For $\mathcal{K}_n^i = \mathcal{K}_{max}$ the birth of a new changepoint is invalid and the Markov chain is left unchanged.

(iii) A changepoint death move (d) on the current state $(\mathcal{K}_n^i, \mathbf{V}_n^i)$ is the reverse of the birth move. There are $\mathcal{K}_n^i - 1$ changepoints and we randomly select and delete one of them. Let $b^\dagger = b_{\mathbf{V}_n^i,j}$ be the selected changepoint and let $\mathbf{V}_n^{i+1}$ be the new candidate allocation vector after deletion of the selected changepoint $b^\dagger$. We obtain for the product of the prior probability ratio and the inverse proposal probability ratio:

$$A_d B_d = \frac{(m - 2\mathcal{K}_n^i - 3)(m - 2\mathcal{K}_n^i - 4)}{(2\mathcal{K}_n^i - 1)(2\mathcal{K}_n^i - 2)} \frac{(b_{\mathbf{V}_n^i,j+1} - b_{\mathbf{V}_n^i,j-1} - 1)}{(b_{\mathbf{V}_n^i,j+1} - b^\dagger - 1)(b^\dagger - b_{\mathbf{V}_n^i,j-1} - 1)} \frac{\mathcal{K}_n^i - 1}{|B^\dagger(\mathbf{V}_n^{i+1})|} \tag{18}$$

where $|B^\dagger(\mathbf{V}_n^{i+1})|$ is the number of valid new changepoint locations that can be added during a birth move. For $\mathcal{K}_n^i = 1$ there is no changepoint that can be deleted during a death move and the Markov chain is left unchanged.

1.4 Sampling parent node sets from the Boltzmann distribution

The Metropolis-Hastings (MH) sampler presented in Section 1.3.1 changes the current graph $\mathcal{G}$ by single-edge operations. An improvement can be achieved by sampling new parent node sets $\pi_n^\star$ for each node X_n directly from the posterior distribution:

$$P(\pi_n^\star | \mathcal{D}_n^{1:N}) = \frac{\Psi(\mathcal{D}_n^{\pi_n^\star})}{\sum_{\pi_n : |\pi_n| \leq \mathcal{F}} \Psi(\mathcal{D}_n^{\pi_n})} \tag{19}$$

where the local $\Psi(.)$-scores of the standard (homogeneous) DBN were specified in Eq. (3) and the sum is over all valid parent node sets π_n subject to a fan-in restrition $\mathcal{F}$. Eq. (19) is similar to Eq. (10) in Friedman and Koller (2003). The main difference is that Friedman and Koller (2003) apply this scheme to static Bayesian networks subject to an order constraint, where the latter has to be imposed on the system to render it modular. A DBN without intra-time-slice connectivities, on the other hand, is intrinsically modular, i.e. Eq. (19) exploits modularities that already exist and do not need to be enforced via an additional constraint.

In standard (homogeneous) DBNs the Boltzmann distributions can be pre-computed and stored for each node so that sampling from them may become computationally very effective and superior to MH samplers that are based on single edge operations. For our changepoint model it turns out that sampling from the Boltzmann distribution is ineffective, as the local scores depend on the node-specific changepoints and would have to be re-computed in every single MCMC step. In our cpBGe model we have the following node-specific Boltzmann distributions conditional on the number of changepoints $\mathcal{K}_n$ and the allocation vector $\mathbf{V}_n$:

$$P(\pi_n^\star|\mathcal{K}_n, \mathbf{V}_n, \mathcal{D}_n^{1:N}) = \frac{\Psi^\dagger(\mathcal{D}_n^{\pi_n^\star}[\mathcal{K}_n, \mathbf{V}_n])}{\sum_{\pi_n:|\pi_n|\leq\mathcal{F}} \Psi^\dagger(\mathcal{D}_n^{\pi_n}[\mathcal{K}_n, \mathbf{V}_n])} = \frac{\prod_{k=1}^{\mathcal{K}_n} \Psi(\mathcal{D}_n^{\pi_n^\star}[k, \mathbf{V}_n])}{\sum_{\pi_n:|\pi_n|\leq\mathcal{F}} \prod_{k=1}^{\mathcal{K}_n} \Psi(\mathcal{D}_n^{\pi_n}[k, \mathbf{V}_n])} \tag{20}$$

where the local cpBGe scores $\Psi^\dagger(\mathcal{D}_n^{\pi_n}[\mathcal{K}_n, \mathbf{V}_n])$ and the local BGe scores $\Psi(\mathcal{D}_n^{\pi_n}[k, \mathbf{V}_n])$ can be computed with Eqn. (6) and (7). Although the three changepoint moves affect only two local BGe scores in the products, the re-computation of the Boltzmann distribution after each changepoint move becomes computationally expensive. The bottleneck becomes obvious when taking into consideration that the three changepoint moves give relatively small steps in the configuration space of the allocation vector $\mathbf{V}_n$ so that a large amount of re-computations is required.
In Sections 1.5 and 1.6 we will discuss a dynamic programming scheme for sampling the node-specific numbers of changepoints $\mathcal{K}_n$ and the node-specific allocation vectors $\mathbf{V}_n$ directly from the conditional posterior distribution: $P(\mathbf{V}_n, \mathcal{K}_n|\pi_n, \mathcal{D}_n^{\pi_n})$. This dynamic programming scheme for sampling from $P(\mathbf{V}_n, \mathcal{K}_n|\pi_n, \mathcal{D}_n^{\pi_n})$ in combination with sampling parent node configurations π_n from the Boltzmann distribution $P(\pi_n|\mathcal{K}_n, \mathbf{V}_n, \mathcal{D}_n^{1:N})$ can be used to construct a Gibbs MCMC sampling scheme.

1.5 Sampling changepoints by dynamic programming

In the proposed cpBGe model we have a parent node set π_n, a number of components $\mathcal{K}_n$, and an allocation vector $\mathbf{V}_n$ for each domain node X_n $(n = 1, \dots, N)$. $\mathcal{K}_n$ can be identified with $\mathcal{K}_n - 1$ changepoints on the *discrete* set $\{2, \dots, m-1\}$ and there is a one-to-one mapping between $\mathbf{V}_n$ and the changepoint vector $\mathbf{b}_{\mathbf{V}_n} := (b_{\mathbf{V}_n,0}, \dots, b_{\mathbf{V}_n,\mathcal{K}_n})$ where $b_{\mathbf{V}_n,0} = 1$ and $b_{\mathbf{V}_n,\mathcal{K}_n} = m$ are pseudo changepoints.
We now want to apply a dynamic programming scheme to sample for each domain node X_n from the joint posterior distribution of $(\mathcal{K}_n, \mathbf{V}_n)$ conditional on the parent node set π_n:

$$P(\mathcal{K}_n, \mathbf{V}_n|\pi_n, \mathcal{D}_n^{\pi_n}) = P(\mathcal{K}_n|\pi_n, \mathcal{D}_n^{\pi_n})P(\mathbf{V}_n|\mathcal{K}_n, \pi_n, \mathcal{D}_n^{\pi_n}) \tag{21}$$

where $\mathcal{D}_n^{\pi_n}$ denotes the set of observations $\{(\mathcal{D}_{n,i}, \mathcal{D}_{\pi_n,i-1}) : 2 \leq i \leq m\}$ pertaining to node X_n and its parent node set π_n. Accordingly, let $\mathcal{D}_n^{\pi_n}[s:t]$ denote the sub-segment $\{(\mathcal{D}_{n,i}, \mathcal{D}_{\pi_n,i-1}) : s \leq i \leq t\}$ of adjacent observations, and we also define $\mathcal{D}_{n,s:t} = \{\mathcal{D}_{n,i} : s \leq i \leq t\}$ and $\mathcal{D}_{\pi_n,s:t} = \{\mathcal{D}_{\pi_n,i} : s-1 \leq i \leq t-1\}$

The local cpBGe score $\Psi^\dagger(\mathcal{D}_n^{\pi_n}[\mathcal{K}_n, \mathbf{V}_n])$ of X_n is the probability of the observations $\mathcal{D}_{n,2:m}$ of X_n given the parent set π_n and its observations $\mathcal{D}_{\pi_n,2:m}$, $\mathcal{K}_n$ mixture components, and the allocation vector $\mathbf{V}_n$. The local score of X_n can be factorized using Eq. (6). Mapping the allocation vector $\mathbf{V}_n$ onto the changepoint vector $\mathbf{b}_{\mathbf{V}_n}$ we obtain as alternative representation:

$$\Psi^\dagger(\mathcal{D}_n^{\pi_n}[\mathcal{K}_n, \mathbf{V}_n]) = P(\mathcal{D}_{n,2:m}|\mathcal{D}_{\pi_n,2:m}, \mathcal{K}_n, \mathbf{b}_{\mathbf{V}_n}) = \prod_{k=0}^{\mathcal{K}_n-1} \Psi(\mathcal{D}_n^{\pi_n}[(b_{\mathbf{V}_n,k}+1) : b_{\mathbf{V}_n,k+1}]) \tag{22}$$

When just conditioning on $\mathcal{K}_n$ with $\mathcal{K}_n > 1$, we obtain the following marginal distribution:

$$P(\mathcal{D}_{n,2:m}|\mathcal{D}_{\pi_n,2:m}, \mathcal{K}_n) = \sum_{\mathbf{b}_n\in\mathcal{B}(\mathcal{K}_n)} P(\mathbf{b}_n) \prod_{k=0}^{\mathcal{K}_n-1} \Psi(\mathcal{D}_n^{\pi_n}[(b_{n,k}+1) : b_{n,k+1}]) \tag{23}$$

where $\mathcal{B}(\mathcal{K}_n)$ is the set of all valid changepoint vectors $\mathbf{b}_n = (b_{n,0}, \ldots, b_{n,\mathcal{K}_n})$ of cardinality $\mathcal{K}_n + 1$ with $b_{n,i+1} - b_{n,i} > 1$, $b_{n,0} = 1$ and $b_{n,\mathcal{K}_n} = m$, and $P(\mathbf{b}_n) = P(\mathbf{V}_n(b_n))$ is the prior probability of the unique allocation vector $\mathbf{V}_n(b_n)$ and can be computed with Eq. (11) after having extracted the allocation vector $\mathbf{V}_n(\mathbf{b}_n)$ from $\mathbf{b}_n$. Now we additionally fix the j-th changepoint location, symbolically: $b_{n,j} = t - 1$, and restrict on the data sub-segment $\mathcal{D}_n^{\pi_n}[t : m]$:

$$P(\mathcal{D}_{n,t:m}|\mathcal{D}_{\pi_n,t:m}, \mathcal{K}_n, b_{n,j} = t-1) = \sum_{\mathbf{b}_n^j \in \mathcal{B}^j(\mathcal{K}_n|b_{n,j}=t-1)} P(\mathbf{b}_n^j) \prod_{k=j}^{\mathcal{K}_n - 1} \Psi(\mathcal{D}_n^{\pi_n}[(b_{n,k}+1) : b_{n,k+1}]) \quad (24)$$

where $\mathcal{B}^j(\mathcal{K}_n|b_{n,j} = t-1)$ is the set of all valid changepoint vectors $\mathbf{b}_n^j = (b_{n,j+1}, \ldots, b_{n,\mathcal{K}_n})$ on the discrete interval $\{t+1, \ldots, m-2\}$ with $b_{n,i+1} - b_{n,i} > 1$, $b_{n,j} = t-1$ and $b_{n,\mathcal{K}_n} = m$. Different from Eq. (23) the prior probability $P(\mathbf{b}_n^j)$ of the changepoint subset $\mathbf{b}_n^j$ cannot be computed in closed-form for $j > 0$.

For $\mathcal{K}_n > 1$ and $j = 0, \ldots, \mathcal{K}_n - 1$ we set $Q_j^{\mathcal{K}_n}(t|n, \pi_n) = P(\mathcal{D}_{n,t:m}|\mathcal{D}_{\pi_n,t:m}, \mathcal{K}_n, b_{n,j} = t-1)$ for $t = 2(j+1), \ldots, m - 2(\mathcal{K}_n - j) + 1$ and let $Q_j^{\mathcal{K}_n}(t|n, \pi_n)$ be zero otherwise, i.e. for $t < 2(j+1)$ and $t > m - 2(\mathcal{K}_n - j) + 1$.

It can be seen from Eq. (23) that $Q_0^{\mathcal{K}_n}(2|n, \pi_n)$ is equal to $P(\mathcal{D}_{n,2:m}|\mathcal{D}_{\pi_n,2:m}, \mathcal{K}_n)$, since $b_{n,0} = 1$ is a fixed pseudo changepoint, and we have for $t = 2\mathcal{K}_n, \ldots, m-1$:

$$Q_{\mathcal{K}_n - 1}^{\mathcal{K}_n}(t|n, \pi_n) = \Psi(\mathcal{D}_n^{\pi_n}[t : m]) \quad (25)$$

so that the Q terms can be computed straightforwardly for $j = \mathcal{K}_n - 1$.

Afterwards – as a special case of the recursions given in Fearnhead (2006) – we obtain the following recursions: For $\mathcal{K}_n > 1$, $j = 0, \ldots, \mathcal{K}_n - 2$ and $t = 2(j+1), \ldots, m - 2(\mathcal{K}_n - j) + 1$:

$$Q_j^{\mathcal{K}_n}(t|n, \pi_n) = \sum_{s=t+1}^{m-2(\mathcal{K}_n - j - 1)} \Psi(\mathcal{D}_n^{\pi_n}[t : s]) Q_{j+1}^{\mathcal{K}_n}(s+1|n, \pi_n) P(b_{n,j} = t-1|b_{n,j+1} = s, \mathcal{K}_n) \quad (26)$$

where the bounds of t as well as the upper summation index allow for the changepoints that still need to be included[1].

In our changepoint model the probability distribution $P(b_{n,j} = t-1|b_{n,j+1} = s, \mathcal{K}_n)$ of changepoint $b_{n,j}$ conditional on $\mathcal{K}_n$ changepoints and the $b_{n,j+1}$ changepoint being located at time point s cannot be computed in closed-form. Following Fearnhead (2006) we set:

$$P(b_{n,j} = t-1|b_{n,j+1} = s, \mathcal{K}_n) = P(m, \mathcal{K}_n, s, t) := \frac{s-t}{\begin{pmatrix} m-2 \\ 2(\mathcal{K}_n - 1) + 1 \end{pmatrix}} \quad (27)$$

This is a 'computational trick' which also yields: $Q_0^{\mathcal{K}_n}(2|n, \pi_n) = P(\mathcal{D}_n^{\pi_n}|\mathcal{K}_n)$ (Fearnhead, 2006). Thus, the modified recursions can be employed to compute: $P(\mathcal{D}_{n,2:m}|\mathcal{D}_{\pi_n,2:m}, \mathcal{K}_n)$ for $\mathcal{K}_n = 2, \ldots, \mathcal{K}_{MAX}$. Note that there is no changepoint for $\mathcal{K}_n = 1$ so that the local cpBGe score (see Eq. (6)) is equal to the local BGe score of X_n (see Eq. (3)).

$$P(\mathcal{D}_{n,2:m}|\mathcal{D}_{\pi_n,2:m}, \mathcal{K}_n = 1) = \Psi(\mathcal{D}_n^{\pi_n}) \quad (28)$$

Subsequently, the marginal posterior probability of the number of mixture components $\mathcal{K}_n$ can be computed as follows:

$$P(\mathcal{K}_n = k^\star|\mathcal{D}_{n,2:m}, \mathcal{D}_{\pi_n,2:m}) = \frac{P(\mathcal{K}_n = k^\star) P(\mathcal{D}_{n,2:m}|\mathcal{D}_{\pi_n,2:m}, \mathcal{K}_n = k^\star)}{\sum_{k=1}^{\mathcal{K}_{MAX}} P(\mathcal{K}_n = k) P(\mathcal{D}_{n,2:m}|\mathcal{D}_{\pi_n,2:m}, \mathcal{K}_n = k)} \quad (29)$$

[1] Note that there must be room for including $j-1$ changepoints $b_{n,1}, \ldots, b_{n,j-1}$ on the locations $2, \ldots, t-2$ with $b_{n,j} - b_{n,j-1} > 1$ $(j = 1, \ldots, j)$, $b_{n,0} = 1$ and $b_{n,j} = t-1$. And there must be room for $\mathcal{K}_n - 1 - j$ changepoints $b_{n,j+1}, \ldots, b_{n,\mathcal{K}_n - 1}$ on the locations $t, \ldots, m-1$ with $b_{n,j} - b_{n,j-1} > 1$ $(j = j+1, \ldots, \mathcal{K}_n)$, $b_{n,j} = t-1$ and $b_{n,\mathcal{K}_n} = m$.

where $P(\mathcal{K}_n)$ is a Poisson distribution with $\lambda = 1$ truncated to $1 \leq \mathcal{K}_n \leq \mathcal{K}_{MAX}$ in our cpBGe model.

After having sampled $\mathcal{K}_n = k$ from $P(\mathcal{K}_n|\mathcal{D}_{n,2:m}, \mathcal{D}_{\pi_n,2:m})$, we can sample an allocation vector $\mathbf{V}_n$ from $P(\mathbf{V}_n|\mathcal{K}_n = k, \mathcal{D}_{n,2:m}, \mathcal{D}_{\pi_n,2:m})$ by sampling the j-th changepoint $b_{\mathbf{V}_n,j}$ conditional on the $(j-1)$-th changepoint $b_{\mathbf{V}_n,j-1}$ for $j = 1, \dots, k-1$ from the following distribution:

$$P(b_{\mathbf{V}_n,j} = s|b_{\mathbf{V}_n,j-1}, \mathcal{D}_n^{\pi_n}, \mathcal{K}_n = k) = \frac{\Psi(\mathcal{D}_n^{\pi_n}[(b_{\mathbf{V}_n,j-1}+1) : s])Q_j^k(s+1|n,\pi_n)P(m,k,s,b_{\mathbf{V}_n,j-1}+1)}{Q_{j-1}^k(b_{\mathbf{V}_n,j-1}+1|n,\pi_n)} \tag{30}$$

as shown in Fearnhead (2006). The dynamic programming scheme works as follows: (i) We sample $\mathcal{K}_n = k$ from Eq. (29). (ii) For $k = 1$ we have no changepoints and for $k > 1$ we can subsequently employ Eq. (30) to sample the locations of the $k-1$ changepoints. Because of the one-to-one mapping between changepoints and allocation vectors, the sampled changepoints $b_{\mathbf{V}_n,1}, \dots, b_{\mathbf{V}_n,k-1}$ give a unique allocation vector $\mathbf{V}_n$ which can be seen as directly sampled from $P(\mathbf{V}_n|\mathcal{K}_n = k, \mathcal{D}_{n,2:m}, \mathcal{D}_{\pi_n,2:m})$.

As a summary: By employing the dynamic programming scheme presented in this Section for each node X_n with parent set π_n, the number of mixture components $\mathcal{K}_n$ and the allocation vector $\mathbf{V}_n$ can be sampled from the conditional posterior distribution of $P(\mathcal{K}_n, \mathbf{V}_n|\pi_n, \mathcal{D}_n^{\pi_n})$.

1.6 Sampling changepoints from a point process prior

As shown by Fearnhead (2006) the computational costs of the dynamic programming scheme can be reduced by a slightly modified prior distribution for $(\mathcal{K}_n, \mathbf{V}_n)$. Instead of modelling $P(\mathcal{K}_n)$, and afterwards the allocation vectors $\mathbf{V}_n$ conditional on $\mathcal{K}_n$, a point process prior can be used to model the distances between successive changepoints. In the point process model $g(t)$ $(t = 1, 2, 3, \dots)$ denotes the prior probability that there are t time points between two successive changepoints $b_{n,j-1}$ and $b_{n,j}$ on the discrete interval $\{2, \dots, m-1\}$. The prior probability of $\mathcal{K}_n - 1$ changepoints being located at time points $b_{n,1}, \dots, b_{n,\mathcal{K}_n-1}$ is:

$$P(b_{n,1}, \dots, b_{n,\mathcal{K}_n-1}) = g_0(b_{n,1}) \left(\prod_{j=2}^{\mathcal{K}_n-1} g(b_{n,j} - b_{n,j-1}) \right) (1 - G(b_{n,\mathcal{K}_n} - b_{n,\mathcal{K}_n-1})) \tag{31}$$

where $b_{n,0} = 1$ and $b_{n,\mathcal{K}_n} = m$ are again pseudo changepoints, $G(t) = \sum_{s=1}^{t} g(t)$, and $g_0(.)$ is the prior distribution for the first changepoint $b_{n,1}$. For $g(.)$ the probability mass function of the negative binomial distribution NBIN(p,a) with parameters p and a can be used:

$$g(t) = \left(\begin{array}{c} t-1 \\ a-1 \end{array} \right) p^k (1-p)^{t-a} \tag{32}$$

In a point process model on the positive *and* negative integers the probability mass function of the first changepoint $b_{n,1} \in \{2, \dots, m-1\}$ is a mixture of k negative binomial distributions:

$$g_0(b_{n,1}) = \frac{1}{k} \sum_{i=1}^{k} \left(\begin{array}{c} (b_{n,1}-1) - 1 \\ i-1 \end{array} \right) p^i (1-p)^{(b_{n,1}-1)-i} \tag{33}$$

For each node X_n we define $Q(t|n, \pi_n)$ as the probability of its observations $\mathcal{D}_{n,t:m}$ given the observations $\mathcal{D}_{\pi_n,(t-1):(m-1)}$ of π_n and a changepoint $b^\dagger$ at time point $t-1$ $(t = 2, \dots, m)$:

$$Q(t|n, \pi_n) = P(\mathcal{D}_{n,t:m}|\mathcal{D}_{\pi_n,(t-1):(m-1)}, b^\dagger = t-1) \tag{34}$$

$Q(m|n, \pi_n)$ is then equal to $\Psi(\mathcal{D}_n^{\pi_n}[m : m])$, defined below Eq. (21). For $t = 3, \dots, m-1$ the following recursion can be used:

$$Q(t|n, \pi_n) = \left(\sum_{s=t}^{m-1} \Psi(\mathcal{D}_n^{\pi_n}[t : s]) Q(s+1|n, \pi_n) g(s+1-t) \right) + \Psi(\mathcal{D}_n^{\pi_n}[t : m])(1 - G(m-t)) \tag{35}$$

and

$$Q(2|n,\pi_n) = \left(\sum_{s=2}^{m-1} \Psi(\mathcal{D}_n^{\pi_n}[2:s])Q(s+1|n,\pi_n)g_0(s-1)\right) + \Psi(\mathcal{D}_n^{\pi_n})(1-G_0(m-2)) \tag{36}$$

where $G_0(t) = \sum_{s=1}^{t} g_0(s)$. The posterior distribution of the first changepoint $b_{n,1}$ given the parent set π_n is:

$$P(b_{n,1} = t|\mathcal{D}_n^{\pi_n}) = \Psi(\mathcal{D}_n^{\pi_n}[2:t])Q(t+1|n,\pi_n)\frac{g_0(t-1)}{Q(2|n,\pi_n)} \tag{37}$$

for $t = 2, \dots, m-1$ and the probability of no changepoint ($P(\mathcal{K}_n = 1)$) is given by:

$$P(\mathcal{K}_n = 1|\pi_n, \mathcal{D}_n^{\pi_n}) = \Psi(\mathcal{D}_n^{\pi_n}[2:m])\frac{1-G_0(m-2)}{Q(2|n,\pi_n)} \tag{38}$$

The posterior distribution of the j-th changepoint $b_{n,j}$ given the parent node set π_n and the previous changepoint $b_{n,j-1}$ is:

$$P_t := P(b_{n,j} = t|b_{n,j-1}, \mathcal{D}_n^{\pi_n}) = \Psi(\mathcal{D}_n^{\pi_n}[(b_{n,j-1}+1):t])Q(t+1|n,\pi_n)\frac{g(t-b_{n,j-1})}{Q(b_{n,j-1}+1|n,\pi_n)} \tag{39}$$

for $t = b_{n,j-1}+1, \dots, m-1$ and the probability of no further changepoint is given by:

$$P_{\geq m} := \Psi(\mathcal{D}_n^{\pi_n}[(b_{n,j-1}+1):m])\frac{1-G_0(m-b_{n,j-1}-1)}{Q(b_{n,j-1}+1|n,\pi_n)} \tag{40}$$

Consequently, if there is a changepoint at $b_{n,j-1} = t$, then the location of the next changepoint can be sampled from the discrete mass probability distribution $[P_{b_{n,j-1}+1}, \dots, P_{m-1}, P_{\geq m}]$ where $P_{\geq m}$ is the probability for no further changepoints. Having sampled changepoints $b_{n,1}, \dots, b_{n,k-1}$ from these conditional distributions, the number of mixture components is $\mathcal{K}_n = k$ and the allocation vector $\mathbf{V}_n$ can be computed from the changepoints.
As a summary: For each node X_n with parent set π_n, $(\mathcal{K}_n, \mathbf{V}_n)$ can be sampled from $P(\mathcal{K}_n, \mathbf{V}_n|\pi_n, \mathcal{D}_n^{\pi_n})$ when the prior distribution $P(\mathcal{K}_n, \mathbf{V}_n)$ is replaced by a point-process model as described above.

1.7 Sampling changepoints from a point process prior for the regularized cpBGe model

The dynamic programming scheme presented in Section 1.6 can also be used to sample changepoints for the novel regularized cpBGe model. In this Section we describe the modifications that have to be made. We employ the same point process prior for cluster-specific changepoints. The prior probability that there are $\mathcal{K}_i - 1$ changepoints being located at time points $b_{i,1}, \dots, b_{i,\mathcal{K}_i-1}$ for the nodes in the ith cluster is given by:

$$P(b_{i,1}, \dots, b_{i,\mathcal{K}_i-1}) = g_0(b_{i,1})\left(\prod_{j=2}^{\mathcal{K}_i-1} g(b_{i,j} - b_{i,j-1})\right)(1 - G(b_{i,\mathcal{K}_i} - b_{i,\mathcal{K}_i-1})) \tag{41}$$

where $g(.)$, $G(.)$, $g_0(.)$ have been specified in Section 1.6 (see Eqn. (32)-(33)).

Different from the original cpBGe model we now have changepoints for each of c clusters of nodes induced by the clustering $\mathcal{C}$ rather than node-specific changepoints for each individual node. We want to sample changepoints for each cluster, which are then common to all the nodes in that cluster. We consider the ith cluster ($1 \leq i \leq c$), that is the set of nodes $\{X_n : \mathcal{C}(n) = i\}$. The nodes in the ith cluster share K_i components and there is a set of changepoints $b_{i,1}, \dots, b_{i,\mathcal{K}_i-1}$

that can be mapped onto the allocation vector of the ith cluster $\mathbf{V}_i^{\mathcal{C}}$: $\mathbf{V}_i^{\mathcal{C}}(t) = k \Leftrightarrow b_{i,k-1} < t \leq b_{i,k}$ ($t = 2, \dots, m$ and $k = 1, \dots, \mathcal{K}_i$).

We define $Q(t|i, C, \mathcal{G})$ as the probability of the observations for the nodes in the ith cluster $\mathcal{D}_{n,t:m}$ ($n : \mathcal{C}(n) = i$) conditional on the corresponding realisations of the parent nodes $\mathcal{D}_{\pi_n,(t-1):(m-1)}$ ($n : \mathcal{C}(n) = i$) *and* a changepoint $b^\dagger$ at time point $t-1$ ($t = 2, \dots, m$).

For $t = m$ we have:

$$Q(m|i, \mathcal{C}, \mathcal{G}) = \prod_{n:\mathcal{C}(n)=i} \Psi(\mathcal{D}_n^{\pi_n}[m : m]) \tag{42}$$

and for $t = 3, \dots, m-1$ the same recursion as in Section 1.6 can be used:

$$\begin{aligned} Q(t|i, \mathcal{C}, \mathcal{G}) &= \sum_{s=t}^{m-1} \left(\prod_{n:\mathcal{C}(n)=i} \Psi(\mathcal{D}_n^{\pi_n}[t : s]) \right) Q(s+1|i, \mathcal{C}, \mathcal{G}) g(s+1-t) && (43) \\ &+ \left(\prod_{n:\mathcal{C}(n)=i} \Psi(\mathcal{D}_n^{\pi_n}[t : m]) \right) (1 - G(m-t)) && (44) \end{aligned}$$

and

$$\begin{aligned} Q(2|i, \mathcal{C}, \mathcal{G}) &= \sum_{s=2}^{m-1} \left(\prod_{n:\mathcal{C}(n)=i} \Psi(\mathcal{D}_n^{\pi_n}[2 : s]) Q(s+1|i, \mathcal{C}, \mathcal{G}) \right) g_0(s-1) && (45) \\ &+ \left(\prod_{n:\mathcal{C}(n)=i} \Psi(\mathcal{D}_n^{\pi_n}) \right) (1 - G_0(m-2)) && (46) \end{aligned}$$

where $G_0(t) = \sum_{s=1}^{t} g_0(s)$. The posterior distribution of the first changepoint $b_{i,1}$ of cluster i given the graph $\mathcal{G}$ that implies the parent sets for the nodes in the ith cluster, symbolically $\{\pi_n | n : \mathcal{C}(n) = i\}$, is:

$$P(b_{i,1} = t|\mathcal{G}, \mathcal{C}, i) = \left(\prod_{n:\mathcal{C}(n)=i} \Psi(\mathcal{D}_n^{\pi_n}[2 : t]) \right) Q(t+1|i, \mathcal{C}, \mathcal{G}) \frac{g_0(t-1)}{Q(2|i, \mathcal{C}, \mathcal{G})} \tag{47}$$

for $t = 2, \dots, m-1$ and the probability of no changepoint for the ith cluster ($P(\mathcal{K}_i = 1)$) is given by:

$$P(\mathcal{K}_i = 1|i, \mathcal{C}, \mathcal{G}) = \left(\prod_{n:\mathcal{C}(n)=i} \Psi(\mathcal{D}_n^{\pi_n}[2 : m]) \right) \frac{1 - G_0(m-2)}{Q(2|i, \mathcal{C}, \mathcal{G})} \tag{48}$$

The posterior distribution of the j-th changepoint for the ith cluster $b_{i,j}$ given the parent node sets π_n ($\{n : \mathcal{C}(n) = i\}$) and the previous changepoint $b_{i,j-1}$ is:

$$P_t := P(b_{i,j} = t|b_{i,j-1}, i, \mathcal{C}, \mathcal{G}) = \left(\prod_{n:\mathcal{C}(n)=i} \Psi(\mathcal{D}_n^{\pi_n}[(b_{i,j-1}+1) : t]) \right) Q(t+1|i, \mathcal{C}, \mathcal{G}) \frac{g(t - b_{i,j-1})}{Q(b_{i,j-1}+1|i, \mathcal{C}, \mathcal{G})} \tag{49}$$

for $t = b_{i,j-1}+1, \dots, m-1$ and the probability of no further changepoint is given by:

$$P_{\geq m} := \left(\prod_{n:\mathcal{C}(n)=i} \Psi(\mathcal{D}_n^{\pi_n}[(b_{i,j-1}+1) : m]) \right) \frac{1 - G_0(m - b_{i,j-1} - 1)}{Q(b_{i,j-1}+1|i, \mathcal{C}, \mathcal{G})} \tag{50}$$

We note that Eqn. (49-50) are the regularized cpBGe equivalents of Eqn. (39-40) in Section 1.6. If there is a changepoint at $b_{i,j-1} = t$, then the location of the next changepoint can be sampled from the discrete mass probability distribution $[P_{b_{i,j-1}+1}, \dots, P_{m-1}, P_{\geq m}]$ where $P_{\geq m}$ is the probability for no further changepoints. Having sampled changepoints $b_{i,1}, \dots, b_{i,k-1}$ from these conditional distributions, the number of mixture components for the ith cluster of nodes is $\mathcal{K}_i = k$ and the allocation vector for the nodes in the ith cluster $\mathbf{V}_i^{\mathcal{C}}$ can be extracted from the changepoints: $\mathbf{V}_i^{\mathcal{C}}(t) = k \Leftrightarrow b_{i,k-1} < t \leq b_{i,k}$ $(t = 2, \dots, m$ and $k = 1, \dots, \mathcal{K}_i)$.

As a summary: Conditional on the graph $\mathcal{G}$ for each cluster i $(1 \leq i \leq c)$ the number of changepoints and the changepoint locations, symbolically $(\mathcal{K}_i, \mathbf{V}_i^{\mathcal{C}})$ can be sampled from $P(\mathcal{K}_i, \mathbf{V}_i^{\mathcal{C}} | i, \mathcal{C}, \mathcal{G})$.

With regard to Section 1.9 we note that $Q(t|i, \mathcal{C}, \mathcal{G})$ was defined such that we have for $t = 2$:

$$Q(2|i, \mathcal{C}, \mathcal{G}) = \sum_{\mathbf{V}_j^{\mathcal{C}}} P(\mathbf{V}_j^{\mathcal{C}} | \mathcal{C}) \prod_{n:\mathcal{C}(n)=j} \Psi^{\dagger}(\mathcal{D}_n^{\pi_n}[\mathbf{V}_j^{\mathcal{C}}]) \tag{51}$$

where the sum is over all possible allocation vectors $\mathbf{V}_j^{\mathcal{C}}$ for the jth cluster induced by the clustering $\mathcal{C}$. The probability of the observations for the nodes in the jth cluster $\mathcal{D}_{n,2:m}$ $(n : \mathcal{C}(n) = j)$ conditional on the corresponding realisations of the parent nodes $\mathcal{D}_{\pi_n,1:m-1}$ $(n : \mathcal{C}(n) = j)$ can be thought of as the marginal distribution over all possible allocation vectors. In Section 1.9 and in the main paper we refer to $Q(2|j, \mathcal{C}, \mathcal{G})$ as $Q_j(\mathcal{D}, \mathcal{C}, \mathcal{G})$, and as we have seen in this section $Q_j(\mathcal{D}, \mathcal{C}, \mathcal{G}) = Q(2|j, \mathcal{C}, \mathcal{G})$ can be computed efficiently by applying the recursions of Fearnhead (2006).

1.8 MCMC convergence

For our Matlab implementation of the cpBGe model we observed for the Arabidopsis data sets with $N = 9$ variables and $m = 49$ data points that the computational costs of 2000 MCMC iterations of the Metropolis-Hastings (MH) RJMCMC sampling scheme are comparable to the computational costs of approximately 1 Gibbs sampling step, when the same Poisson/changepoint process prior is used and the maximal number of components is set to $\mathcal{K}_{MAX} = 10$. Each single Metropolis-Hastings step proposes the change of either a parent node set π_n *or* a node-specific allocation vector $\mathbf{V}_n$. Each Gibbs iteration consists of two steps, i.e. a new parent node set π_n *and* a new node-specific allocation vector $\mathbf{V}_n$ are sampled. We refer to this Gibbs sampler as *Gibbs*$(K = 10)$. We tried two other variants of this Gibbs sampling scheme, with the objective to increase the number of Gibbs steps at the same computational costs. (i) Setting $\mathcal{K}_{MAX} = 5$ approximately halves the computational costs of the Gibbs sampler, so that 2 moves are approximately as expensive as 2000 MH iterations. We refer to this version of the Gibbs sampler as Gibbs(K=5). (ii) For the Poisson/changepoint process prior with the hyperparameters $p = 0.05$ and $a = 2$ of the negative binomial distribution gained a tenfold increase in the number of Gibbs steps at the same computational costs. We will refer to this version of the Gibbs sampler as Gibbs-NBIN, and we note that performing 10 Gibbs-NBIN steps required the same computational costs as 2000 MH steps.
During the sampling phase the cpBGe model outputs a graph sample $\mathcal{G}^1, \dots, \mathcal{G}^I$ from the posterior distribution from which marginal edge posterior probabilities can be computed. For a network domain with N nodes an estimator $e_{n,j}$ for the marginal posterior probability of the individual edge $X_n \to X_j$ $(\mathcal{G}(n, j))$ is given by:

$$e_{n,j} = \frac{1}{I} \sum_{i=1}^{I} \mathcal{G}^i(n, j) \tag{52}$$

where $\mathcal{G}^i(n,j)$ is an indicator function which is 1 if the ith graph in the sample contains the edge $X_n \to X_j$, and 0 otherwise $(n,j \in \{1,\dots,N\})$. A standard diagnostic that we apply to evaluate convergence is based on potential scale reduction factors (PSRFs), which are usually monitored along the number of MCMC iterations. In the following representation we assume that H independent MCMC simulations with $2s$ iterations each have been performed on the same single data set. Discarding the first s iterations as burn-in phase, I_s graph samples can be taken from the remaining s MCMC iterations. Note that the number of samples I_s that can be taken in the sampling-phase is limited by the number of MCMC iterations s and the distance (no. of iterations) between samples.

For each of the H independent MCMC simulations $h = 1,\dots,H$ we compute the posterior probabilities of all edges $e_{n,j,h}$ $(n,j \in \{1,\dots,N\})$ from the graph samples $\mathcal{G}^{h,1},\dots,\mathcal{G}^{h,I_s}$ as described above. For each individual edge $X_n \to X_j$ the 'between-chain' variance $\mathcal{B}(n,j)$ and the 'within-chain' variance $\mathcal{W}(n,j)$ of its edge posterior probability are defined as (see Brooks and Gelman (1998)):

$$\mathcal{B}(n,j) = \frac{1}{H-1}\sum_{h=1}^{H}(e_{n,j,h} - \overline{e}_{n,j,.})^2 \tag{53}$$

where $\overline{e}_{n,j,.}$ is the mean of $e_{n,j,1},\dots,e_{n,j,H}$, and:

$$\mathcal{W}(n,j) = \frac{1}{H(I_s-1)}\sum_{h=1}^{H}\sum_{i=1}^{I_s}(G^{h,i}(n,j) - e_{n,j,h})^2 \tag{54}$$

where $G^{h,i}(n,j)$ is 1 if the ith graph in the sample taken in the hth simulation contains the edge $X_n \to X_j$, and 0 otherwise. Following Brooks and Gelman (1998) the $PSRF(n,j)$ of the individual edge $X_n \to X_j$ is then given by:

$$PSRF(n,j) = \frac{(1-\frac{1}{I_s})\mathcal{W}(n,j) + (1+\frac{1}{H})\mathcal{B}(n,j)}{\mathcal{W}(n,j)} \tag{55}$$

where PSRF values near 1 indicate that each of the H MCMC simulations is close to the stationary distribution. In our study we use as PSRF-based convergence diagnostic the fraction of edges $\mathcal{C}(\xi)$ whose PSRF is lower than a pre-defined threshold value ξ:

$$\mathcal{C}(\xi) = \frac{1}{N^2}\sum_{n=1}^{N}\sum_{j=1}^{N} Z_{PSRF<\xi}(PSRF(n,j)) \tag{56}$$

where $Z_{PSRF<\xi}(PSRF(n,j))$ is 1 if $PSRF(n,j) < \xi$ and 0 otherwise.

For the *Arabidopsis thaliana* data $2s = 1100k$ MCMC iterations were performed. From the last $s = 550k$ iterations we sampled $I_s = 550$ graphs by sampling every 1000th iteration. The focus of our study is on the convergence of the four MCMC sampling schemes for the cpBGe model. We perform $H = 10$ independent MCMC simulations and consider three different thresholds for ξ $(\xi = 1.02, 1.05, 1.1)$.

1.9 Information coupling between nodes based on Bayesian clustering (Extended version of the main paper)

We instantiate the *class 2* model from Eq. (4) of the main paper by following Fearnhead (2006) and employing the point process prior for the changepoint locations defined in Eq. (5) of the main paper, i.e. the terms $\mathbf{K}$ and $\mathcal{K}_n$ in Eqn. (1-4) become obsolete. We extend the *class 2* model by introducing a cluster function $\mathcal{C}(.)$ that allocates the nodes $X_1, \ldots, X_n$ to c ($1 \leq c \leq N$) non-empty clusters, each characterized by its own changepoint vector $\mathbf{V}_i^{\mathcal{C}}$, $1 \leq i \leq c$:

$$\begin{aligned} P(\mathcal{G}, \mathbf{V}^{\mathcal{C}}, \mathcal{D}, \mathcal{C}) &= P(\mathcal{C})P(\mathbf{V}^{\mathcal{C}}|\mathcal{C})P(\mathcal{G})P(\mathcal{D}|\mathcal{G}, \mathbf{V}^{\mathcal{C}}, \mathcal{C}) \\ &= P(\mathcal{C})\left(\prod_{i=1}^{c} P(\mathbf{V}_i^{\mathcal{C}}|\mathcal{C})\right)\prod_{n=1}^{N} P(\pi_n)\Psi^{\dagger}(\mathcal{D}_n^{\pi_n}[\mathbf{V}_{\mathcal{C}(n)}^{\mathcal{C}}]) \end{aligned} \tag{57}$$

with $\mathbf{V}^{\mathcal{C}} = (\mathbf{V}_1^{\mathcal{C}}, \ldots, \mathbf{V}_c^{\mathcal{C}})$, where c is the number of non-empty node clusters induced by $\mathcal{C}$. We assume for P($\mathcal{C}$) a uniform distribution on all functions $\mathcal{C}$ that give c ($1 \leq c \leq N$) clusters. The key idea behind the model of Eq. (57) is to encourage information sharing among nodes with respect to changepoint locations. Moreover, nodes that are in the same cluster i ($1 \leq i \leq c$) share the same allocation vector $\mathbf{V}_i^{\mathcal{C}}$ and will be "penalized" only once[2]. Note that the novel model is a generalization that subsumes both *class 1* and *class 2* models as limiting cases. It corresponds to *class 1* for $c = 1$ and to *class 2* for $c = N$. Inference can follow a slightly extended Gibbs sampling procedure, where we iteratively sample the latent variables from $P(\mathbf{V}_i^{\mathcal{C}}|\mathcal{G}, \mathcal{D}, \mathcal{C})$, a new network structure from $P(\mathcal{G}|\mathbf{V}_i^{\mathcal{C}}, \mathcal{D}, \mathcal{C})$, and a new cluster formation from $P(\mathcal{C}|\mathbf{V}_i^{\mathcal{C}}, \mathcal{D}, \mathcal{G})$. The first two steps follow the procedure discussed in Section 2.2 of the main paper.

For the third step, sampling from $P(\mathcal{C}|\mathbf{V}_i^{\mathcal{C}}, \mathcal{D}, \mathcal{G})$, we adopt an RJMCMC (Green, 1995) scheme based on cluster birth (b), death (d), and re-clustering (r) moves.[3] In a cluster birth move we randomly select a node cluster i that contains at least 2 nodes, and we randomly choose a node contained in it. The move tries to re-cluster this node from the ith cluster to a new cluster $c + 1$. Denote by $\mathcal{C}^{\star}$ the new cluster formation thus obtained. For the ith cluster and for the new $(c + 1)$th cluster we propose new changepoint allocation vectors $\mathbf{V}_i^{\mathcal{C}^{\star}}$ and $\mathbf{V}_{c+1}^{\mathcal{C}^{\star}}$ by sampling them from the distributions $P(\mathbf{V}_{c+1}^{\mathcal{C}^{\star}}|\mathcal{G}, \mathcal{D}, \mathcal{C}^{\star})$ and $P(\mathbf{V}_i^{\mathcal{C}^{\star}}|\mathcal{G}, \mathcal{D}, \mathcal{C}^{\star})$, defined in Eq. (59), with Fearnhead's dynamic programming scheme (Fearnhead, 2006), as discussed in Section 2.2 of the main paper. In a cluster death move we randomly select one of the clusters that contain only a single node, and we re-allocate this node to one of the other existing clusters, chosen randomly. The first cluster disappears and for cluster j, which absorbs the node, we propose a new changepoint allocation vector $\mathbf{V}_j^{\mathcal{C}^{\star}}$ from $P(\mathbf{V}_j^{\mathcal{C}^{\star}}|\mathcal{G}, \mathcal{D}, \mathcal{C}^{\star})$ with dynamic programming (Fearnhead, 2006), where $\mathcal{C}^{\star}$ denotes the proposed cluster formation. In a re-clustering move we randomly choose two clusters i and j ($i \neq j$) as follows. First, cluster i is randomly selected among those that contain at least 2 nodes. Next, cluster j is randomly selected among the remaining clusters. We then randomly chose one of the nodes from cluster i and re-allocate the selected node to cluster j. Denote by $\mathcal{C}^{\star}$ the new cluster formation obtained. (Since cluster i contains at least 2 nodes, this does not affect c.) For both clusters i and j we propose new changepoint allocation vectors $\mathbf{V}_i^{\mathcal{C}^{\star}}$ and $\mathbf{V}_j^{\mathcal{C}^{\star}}$ from $P(\mathbf{V}_i^{\mathcal{C}^{\star}}|\mathcal{G}, \mathcal{D}, \mathcal{C}^{\star})$ and $P(\mathbf{V}_j^{\mathcal{C}^{\star}}|\mathcal{G}, \mathcal{D}, \mathcal{C}^{\star})$ with Fearnhead's dynamic programming scheme (Fearnhead, 2006).
The acceptance probabilities of these three RJMCMC moves are given by the product of the likelihood ratio (LR), the prior ratio (PR), the inverse proposal probability ratio or Hastings factor (HR), and the Jacobian (J) in the standard way (Green, 1995): $A_{(b,d,r)} = min\{1, R_{(b,d,r)}\}$, where $R_{(b,d,r)} = LR \times PR \times HR \times J$. Since this is a discrete problem, the Jacobian is $J = 1$, and for the chosen uniform prior on $\mathcal{C}$, the prior ratio is $PR = 1$. For a cluster birth move (b), symbolically $(\mathcal{C}, \mathbf{V}^{\mathcal{C}}) \rightarrow (\mathcal{C}^{\star}, \mathbf{V}^{\mathcal{C}^{\star}})$, we thus get: $R_{(b)} = LR \times HR$

$$R_{(b)} = \frac{P(\mathcal{G}, \mathbf{V}^{\mathcal{C}^{\star}}, \mathcal{C}^{\star}, \mathcal{D})}{P(\mathcal{G}, \mathbf{V}^{\mathcal{C}}, \mathcal{C}, \mathcal{D})} \times \frac{c^{\dagger} n^{i} P(\mathbf{V}_i^{\mathcal{C}}|\mathcal{G}, \mathcal{D}, \mathcal{C})}{c^{\star}(c^{\ddagger} - 1)P(\mathbf{V}_{c+1}^{\mathcal{C}^{\star}}|\mathcal{G}, \mathcal{D}, \mathcal{C}^{\star})P(\mathbf{V}_i^{\mathcal{C}^{\star}}|\mathcal{G}, \mathcal{D}, \mathcal{C}^{\star})} \tag{58}$$

where $c^{\dagger}$ is the number of clusters induced by $\mathcal{C}$ with at least two nodes, n^i is the number of nodes in the ith cluster (that was selected), $c^{\star}$ is the number of clusters induced by $\mathcal{C}^{\star}$ that contain only a single node, and $c^{\ddagger}$ is the total number of clusters induced by $\mathcal{C}^{\star}$. In our *regularized class 2* model

[2] Rather than "penalizing" nodes with identical allocation vectors independently, like the model in Grzegorczyk and Husmeier (2009).

[3] Each RJMCMC step was repeated 5 times.

the recursions of Fearnhead (2006) can be employed as described in Section 1.7 to sample the j-th $(1 \leq j \leq c)$ allocation vector $\mathbf{V}_j^{\mathcal{C}}$. We have:

$$P(\mathbf{V}_j^{\mathcal{C}}|\mathcal{G},\mathcal{D},\mathcal{C}) = \frac{q_j(\mathcal{D},\mathcal{C},\mathcal{G},\mathbf{V}_j^{\mathcal{C}})}{\sum_{\mathbf{V}_j^{\mathcal{C}^\star}} q_j(\mathcal{D},\mathcal{C}^\star,\mathcal{G},\mathbf{V}_j^{\mathcal{C}^\star})} \tag{59}$$

where

$$q_j(\mathcal{D},\mathcal{C},\mathcal{G},\mathbf{V}_j^{\mathcal{C}}) = P(\mathbf{V}_j^{\mathcal{C}}|\mathcal{C}) \prod_{n:\mathcal{C}(n)=j} \Psi^\dagger(\mathcal{D}_n^{\pi_n}[\mathbf{V}_j^{\mathcal{C}}]) \tag{60}$$

and the sum in Eq. (59) is over all valid allocation vectors $\mathbf{V}_j^{\mathcal{C}^\star}$ for the variables in the jth cluster of $\mathcal{C}^\star$.

It follows from Eqn. (57-58) that all factors except for the $(c+1)$th in the nominator and the ith ones cancel out in the likelihood ratio:

$$LR = \frac{q_i(\mathcal{D},\mathcal{C}^\star,\mathcal{G},\mathbf{V}_i^{\mathcal{C}^\star}) \cdot q_{c+1}(\mathcal{D},\mathcal{C}^\star,\mathcal{G},\mathbf{V}_{c+1}^{\mathcal{C}^\star})}{q_i(\mathcal{D},\mathcal{C},\mathcal{G},\mathbf{V}_i^{\mathcal{C}})} \tag{61}$$

Hence, $R_{(b)} = LR \times HR$ in Eq. (58) reduces to:

$$R_{(b)} = \frac{c^\dagger n^i}{c^\star(c^\ddagger - 1)} \frac{Q_i(\mathcal{D},\mathcal{C}^\star,\mathcal{G})Q_{c+1}(\mathcal{D},\mathcal{C}^\star,\mathcal{G})}{Q_i(\mathcal{D},\mathcal{C},\mathcal{G})} \tag{62}$$

where the terms

$$Q_j(\mathcal{D},\mathcal{C},\mathcal{G}) = \sum_{\mathbf{V}_j^{\mathcal{C}}} q_j(\mathcal{D},\mathcal{C},\mathcal{G},\mathbf{V}_j^{\mathcal{C}}) \tag{63}$$

can be computed efficiently with Fearnhead's dynamic programming scheme as described in Section 1.7. More precisely, as explained in the paragraph below Eq. (51) we have

$$Q_j(\mathcal{D},\mathcal{C},\mathcal{G}) = Q(2|j,\mathcal{C},\mathcal{G}) \tag{64}$$

where $Q(2|j,\mathcal{C},\mathcal{G})$ was specified in Section 1.7 (see Eq. (45)) and can be computed efficiently with Fearnhead's recursions.

The acceptance probabilities for cluster death and re-clustering moves can be derived as follows: For the cluster death move (d), $(\mathcal{C},\mathbf{V}^{\mathcal{C}}) \rightarrow (\mathcal{C}^\star,\mathbf{V}^{\mathcal{C}^\star})$, we assume that $c^\dagger$ is the number of clusters induced by $\mathcal{C}$ with one single node and that the ith cluster belongs to this group and is selected. Removing the single node from the ith cluster, such that the ith cluster is unoccupied and can be removed, and adding this node to the jth $(i \neq j)$ cluster induced by $\mathcal{C}$ gives a new clustering $\mathcal{C}^\star$. We then get: $R_{(d)} = LR \times HR$

$$R_{(d)} = \frac{P(\mathcal{G},\mathbf{V}^{\mathcal{C}^\star},\mathcal{C}^\star,\mathcal{D})}{P(\mathcal{G},\mathbf{V}^{\mathcal{C}},\mathcal{C},\mathcal{D})} \times \frac{c^\dagger(c^\ddagger - 1)P(\mathbf{V}_j^{\mathcal{C}}|\mathcal{G},\mathcal{D},\mathcal{C})P(\mathbf{V}_i^{\mathcal{C}}|\mathcal{G},\mathcal{D},\mathcal{C})}{c^\star n^j P(\mathbf{V}_j^{\mathcal{C}^\star}|\mathcal{G},\mathcal{D},\mathcal{C}^\star)} \tag{65}$$

where $c^\dagger$ is the number of clusters induced by $\mathcal{C}$ that contain only one single node, $c^\ddagger$ is the total number of clusters induced by $\mathcal{C}$, $c^\star$ is the number of clusters induced by $\mathcal{C}^\star$ with at least two nodes, and n^j is the number of nodes in cluster j.

It follows from Eqn. (57) and(65) that all factors except for the ith ones and the jth ones in the denominator cancel out in the likelihood ratio:

$$LR = \frac{q_i(\mathcal{D},\mathcal{C}^\star,\mathcal{G},\mathbf{V}_i^{\mathcal{C}^\star})}{q_i(\mathcal{D},\mathcal{C},\mathcal{G},\mathbf{V}_j^{\mathcal{C}})q_j(\mathcal{D},\mathcal{C},\mathcal{G},\mathbf{V}_j^{\mathcal{C}})} \tag{66}$$

Hence, Eq. (65) reduces to:

$$R_{(d)} = \frac{c^{\dagger}(c^{\ddagger}-1)}{c^{\star}n^{j}} \frac{Q_i(\mathcal{D},\mathcal{C}^{\star},\mathcal{G})}{Q_i(\mathcal{D},\mathcal{C},\mathcal{G})Q_j(\mathcal{D},\mathcal{C},\mathcal{G})} \tag{67}$$

where the $Q(.)$ terms defined in Eq. (63) can be computed efficiently as described in Section 1.7.

For the re-clustering move (r), $(\mathcal{C},\mathbf{V}^{\mathcal{C}}) \to (\mathcal{C}^{\star},\mathbf{V}^{\mathcal{C}^{\star}})$, we assume that $\mathcal{C}$ induces c clusters, and we further assume there are $c^{\dagger}$ clusters with at least two nodes and that the ith cluster belongs to this group and is selected. One of the nodes from the ith cluster is randomly selected and moved to the jth $(i \neq j)$ cluster of $\mathcal{C}$. Let n^i and n^j be the numbers of nodes in the ith and jth cluster of $\mathcal{C}$. We obtain: $R_{(r)} = LR \times HR$

$$R_{(r)} = \frac{P(\mathcal{G},\mathbf{V}^{\mathcal{C}^{\star}},\mathcal{C}^{\star},\mathcal{D})}{P(\mathcal{G},\mathbf{V}^{\mathcal{C}},\mathcal{C},\mathcal{D})} \times \frac{c^{\dagger}n^{i}(c-1)P(\mathbf{V}_i^{\mathcal{C}}|\mathcal{G},\mathcal{D},\mathcal{C})P(\mathbf{V}_j^{\mathcal{C}}|\mathcal{G},\mathcal{D},\mathcal{C})}{c^{\diamond}(n^j+1)(c-1)P(\mathbf{V}_i^{\mathcal{C}^{\star}}|\mathcal{G},\mathcal{D},\mathcal{C}^{\star})P(\mathbf{V}_j^{\mathcal{C}^{\star}}|\mathcal{G},\mathcal{D},\mathcal{C}^{\star})} \tag{68}$$

where $c^{\diamond}$ is the number of clusters induced by $\mathcal{C}^{\star}$ that contain at least 2 nodes.

It follows from Eqn. (57) and (68) that all factors except for the ith and the jth ones cancel out in the likelihood ratio:

$$LR = \frac{q_i(\mathcal{D},\mathcal{C}^{\star},\mathcal{G},\mathbf{V}_i^{\mathcal{C}^{\star}})q_j(\mathcal{D},\mathcal{C}^{\star},\mathcal{G},\mathbf{V}_j^{\mathcal{C}^{\star}})}{q_i(\mathcal{D},\mathcal{C},\mathcal{G},\mathbf{V}_j^{\mathcal{C}})q_j(\mathcal{D},\mathcal{C},\mathcal{G},\mathbf{V}_j^{\mathcal{C}})} \tag{69}$$

Hence, Eq. (68) reduces to:

$$R_{(r)} = \frac{c^{\dagger}n^{i}}{c^{\diamond}(n^j+1)} \frac{Q_i(\mathcal{D},\mathcal{C}^{\star},\mathcal{G})Q_j(\mathcal{D},\mathcal{C}^{\star},\mathcal{G})}{Q_i(\mathcal{D},\mathcal{C},\mathcal{G})Q_j(\mathcal{D},\mathcal{C},\mathcal{G})} \tag{70}$$

where the $Q(.)$ terms can be computed effiviently as described in Section 1.7.

2 *Arabidopsis thaliana* gene expression time series

Plants assimilate carbon via photosynthesis during the day, but have a negative carbon balance at night. They buffer these daily alternations in their carbon budget by storing some of the assimilated carbon as starch in their leaves in the light, and utilising it as a carbon supply during the night. In order to synchronize these processes with the external 24 hour photo period, plants possess a circadian clock that can potentially provide predictive, temporal regulation of metabolic processes over the day/night cycle. The proper working of this circadian regulation is paramount to biomass production and growth, and considerable research efforts are therefore underway to elucidate its underlying molecular mechanism. In the present article, we aim to reconstruct the regulatory network of nine circadian genes in the model plant *Arabidopsis thaliana*.
We apply our method to microarray gene expression time series related to the study of circadian regulation in plants. *Arabidopsis thaliana* seedlings, grown under artificially controlled T_e-hour-light/T_e-hour-dark cycles, were transferred to constant light and harvested at 13 time points in τ-hour intervals. From these seedlings, RNA was extracted and assayed on Affymetrix GeneChip oligonucleotide arrays. The data were background-corrected and normalized according to standard procedures[4], using the GeneSpring© software (Agilent Technologies).

We combine four time series, which differed with respect to the pre-experiment entrainment condition and the time intervals: $T_e \in \{10h, 12h, 14h\}$, and $\tau \in \{2h, 4h\}$. The data, with detailed information about the experimental protocols, can be obtained from Edwards *et al.* (2006), Grzegorczyk *et al.* (2008), and Mockler *et al.* (2007). For an overview see Table 1. We focus our analysis

[4] We used RMA rather than GCRMA for reasons discussed in Lim *et al.* (2007).

	Segment 1	Segment 2	Segment 3	Segment 4
Source	Mockler et al.(2007)	Edwards et al. (2006)	Grzegorcyk et al. (2008)	Grzegorcyk et al. (2008)
Time points	12	13	13	13
Time interval	4h	4h	2h	2h
Pretreatment entrainment	12h:12h light:dark cycle	12h:12h light:dark cycle	10h:10h-dark light:dark cycle	14h:14h light:dark cycle
Measurements	Constant light	Constant light	Constant light	Constant light
Laboratory	Kay Lab	Millar Lab	Millar Lab	Millar Lab

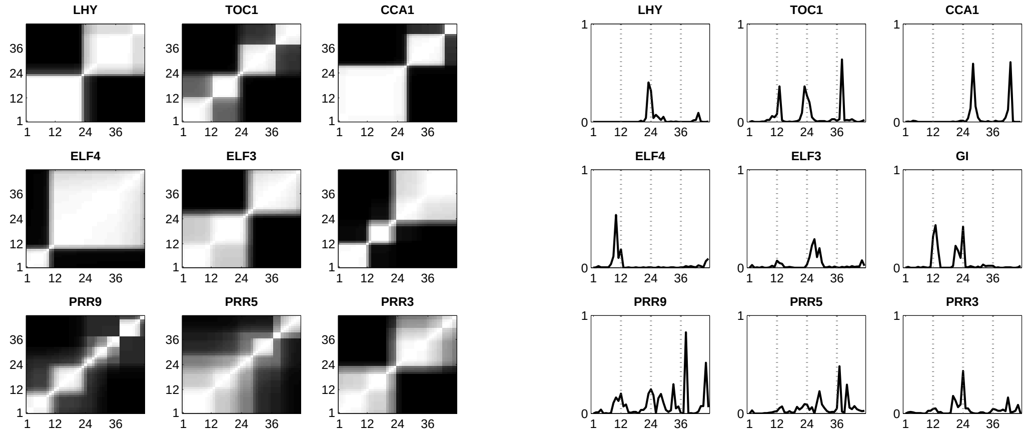
Table 1: **Gene expression time series segments for Arabidopsis.** The table contains an overview of the experimental conditions under which each of the gene expression experiments was carried out.

on 9 circadian genes: LHY, TOC1, CCA1, ELF4, ELF3, GI, PRR9, PRR5, and PRR3, and we merge all four time series into one single data set. The objective is to employ the cpBGe model (Grzegorczyk and Husmeier, 2009), a (*class 2*) model with node-specific changepoints, to detect the different experimental phases. Since the gene expression values at the first time point of a time series segment have no relation with the expression values at the last time point of the preceding segment, the corresponding boundary time points are appropriately removed from the data as described in Grzegorczyk and Husmeier (2009). This ensures that for all pairs of consecutive time points a proper conditional dependence relation determined by the nature of the regulatory cellular processes is given.

We elected to use these data as a test case for evaluating the efficiency of different sampling schemes for the cpBGe model (Grzegorczyk and Husmeier, 2009). Figure 1 of the main paper shows that the three Gibbs sampling schemes outperform the original RJMCMC sampler proposed in Grzegorczyk and Husmeier (2009) in terms of convergence and mixing. Since it appears that the GIBBS-NBIN algorithm performs slightly better than the other two Gibbs sampling schemes (see Figure 1 of the main paper), we report the results obtained with the GIBBS-NBIN algorithm:

Figure 2 shows the marginal posterior probability of the changepoint locations (right panel), and the posterior probability of the co-allocation of two time points to the same component (left panel). It is seen that, overall, the true segment boundaries tend to be detected. Different genes tend to be affected by the concatenation of the expression time series differently, though. For two genes (TOC1 and PRR9), all true changepoints are correctly predicted. Gene PRR9 shows various additional changepoints; this might indicate that it is affected by additional heterogeneities beyond the four experimental phases. Three of the genes (CCA1, ELF3, GI) show two changepoints, at the true locations (GI) or with a short time lag (CCA1). For genes LHY and ELF4 only one changepoint is predicted, at the location of the first or second concatenation point. A comparison of Table 1 with the locations of the peaks in Figure 2 suggests that gene CCA1 is mainly affected by a change of the entrainment condition, gene ELF4 is mainly affected by factors associated with the laboratory context, and genes ELF3 and PRR3 are mainly affected by a change of the sampling time interval (2 versus 4 hours). This deviation indicates that the genes are affected by the changing experimental conditions (entrainment, time interval) in different ways and that the node-specific changepoint model can be exploited as an exploratory tool for hypothesis generation.

Figure 3 shows the gene interaction network that is predicted when keeping all edges with marginal posterior probability above 0.5. There are two groups of genes. Empty circles in the figure represent morning genes (i.e. genes whose expression peaks in the morning), shaded circles represent evening genes (i.e. genes whose expression peaks in the evening). There are several directed edges pointing from the group of morning genes to the evening genes, mostly originating from gene CCA1. This result is consistent with the findings in McClung (2006), where the morning genes were found



(a) Connectivity structures

(b) Transition probabilities

Figure 2: **Results on the Arabidopsis gene expression time series. Panel (a)**: Co-allocation matrices for the nine circadian genes. The axes represent time. The grey shading indicates the posterior probability of two time points being assigned to the same mixture component, ranging from 0 (black) to 1 (white). **Panel (b)**: Average posterior probability of a changepoint (vertical axis) at a specific transition time plotted against the transition time (horizontal axis) for the nine circadian genes. The vertical dotted lines indicate the boundaries of the time series segments, which are related to different experimental conditions (see Table 1).

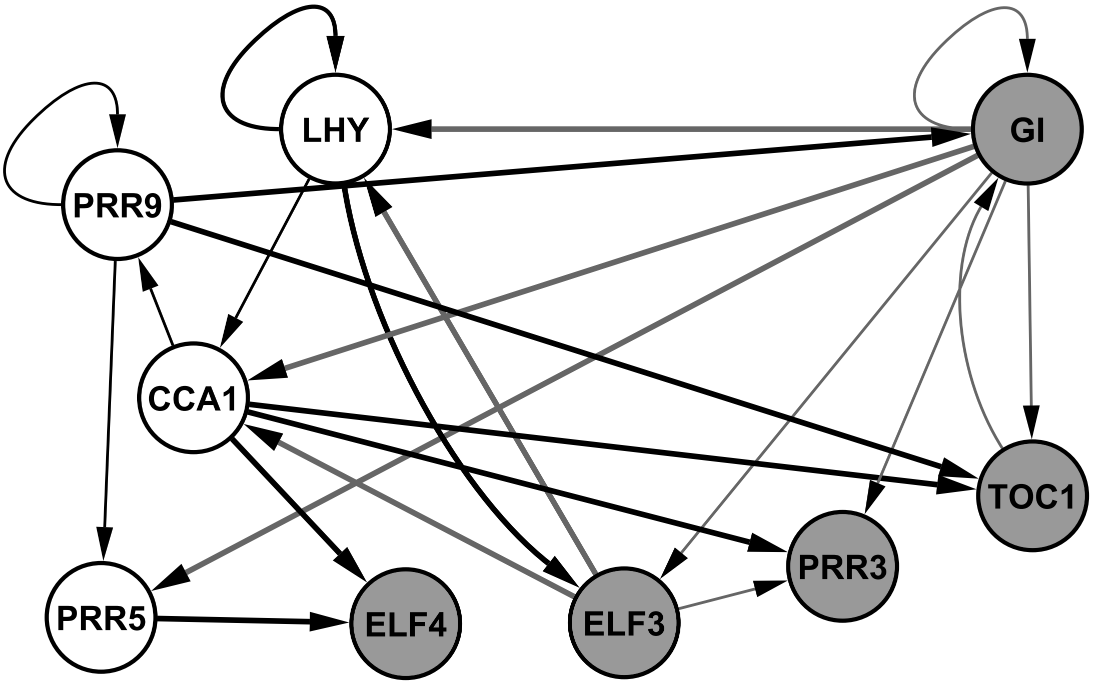


Figure 3: **Circadian gene regulatory network in Arabidopsis learnt from gene expression time series.** Predicted regulatory network of nine circadian genes in *Arabidopsis thaliana*. Empty circles represent morning genes. Shaded circles represent evening genes. Edges indicate predicted interactions with a marginal posterior probability greater than 0.5.

to activate the evening genes, with CCA1 and/or its partially redundant homologue LHY (Miwa *et al.*, 2007) being central regulators. E.g. Alabadi *et al.* (2001) found that CCA1 (and/or LHY) repress TOC1 and potentially other evening genes, and Kikis *et al.* (2005) report that CCA1 (and LHY) act negatively on ELF4 expression. Our reconstructed network also contains edges pointing into the opposite direction, from the evening genes back to the morning genes. This finding is also consistent with McClung (2006), where the evening genes were found to inhibit the morning genes via a negative feedback loop. E.g. the edges $ELF3 \rightarrow CCA1$ and $ELF3 \rightarrow LHY$ in Figure 3 are consistent with the biological finding in Kikis *et al.* (2005) that ELF3 is necessary for light-induced CCA1 and LHY expression. Moreover, it is also known that GI and ELF3 play important roles in the circadian clock network and in that they are involved in the regulatory interactions between the morning genes LHY/CCA1 and the evening gene TOC1 (Miwa *et al.*, 2006). Within the group of evening genes, the reconstructed network contains a feedback loop between GI and TOC1, symbolically $GI \leftrightarrow TOC1$. This feedback loop has also been found in Locke *et al.* (2005) and is an improvement on our earlier work (Grzegorczyk and Husmeier, 2009), where only a unidirectional interaction $GI \rightarrow TOC1$ was extracted.

Hence while a proper evaluation of the reconstruction accuracy is currently unfeasible – like Robinson and Hartemink (2009) and many related studies, we lack a gold-standard owing to the unknown nature of the true interaction network – our study suggests that the essential features of the reconstructed network are biologically plausible and consistent with the literature.

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