NONREVERSIBLE POPULATION MCMC WITH APPLICATIONS

Jukka Corander

Department of Mathematics and Statistics

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Primer on Bayesian model selection - I

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- Here δ is taken as the structural layer of a probability model, such the set of covariates in regression, set of edges in a graphical model, etc.
- The parameter $\theta_\delta \in \Theta_\delta$ represents the quantitative layer, taking values on a space dependent on the specific structure δ.

Primer on Bayesian model selection - II

- The Bayesian approach specifies formally the predictive, or marginal data distribution as the mixture

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- We assume that the integral $\int_{\Theta_\delta} p(\mathbf{x}|\theta_\delta) d\mu(\theta_\delta)$ can be calculated analytically, either exactly or approximately.

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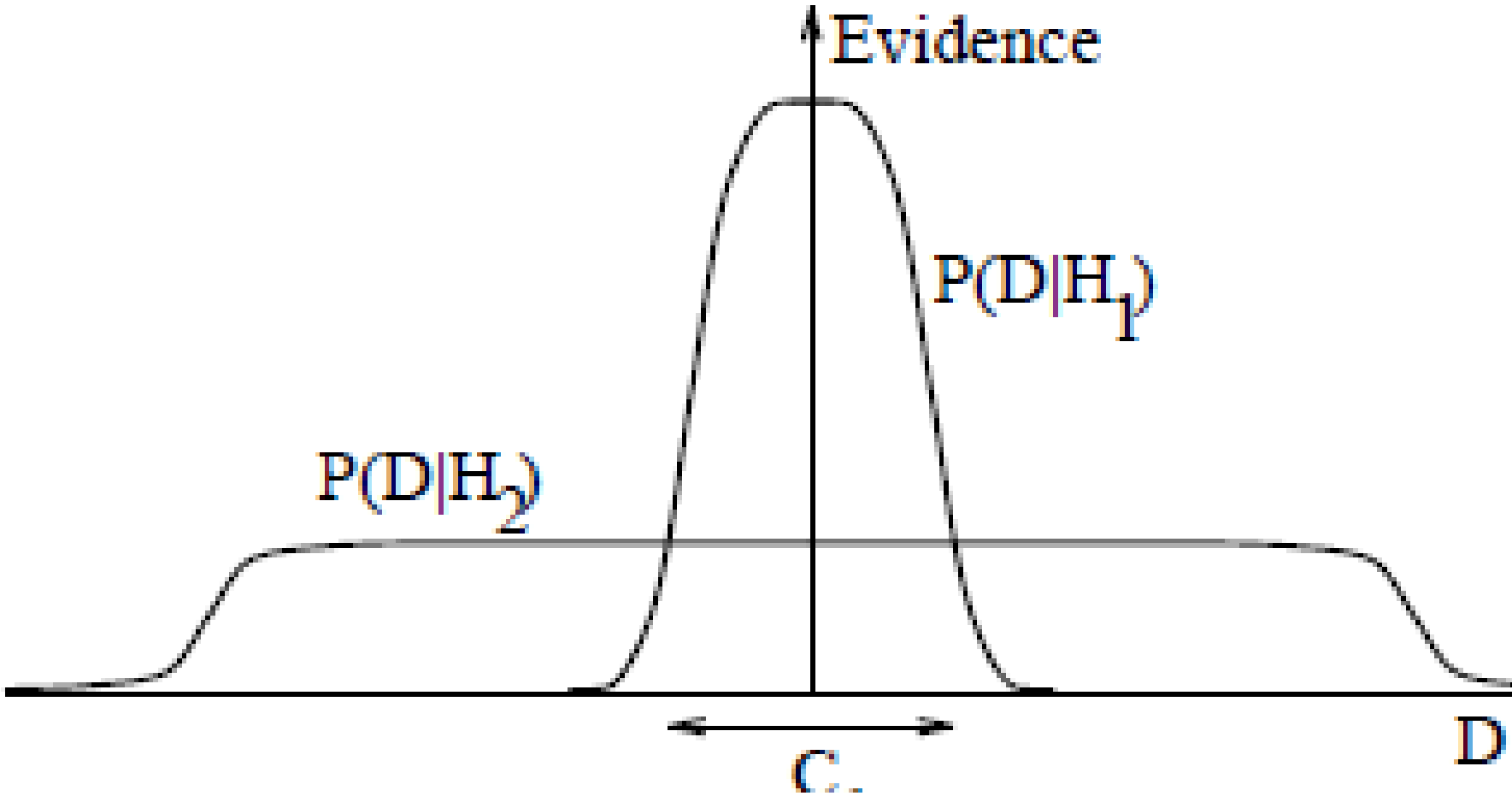
- Calculation of the posterior probabilities is in general intractable due to the size of Δ, but they can be approximated with MCMC, or one can e.g. try to estimate the mode

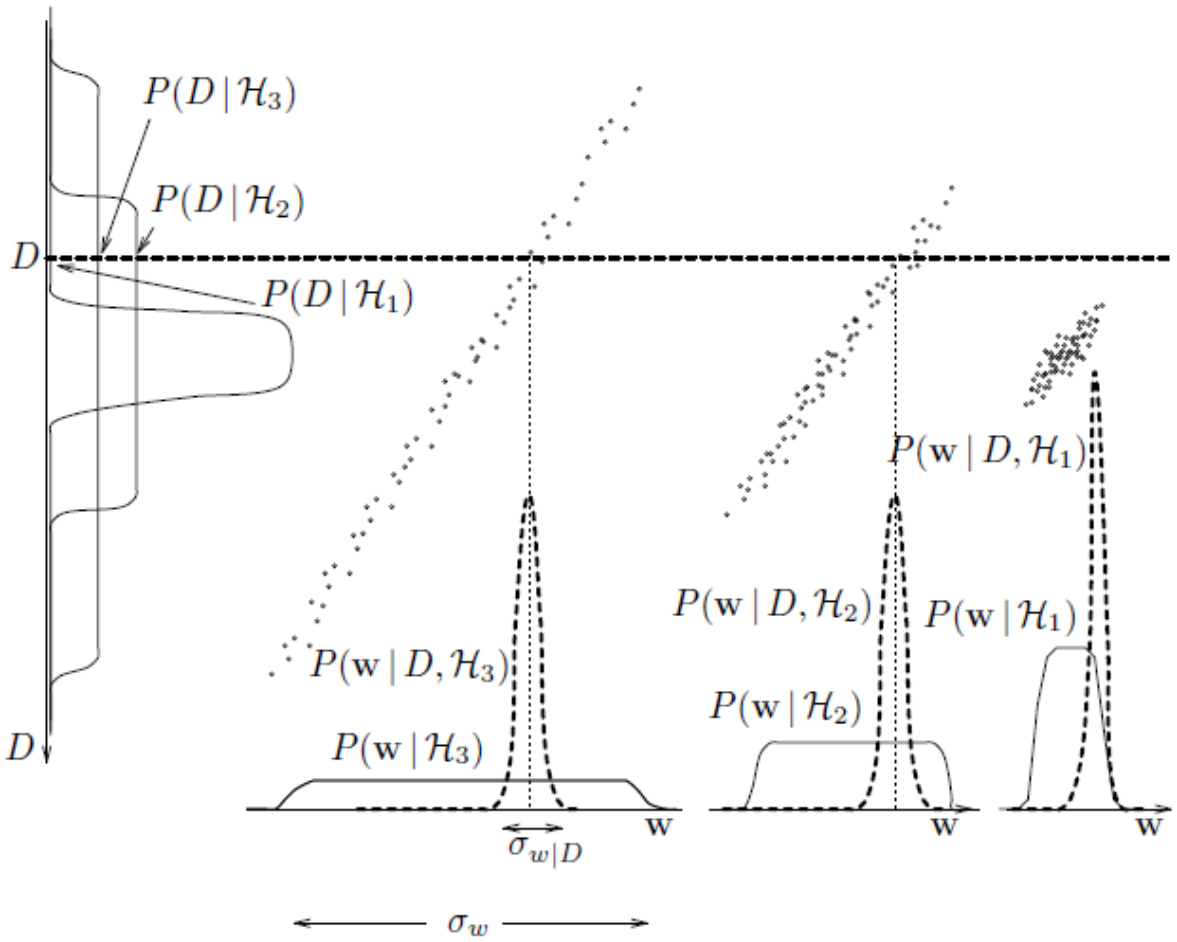
$$\arg\max_{\delta \in \Delta} p(\delta|\mathbf{x})$$

Model regularization - a primer by David MacKay, part I



Bayesian models specify a predictive distribution in the data space!

Model regularization - a primer by David MacKay, part II



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- and $q(\delta_t|\delta^*)$ is the probability of restoration of the current state.

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- From a realization $\{\delta_t, t = 0, 1, ...\}$ of such a chain, the posterior probabilities can be consistently estimated as

$$p_T(\delta|\mathbf{x}) = T^{-1} \sum_{t=1}^{n} I(\delta_t = \delta),$$

such that $p_T(\delta|\mathbf{x}) \longrightarrow p(\delta|\mathbf{x})$, as $T \longrightarrow \infty$.

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- Slow convergence to the relevant areas of the posterior.
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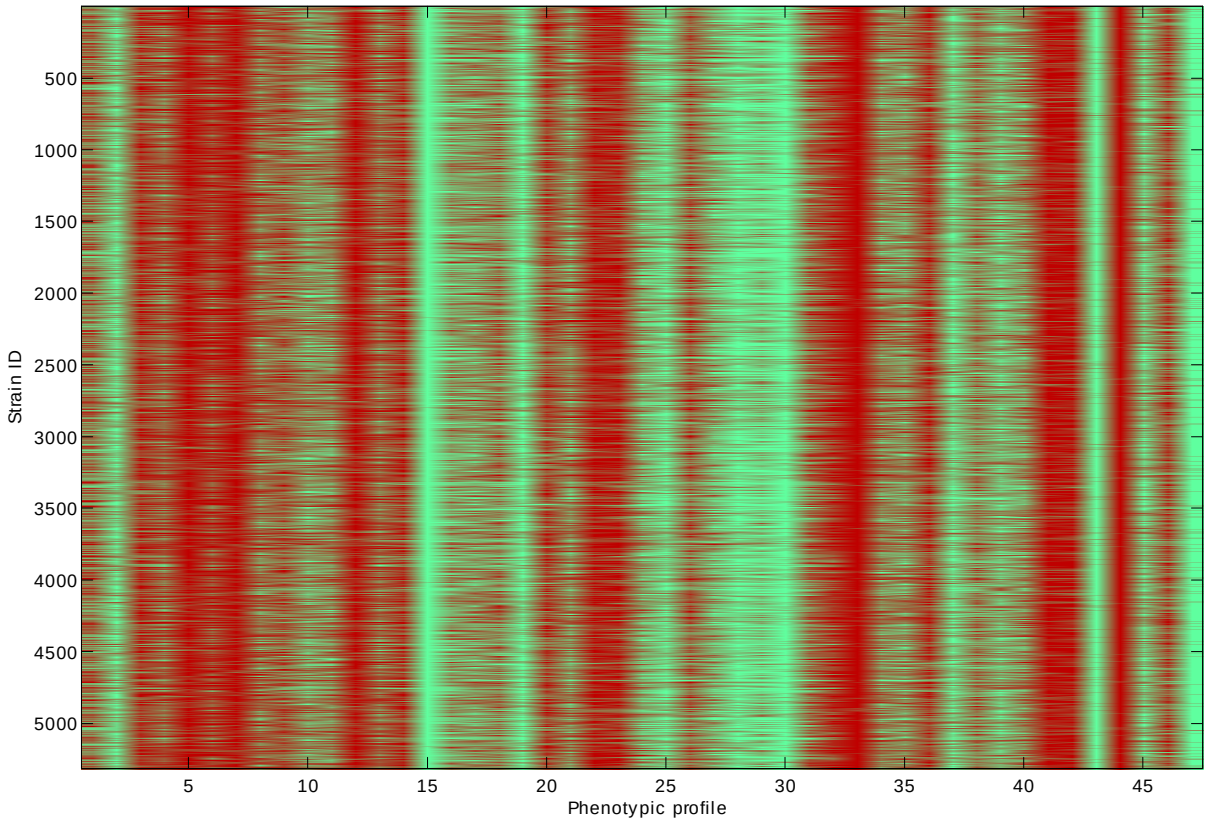
- Missing posterior mode completely in practice.
- Solutions?

What doesn't kill you will only make you stronger (Stronger - Kanye West)!



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- In general we don't know in advance what k should be representative for our data.

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- Allocation of a particular subset of the items into the same cluster s_c implies the use of a common predictive model $p(\mathbf{x}^{(s_c)})$ for their observed features $\mathbf{x}^{(s_c)}$, i.e.

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- Under certain form of exchangeability (more later) this leads to the predictive model $p(\mathbf{x}^{(N)}|S) = \prod_{c=1}^{k} p(\mathbf{x}^{(s_c)})$ for all data, conditional on the partition S.

Bayesian predictive learning in clustering

- The basis of predictive learning is quantified by the probability measure

$$p(\mathbf{x}^{(N)}) = \sum_{S \in \mathcal{S}} p(\mathbf{x}^{(N)}|S)p(S), \tag{1}$$

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- The conditional (posterior) distribution of S given the data is determined by Bayes' rule:

$$p(S|\mathbf{x}^{(N)}) = \frac{p(\mathbf{x}^{(N)}|S)p(S)}{\sum_{S \in \mathcal{S}} p(\mathbf{x}^{(N)}|S)p(S)}.$$

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- Then, we obtain a unique probabilistic characterization of the cluster data as

$$p(\mathbf{x}^{(s)}) = \int_{\Theta_{sc}} \prod_{j=1}^{d} \prod_{l=1}^{r_j} p_{jl}^{n_{jl}} p(\theta_{s_c}),$$

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- The symbol θ_{s_c} refers jointly to all parameters p_{jl} over different values and features.

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- By extending the unrestricted exchangeability assumption to hold over the clusters $s_1, \ldots, s_k$, we obtain the joint probabilistic characterization for $\mathbf{x}^{(N)}$ as

$$p(\mathbf{x}^{(N)}|S) = \int_{\Theta} \prod_{c=1}^{k} \prod_{j=1}^{d} \prod_{l=1}^{r_j} p_{cjl}^{n_{cjl}} p(\theta|S), \tag{2}$$

where n_{cjl} represents now the number of copies of value l for feature j observed among the items in s_c, and p_{cjl}, θ, and $p(\theta|S)$, are defined analogously to the previous slide.

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- It is a representation of the statistical uncertainty arising about genetic population structure under the assumptions of unlinked markers and random mating populations (k is unknown).

Predictive model under generalized exchangeability

- To finally obtain an explicit form of the predictive density, we specify the prior beliefs $p(\theta|S)$, according to the product Dirichlet distribution

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- Then, the explicit predictive probability for the feature data equals

$$p(\mathbf{x}^{(N)}|S) = \prod_{c=1}^{k} \prod_{j=1}^{d} \frac{\Gamma(\sum_{l=1}^{r_j} \lambda_{cjl})}{\Gamma(\sum_{l=1}^{r_j} \lambda_{cjl} + n_{cjl})} \prod_{l=1}^{r_j} \frac{\Gamma(\lambda_{cjk} + n_{cjl})}{\Gamma(\lambda_{cjl})}.$$

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- A solution to such an estimation problem was suggested by Corander *et al.* (2004), where a MH algorithm for searching the space of partitions was introduced.
- One can use also more advanced estimators that average the evidence of merging items to the same cluster, but these are often computationally very demanding.

Ordinary Metropolis-Hastings learning

- A Metropolis-Hastings algorithm for learning classifications can be defined by the transition kernel of a Markov chain, which determines the probability of a transition from a current classification S to a new proposal classification S^*, as

$$\min\left(1, \frac{p(\mathbf{x}^{(N)}|S^*)}{p(\mathbf{x}^{(N)}|S)} \frac{q(S|S^*)}{q(S^*|S)}\right), \tag{3}$$

where $q(S^*|S)$ is the probability of choosing classification S^* as the new candidate when in S, and $q(S|S^*)$ is the probability of restoration of the current classification S.

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- Choose one item randomly from each of two randomly chosen classes s_c and s_{c^*}, and exchange them between the classes.
- These kinds of proposals are very commonly used in Bayesian MCMC for variable-dimensional models.

Estimating the posterior

- For a realization of the Markov chain $\{S_t, t = 0, 1, ...\}$, the standard convergence result holds as

$$\lim_{T \to \infty} p_T(S|\mathbf{x}^{(N)}) = p(S|\mathbf{x}^{(N)}), \tag{4}$$

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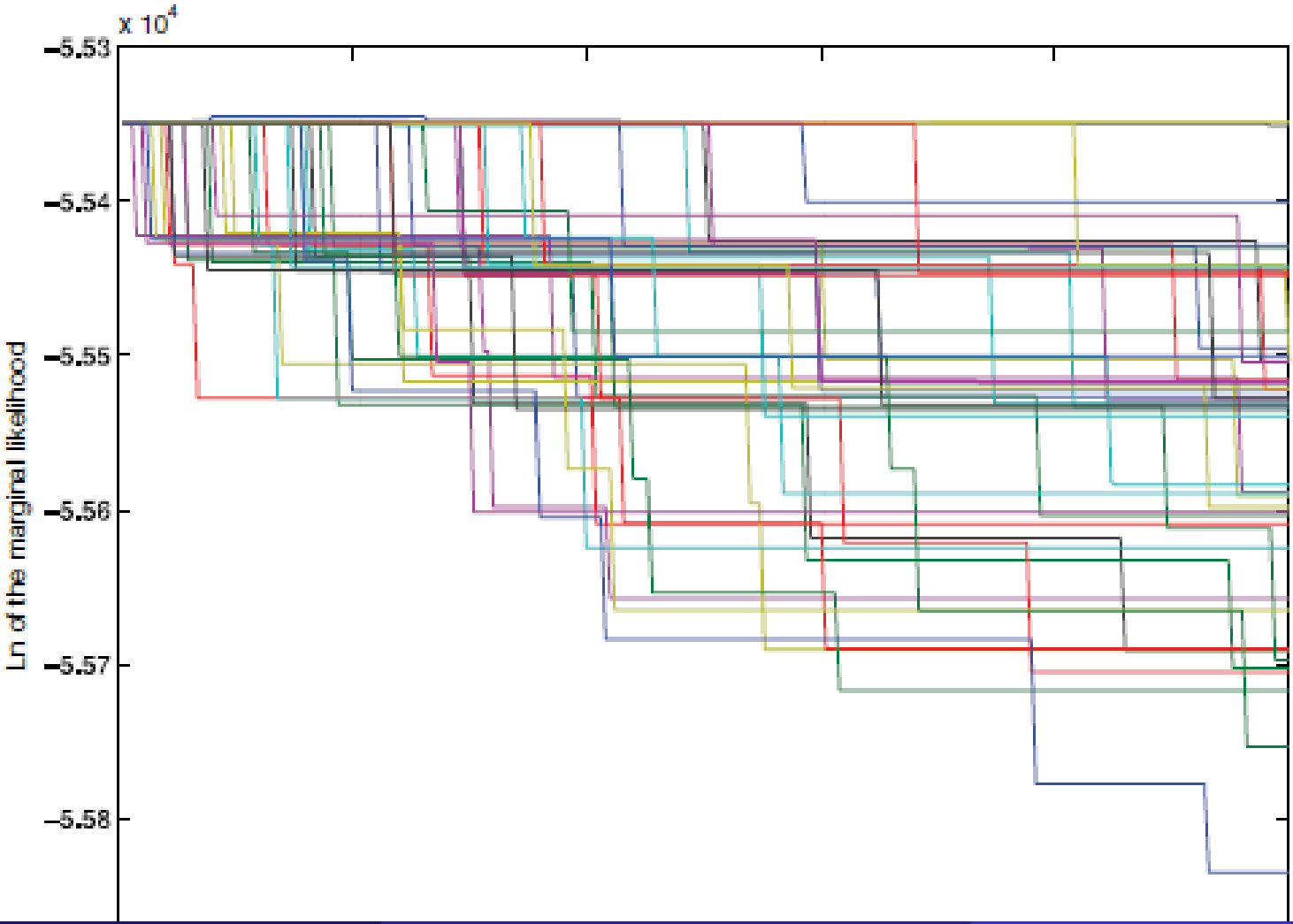
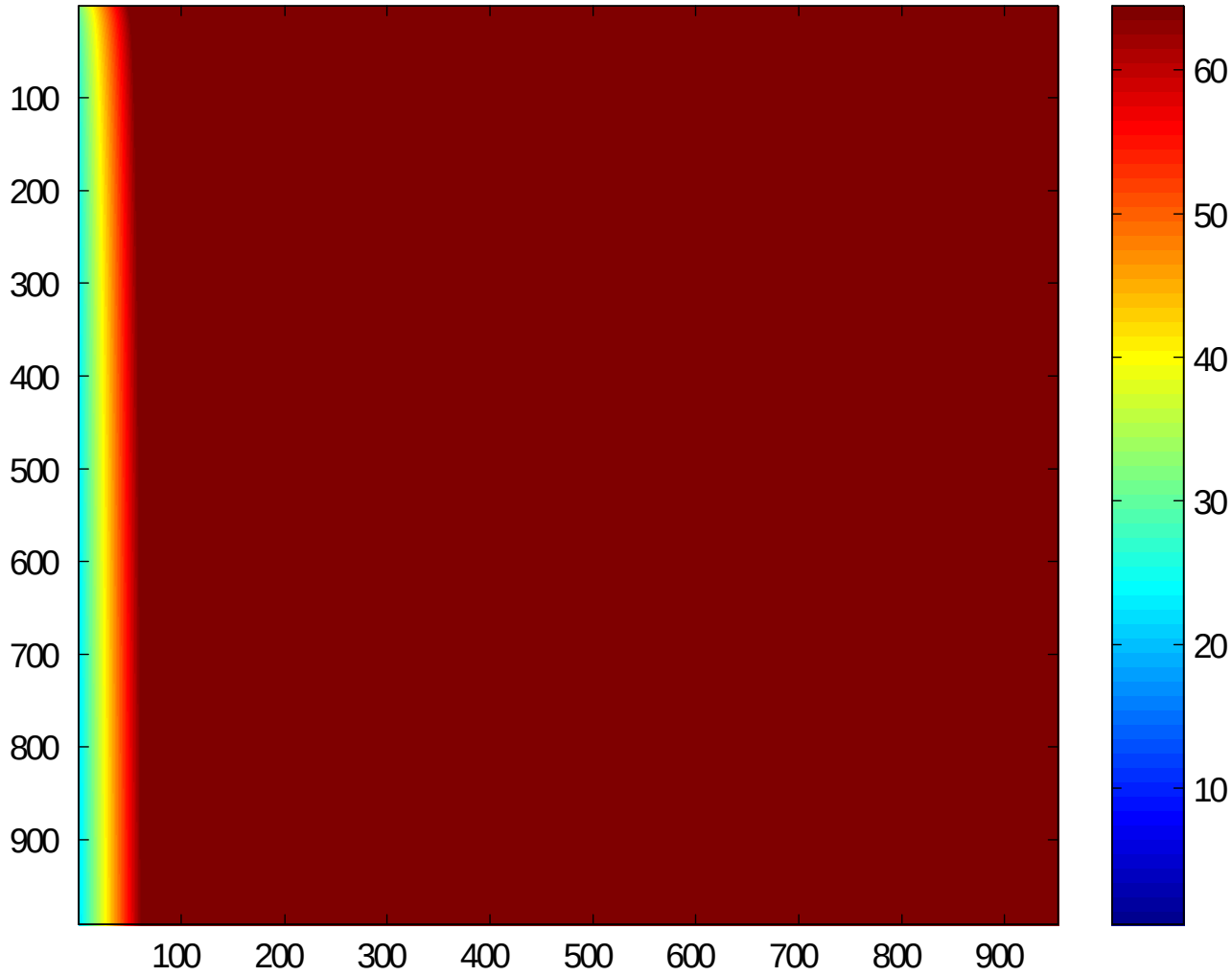
- Also, we know that the true posterior optimum $\hat{S}$ will be identified when $T \to \infty$.
- BUT, the above standard estimates can have enormous variance and be strongly biased in practice, when the state space is large (cf. phylogenetics and estimation of topologies).

What happened when the algorithm was applied to the data shown earlier?



Explicit illustration of the skweness of

$$\log \frac{q(S|S^*)}{q(S^*|S)}$$



How to solve the problem?

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- In the simplest case, such a sampler can use the same proposal distributions as the previous one.
- But we can do even better by allowing multiple processes to learn from each other!

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- *For each* t, *such that* $Z_t = 1$, *transition from* S_{tj} *to the next state* $S_{(t+1)j}$ *is determined according to the following distribution over the space* $\mathcal{S}_t = \{S_{tj}, j = 1, ..., m\}$ *of candidate states:*

$$P_t(S_{(t+1)j} = S_{tj}) = \frac{p(S_{tj})p(\mathbf{x}|S_{tj})}{\sum_{j=1}^{m} p(S_{tj})p(\mathbf{x}|S_{tj})},$$

independently for $j = 1, ..., m$.

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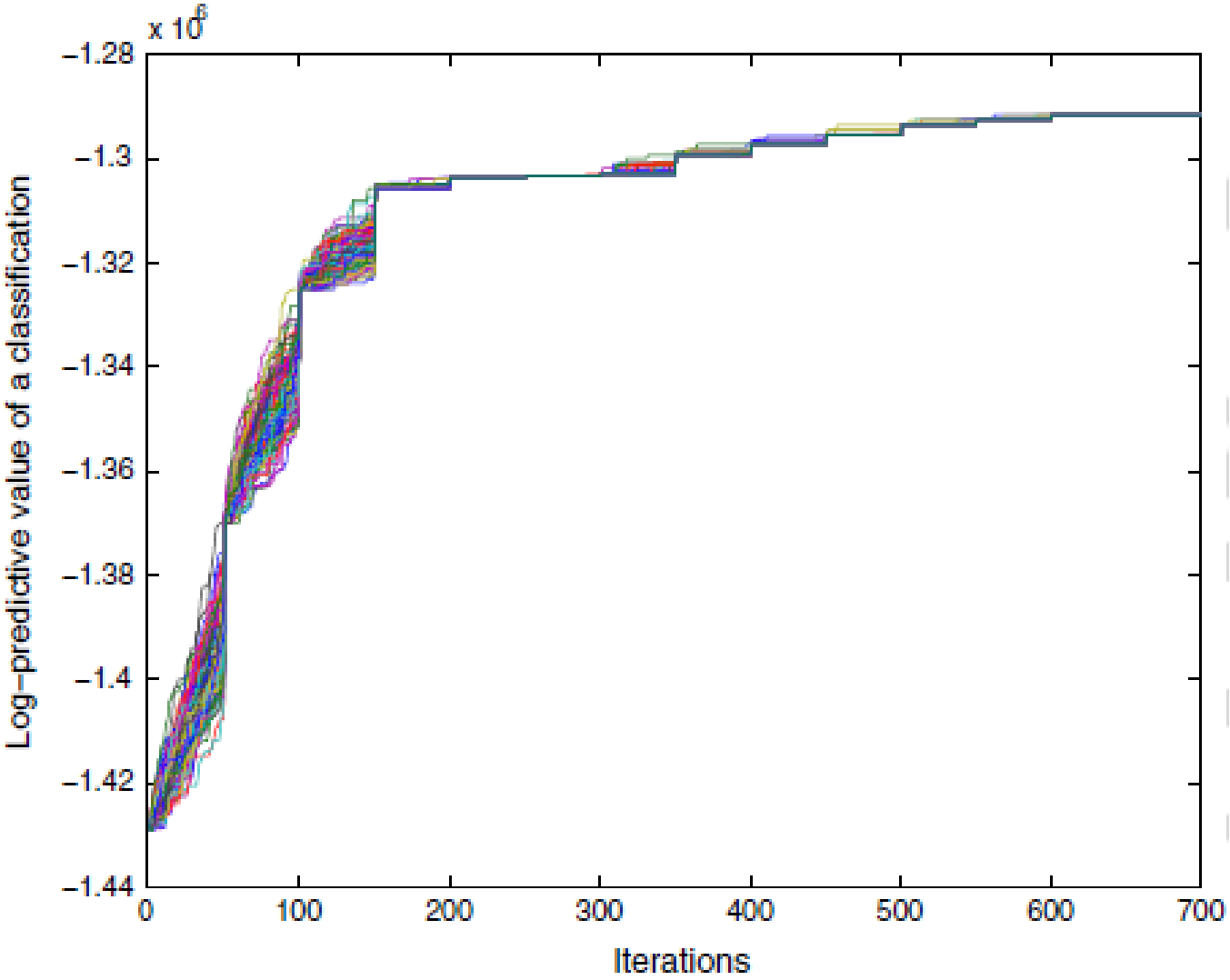
- The following estimate is consistent and it can have much smaller variance than the relative frequency based estimate:

$$\hat{p}(S|\mathbf{x}^{(N)}) = \frac{p(\mathbf{x}^{(N)}|S)p(S)}{\sum_{S \in \mathcal{S}_t} p(\mathbf{x}^{(N)}|S)p(S)},$$

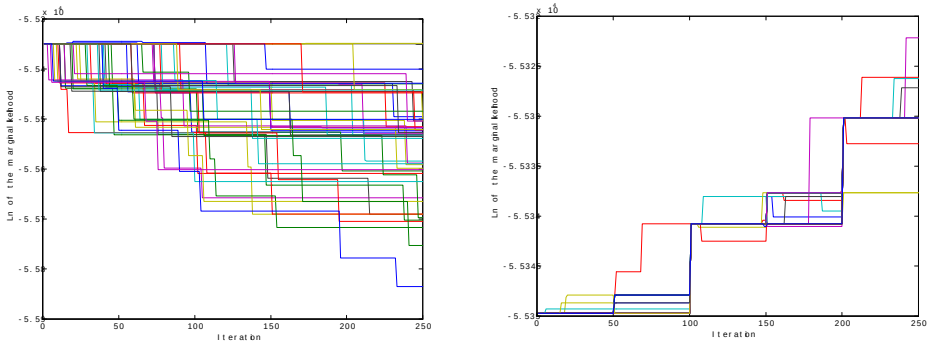
where $\mathcal{S}_n$ is the space of distinct states visited by time n by the non-reversible process.

An illustration of the behavior of parallel processes



$\log_e p(\mathbf{x}|S)$ (vertical axis) of 100 dependent processes for a molecular

Comparison between the reversible and nonreversible processes



Predictive abilities ($\log_e p(\mathbf{x}|S)$, vertical axis) of the Bayesian classification model for the *Enterobacteriaceae* data, over 250 iterations of 50 processes all started at the same initial configuration, produced with the reversible (left) and non-reversible (right) MH algorithms.

Optimization of dynamical graphical models stochastic nonreversible search vs hill-climbing

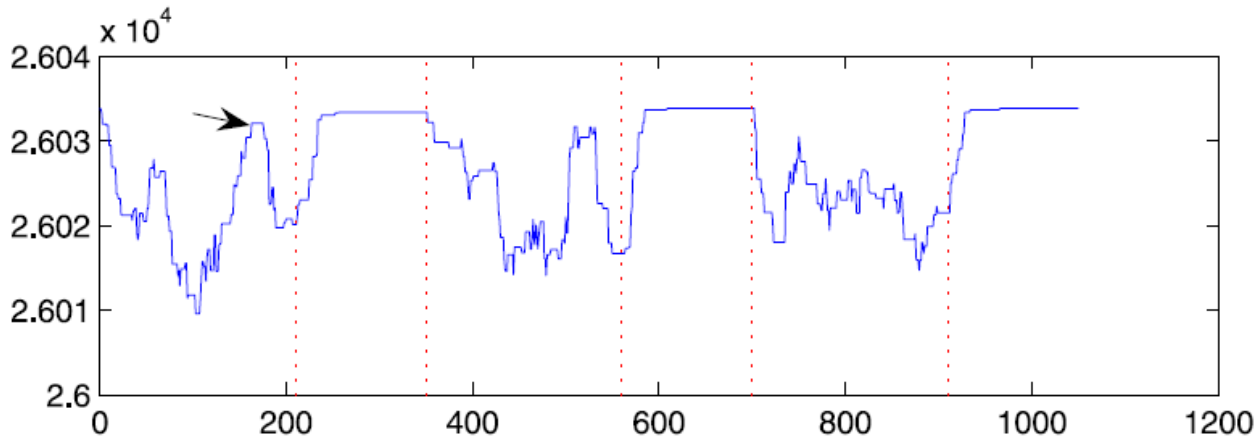
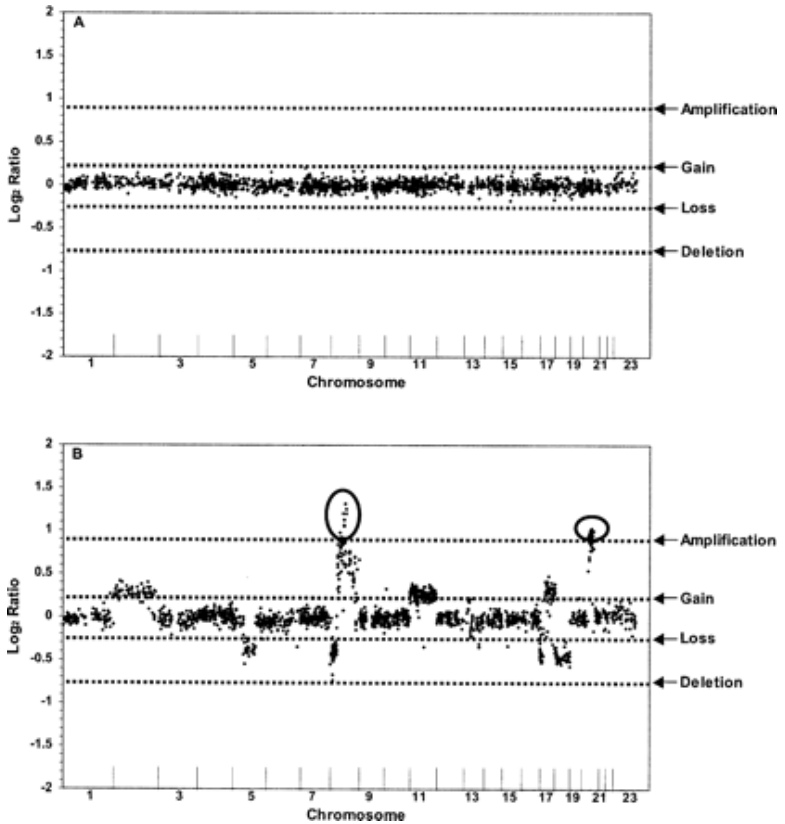


Fig. 4 Trace plot of BEC values of models visited during a search which was started from the optimal model for the air pollution data and carried out by repeating three times a sequence of six stochastic and four greedy iterations. The periods of stochastic and greedy iterations are separated by *dotted vertical lines*. The highest score found during the stochastic iterations is marked with an *arrow* and it is 5.7 times less probable than the overall optimal model

Marttinen and Corander (Machine Learning, 2009)

Bayesian profiling of cancer tissues using comparative genomic hybridization (CGH) data.



Control tissue

Cancer tissue

From Nakao et al. Carcinogenesis 2004.

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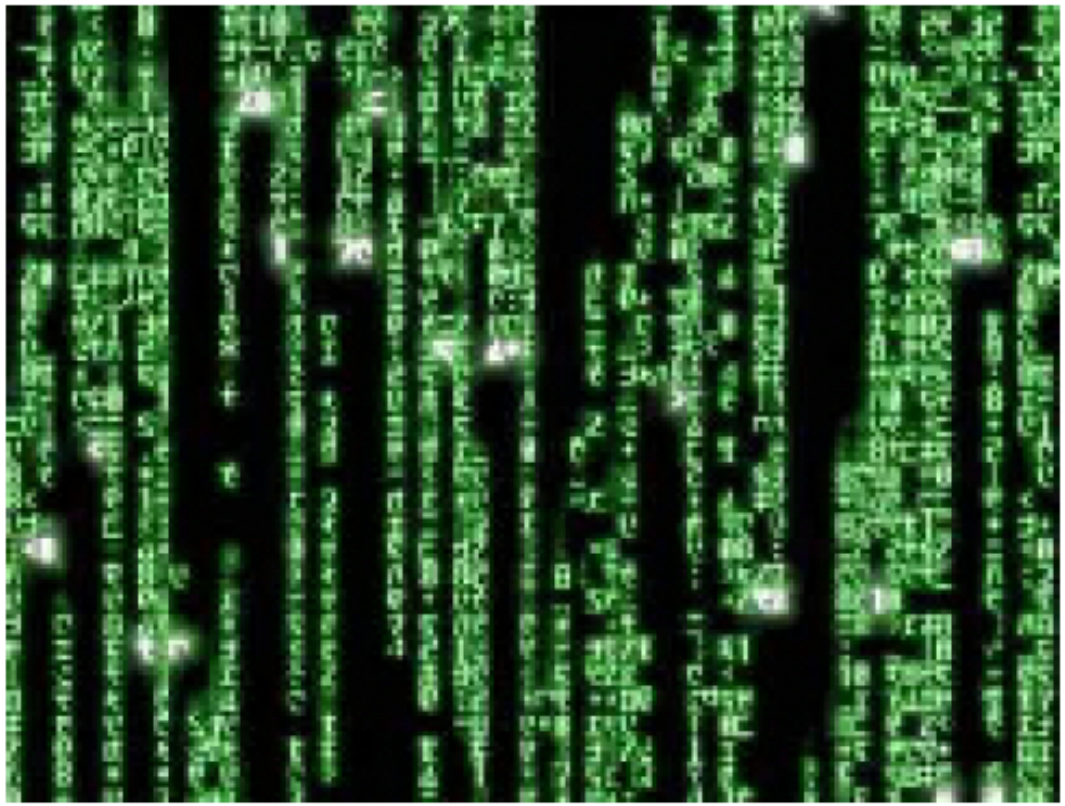
- Identify chromosomic areas that are signatures for certain cancer subtypes?
- Is it really that difficult?

Let's try it out

- Can you see clearly what's in the picture below?



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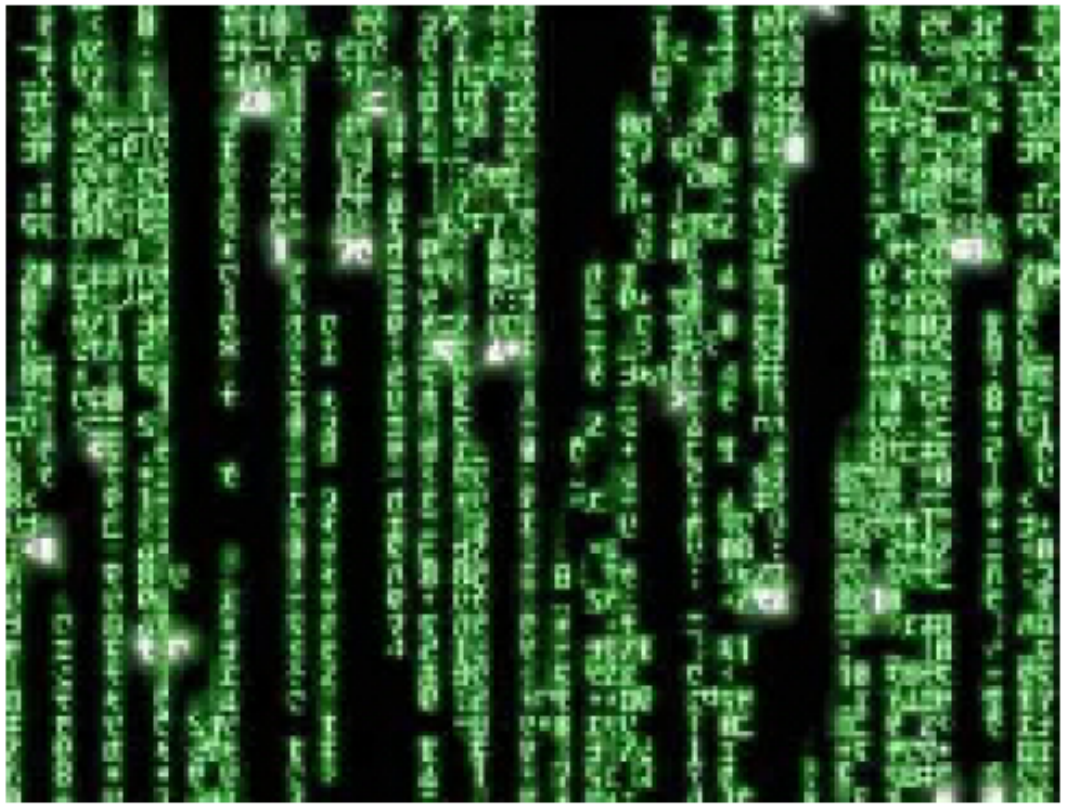
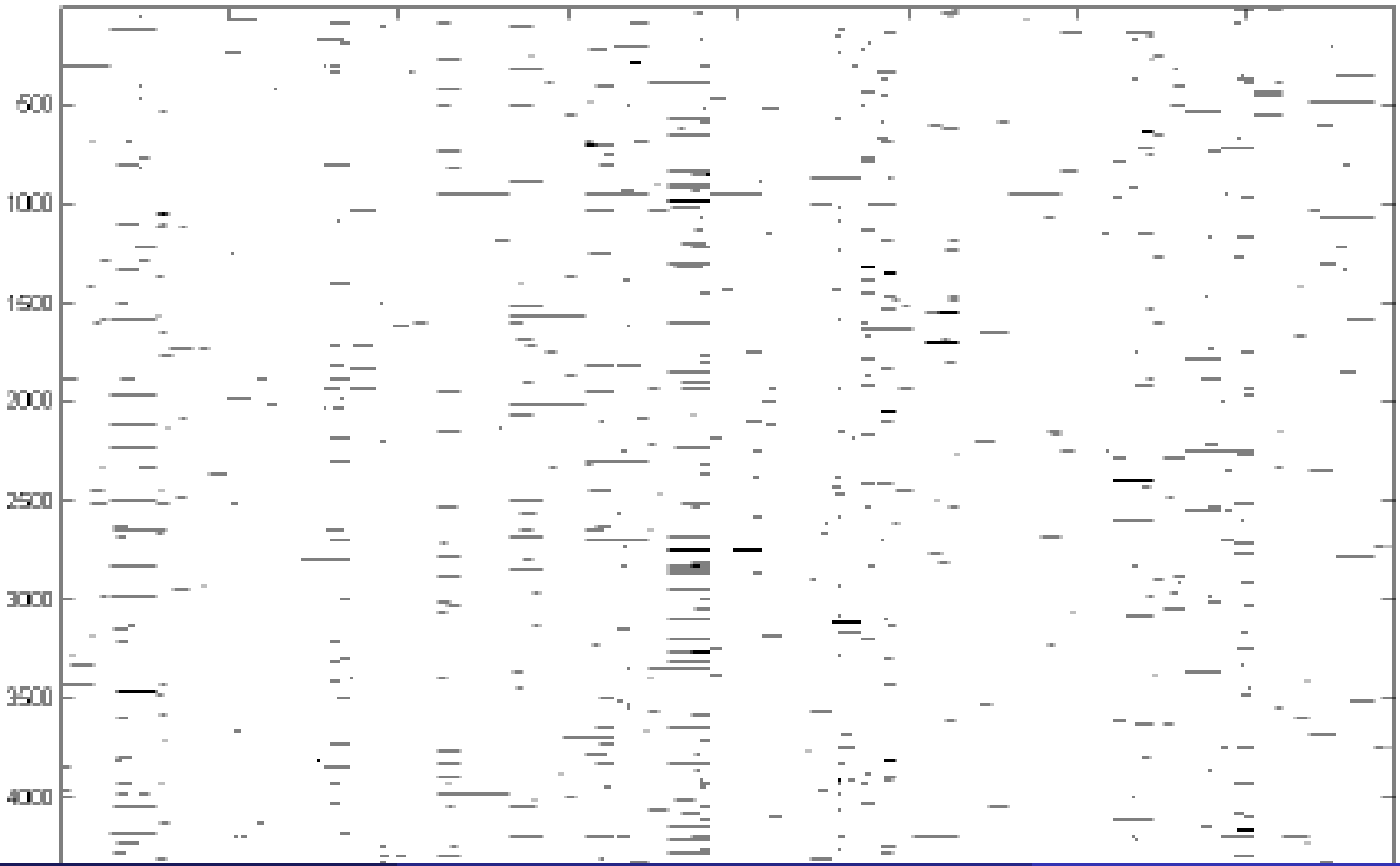


- Oops, wrong picture.

5000 cancer samples (rows) and amplifications (black) on sub-band resolution (columns). Easy to see the patterns, right?



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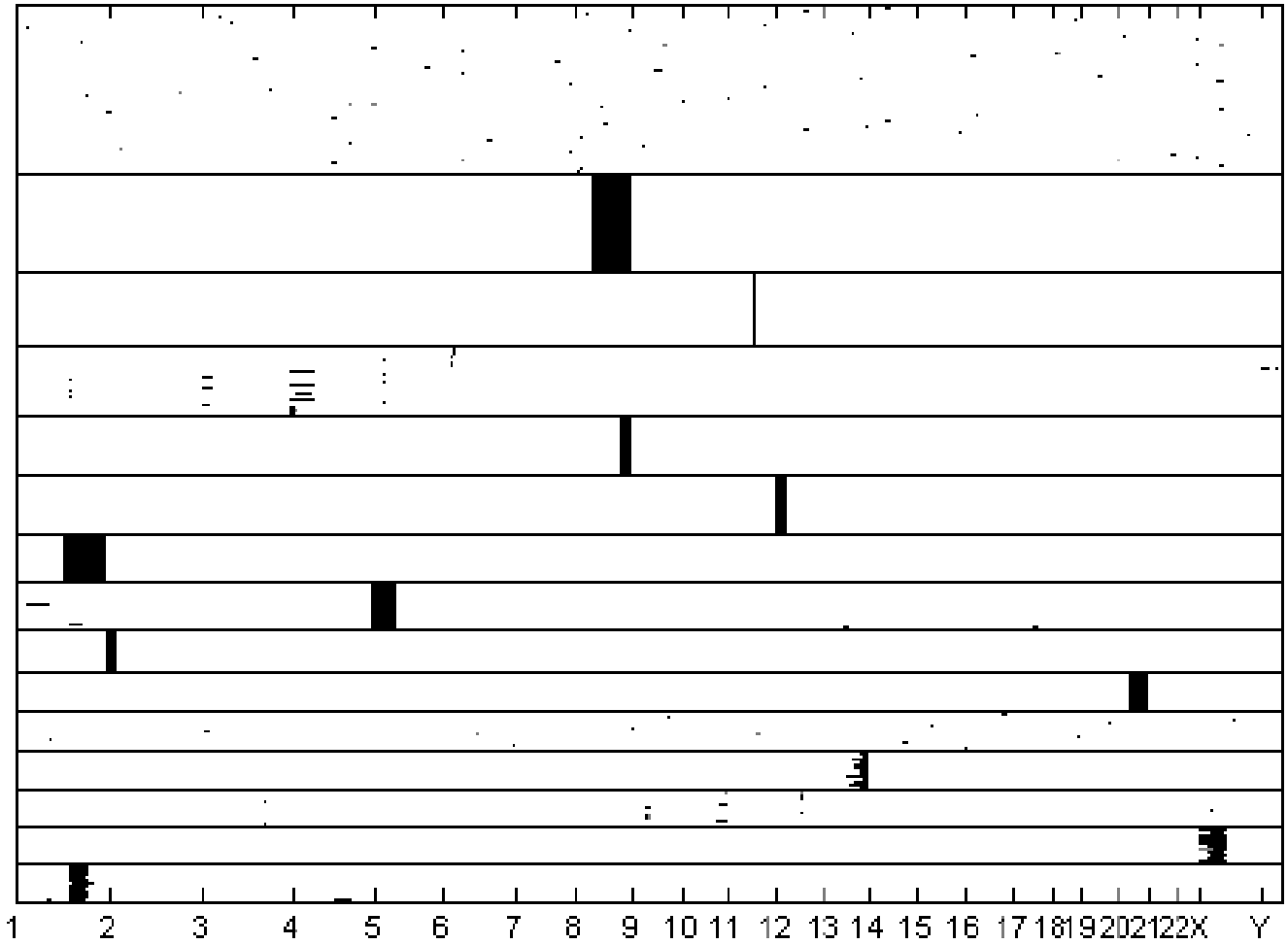
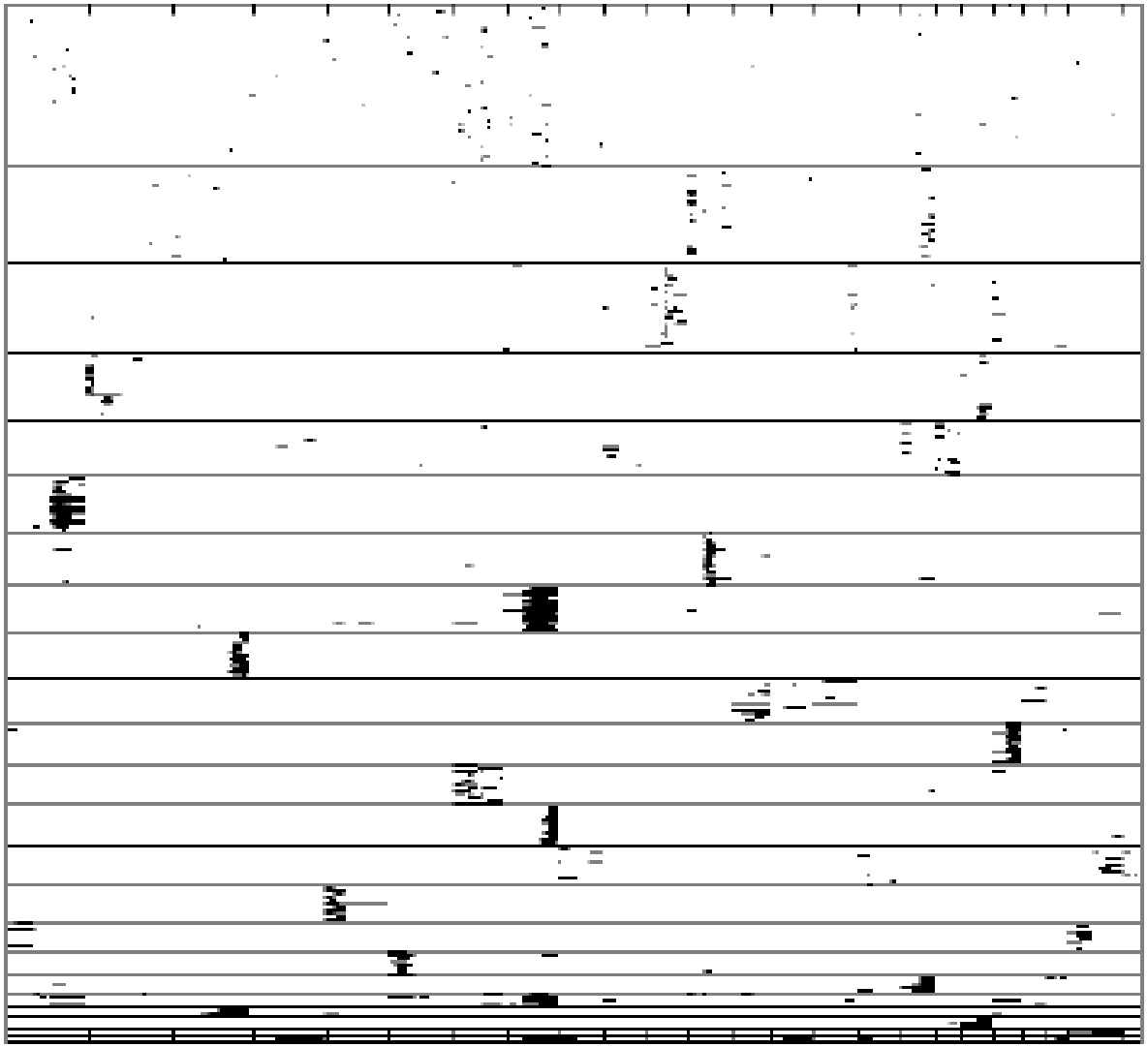
- Model-based methods, e.g. mixture models fitted with EM algorithm or Gibbs sampler.
- More challenging to use and slower, but may provide DIRECT focus on the biologically relevant questions.

Let's try k-means with, say, 291 clusters.



Oops, I forgot k-means cannot estimate k. Let's instead use a Bayesian mixture model which can learn k.



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- How many subgroups of cancer samples do exist in my database, such that they are similar w.r.t. DNA alterations?
- Which DNA alterations are relevant for which subgroups?
- Which genomic regions are simply uninformative (noise) for the clustering purposes?

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2. The DNA alterations that characterize the biological behavior of a certain cancer subtype should be present with high probability if a sample belongs to this subtype.
3. Other, less characteristic DNA alterations may also be present among samples with varying probabilities.

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- Specify prior distributions for all model parameters.

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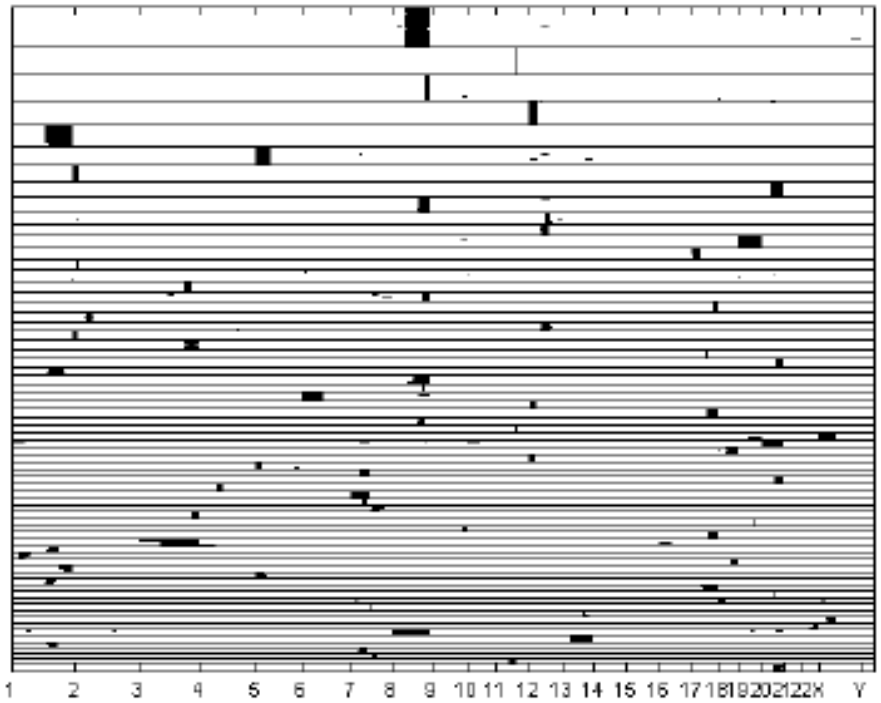
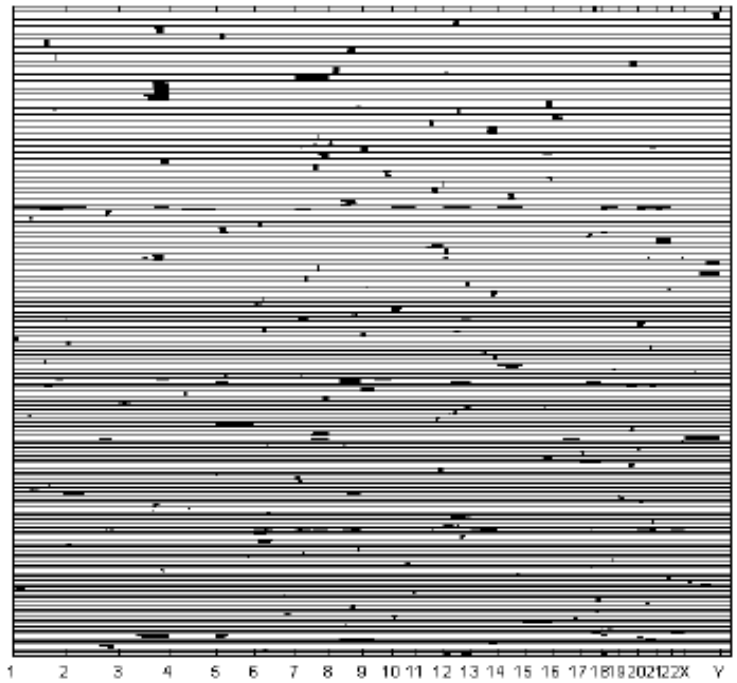
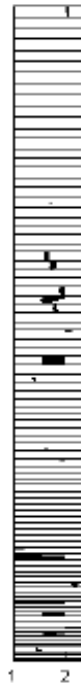
BASTA results for the data (parts I-III).



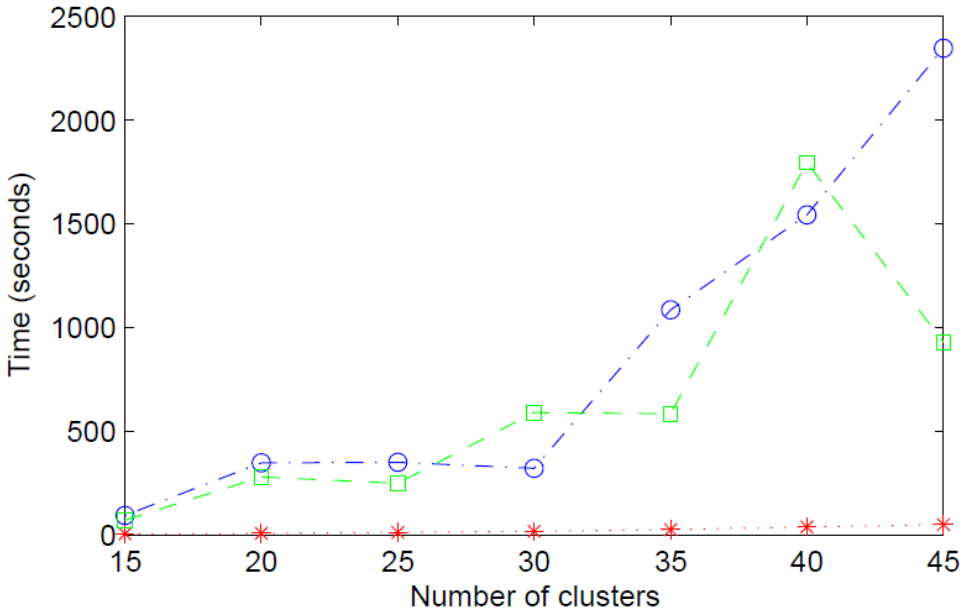


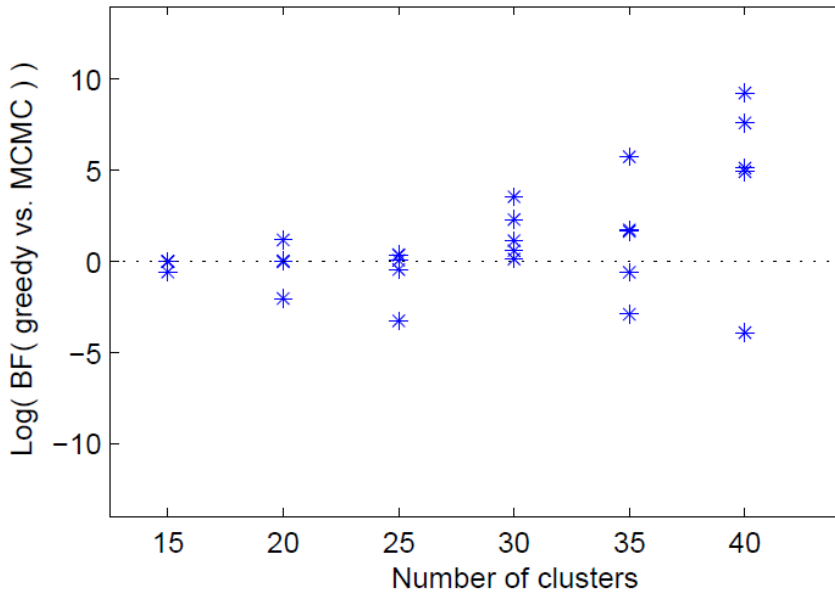


Moral of the story?

It may be quite dangerous to use data mining methods when not aware if the assumptions hidden in them meet the characteristics of the biological observations...

Comparison between a hill-climbing version of the nonreversible process and Gibbs sampler





Left panel: the time complexity of Gibbs sampler as a function of time required to identify as good solution as that found by a smart stochastic search. Right panel: Bayes factor values for the best clustering solutions found by the smart search against those found by Gibbs sampler. In both cases x-axis corresponds to the number of clusters in the generating model.

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- This story ends now, but the work still goes on...