

# A Semiparametric Bayesian Model for Comparing DNA Copy Numbers

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(joint with Y Ji & V. Baladandayuthapani)

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  - Identifying genome aberrations for samples of the same disease subtype
  - Detecting differences across disease subtypes



# Example

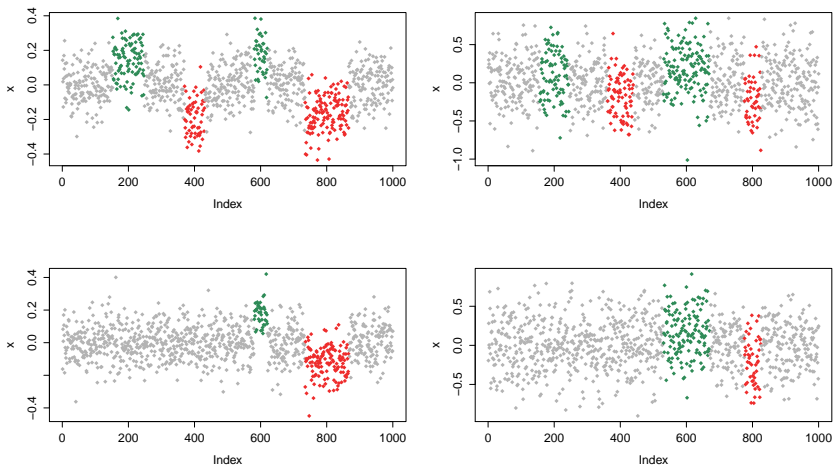


Figure : Simulated genome profile.

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- Baladandayuthapani et al. (2010): Hierarchical Bayesian random segmentation approach for multiple samples
- Yau et al. (2011): mixture model that combines a hidden Markov model for the locations (states), with a Dirichlet process prior for the scales

# Definitions

- Let  $\mathcal{A} = \{t_1, t_2, \dots, t_n\}$  be the index of probes.  
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- We define a common partition  $\{\Omega_k\}_{k=1}^K$  for all arrays as the union of all partition segments over  $j = 1, \dots, J$ . That is,  $\Omega_k = [c_k, c_{k+1})$  with  $\{t_1 = c_1 < c_2 \dots < c_{K+1} = t_n\} = \cup_j \{t_1 = c_1^j < c_2^j \dots < c_{L_j+1}^j = t_n\}$ .

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- Let  $g_j$  indicate the disease subtype for sample  $j$ . Say  $g_j \in \{1, 2\}$ .

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$$Y_{ij} = \sum_{k=1}^K \mu_{k,g_j} I(i \in \Omega_k) + \sum_{l=1}^{L_j} m_{lj} I(i \in \Delta_{lj}) + \epsilon_{ij}, \quad (1)$$

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- That is,  $Y_{ij}$  arises from the sum of a population mean  $\mu_{k,g_j}$ , a sample-specific mean  $m_{lj}$ , plus a measurement error  $\epsilon_{ij}$ .

# Semiparametric model

## Priors:

- Denote by  $\boldsymbol{\mu}_k = (\mu_{k1}, \mu_{k2})$  the vector of population copy number levels for subtypes 1 and 2

$$\boldsymbol{\mu}_k \mid G \stackrel{\text{ind}}{\sim} G, \quad \text{for } k = 1, \dots, K$$

$$G = (1 - \pi)G_0 + \pi G_1$$

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- Introducing a latent indicator  $z_k = I(\mu_{k1} \neq \mu_{k2})$

$$\boldsymbol{\mu}_k \mid z_k, G_0, G_1 \stackrel{\text{ind}}{\sim} G_{z_k}, \quad z_k \stackrel{\text{ind}}{\sim} \text{Ber}(\pi), \quad G_r \stackrel{\text{ind}}{\sim} \mathcal{DP}(a_r, F_r) \quad (2)$$



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- For the precision parameter of the Dirichlet processes:

$$a_r \stackrel{\text{iid}}{\sim} \text{Ga}(a_\alpha, b_\alpha),$$

for  $r = 0, 1$ .

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- Also implement a re-sampling step for  $\mu_k$

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$$(\mu_{k,g_j} + m_{l,j})$$

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- $n = 1,000$  probes, with locations from 1 to  $n$
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- We took level zero for the neutral zones and a positive / negative random value  $\text{Un}(0.1, 0.25)$  for the gain/loss zones
- We added random errors  $N(0, \sigma^2)$  to the mean profiles, with  $\sigma^2 \in \{0.1, 0.3\}$  to show low and high levels of noise in the  $\log_2$  ratios

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- Therefore, we had a total of 6 different scenarios: (3 prevalence levels  $\times$  2 noise levels).

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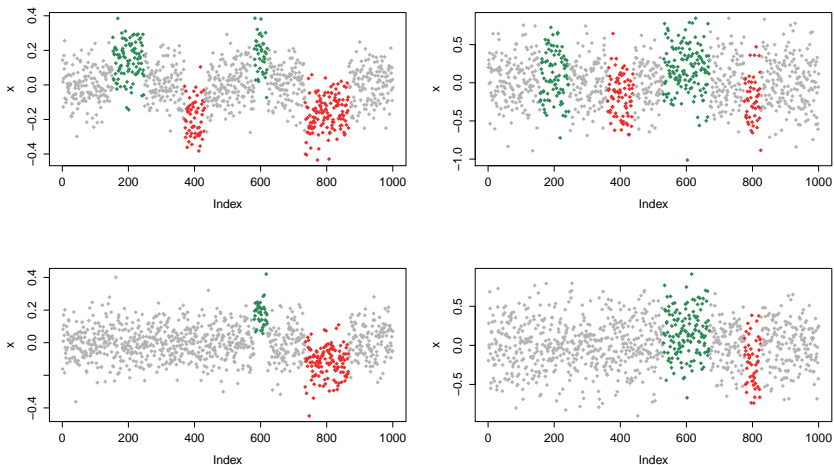


Figure : Simulated genome profile.

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- We took  $(\alpha_\tau, \beta_\tau) = (3, 0.01)$

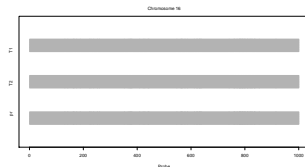
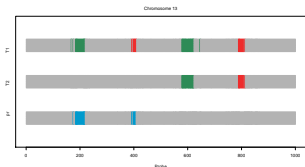
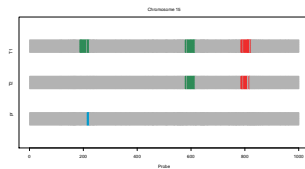
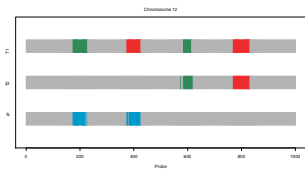
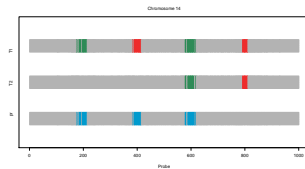
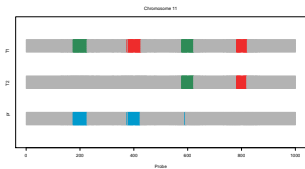
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- We call differential CNAs with a FDR = 5% and thresholds  $c_1 = c_2 = c$  with  $c = 0.10, 0.05, 0.03$  for the 100%, 60% and 30% prevalence levels

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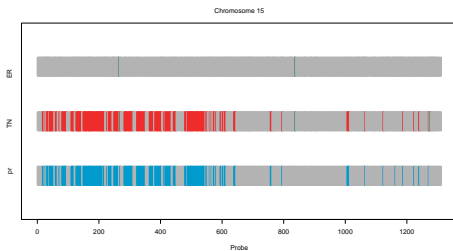
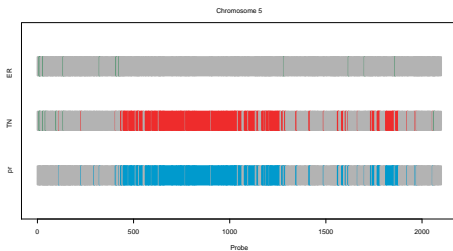
# Breast Cancer Data

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# Breast Cancer Data

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- Chromosome 15 is a new finding

# Breast Cancer Data



# Breast Cancer Data

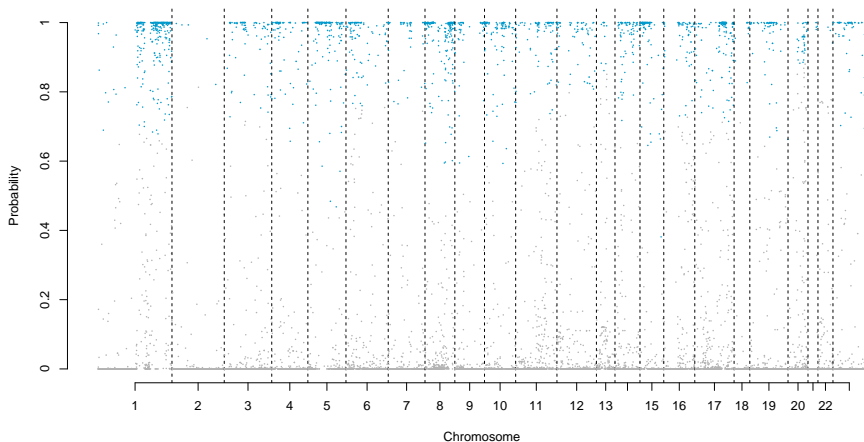


Figure : Differential CNA probabilities for all chromosomes.

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