

BitPhylogeny: a probabilistic framework for reconstructing intra-tumor phylogenies

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Intra-tumor view of carcinogenesis

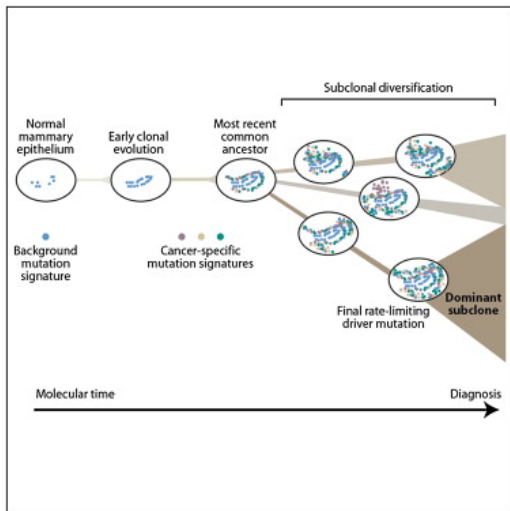


Figure: Nik-Zainal et al., (2012) Cell

Intra-tumor tree of one breast cancer sample

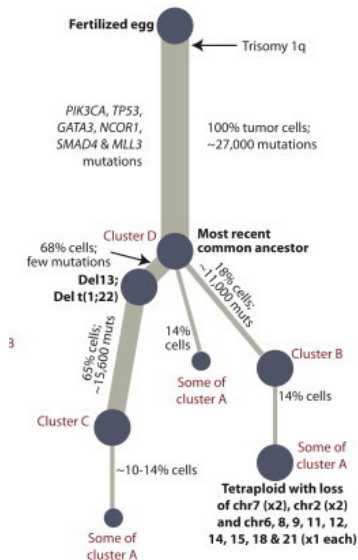
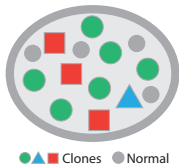


Figure: Nik-Zainal et al., (2012) Cell

Intra-tumor phylogenies

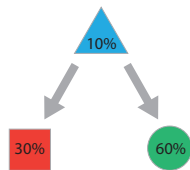
A Poly-clonal tumor



B Classical phylogenetic trees, hierarchical clustering

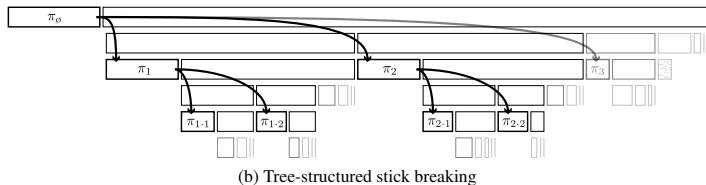


C Differentiation hierarchy



Goal: probabilistic model for differentiation hierarchy

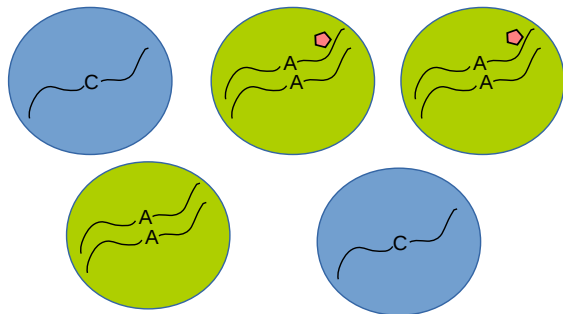
Tree structured Dirichlet process - probabilistic clustering prior



Adams et al. (2010) NIPS

- ▶ Nodes correspond to clones
- ▶ Data is placed in nodes

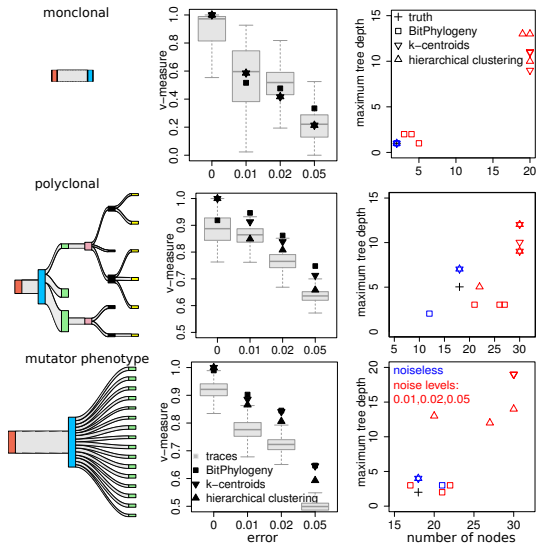
Flexible framework



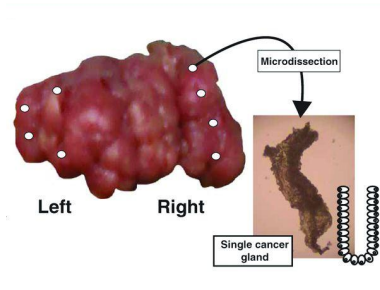
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...ACTACAGCAC..  
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...ACTACAGCAC..
```

- ▶ transition kernel - clone parameters depend on parent clones
 - ▶ provides link to classical phylogeny
 - ▶ back mutation for methylations
 - ▶ no back mutation for single nucleotide variants

Performance - clustering and tree summaries



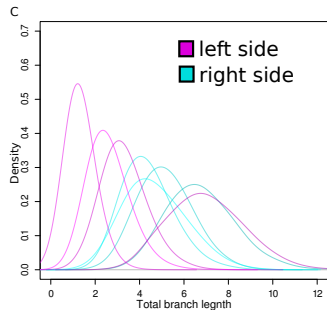
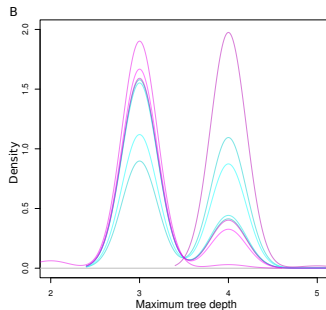
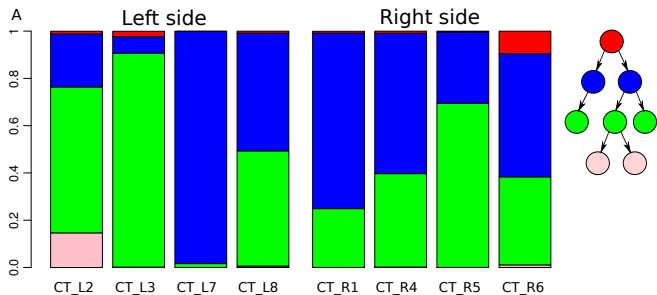
Colon cancer



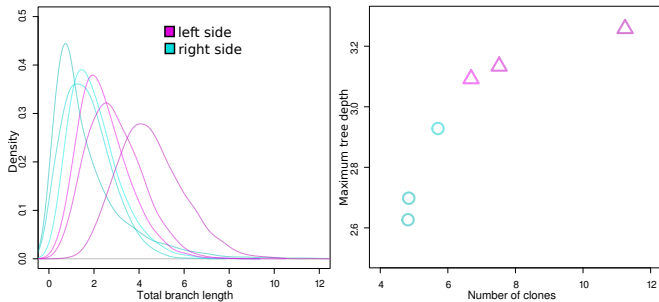
- ▶ about 10.000 cells per sample
- ▶ Bisulfite sequencing (bulk sequencing)
- ▶ IRX2 locus: 201 bp locus
- ▶ span 8 CpG region

Sottoriva et al. (2013)
Cancer Research

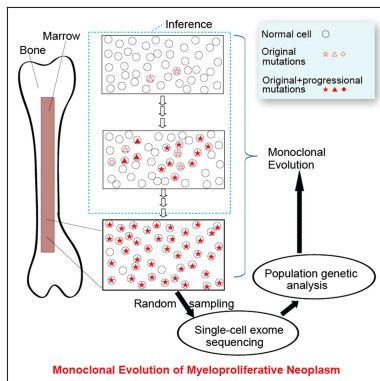
Tumor I



Tumor II



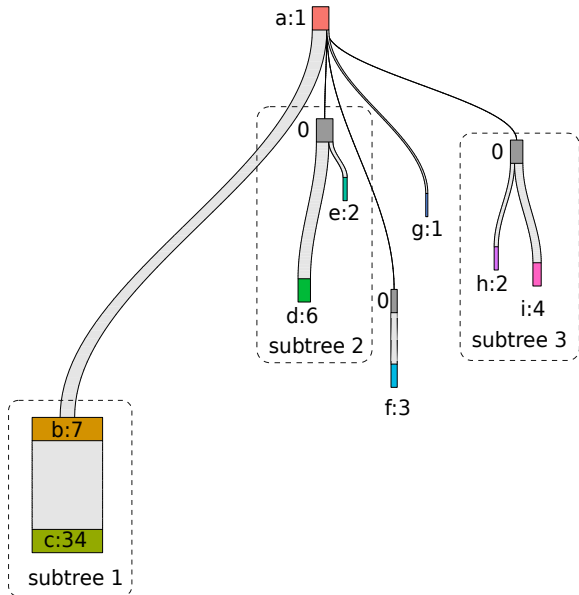
Leukemia - Myeloproliferative neoplasm



- ▶ 56 cancer cells
- ▶ whole-exome sequencing
- ▶ 712 SNVs
- ▶ 43 % allelic dropout rate
- ▶ assumption: infinite sites model

Hou et. al (2013) Cell

Clonal hierarchy



Discussion

- ▶ Probabilistic model for intra-tumor phylogeny reconstruction
- ▶ Faster inference needed
- ▶ Comparison method for evolutionary trees is lacking
- ▶ Vision: patient stratification

Acknowledgement

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- ▶ Florian Markowetz
- ▶ Ke Yuan