UCLA

Tractable and expressive generative models of genetic variation data

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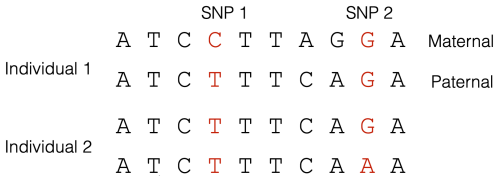
*Tractable and expressive generative models of **genetic variation data***

DNA sequence data



Can be represented as

$$\begin{bmatrix} 1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

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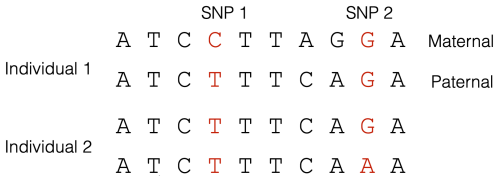

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It has wide applications

$\Rightarrow$ *genotype imputation, haplotype phasing, ancestry inference*

but challenging to learn

- high-dimensional
- data-scarce
- unevenly-distributed

$\Rightarrow$ *1000 Genomes Project studies 2500 individuals, discovers 90 million SNPs, includes >99% of SNPs with with frequency > 1%*

*Tractable and expressive **generative models** of genetic variation data*

Probabilistic models that represent joint probability $p(\mathbf{X})$ over random variables $\mathbf{X}$.

- traditional probabilistic models, such as HMM and Markov chain
- more recent ML approaches, such as VAEs and GANs

Tractable and expressive *generative models of genetic variation data*

expressive

$\Rightarrow$ *how well it captures the data*

tractable

$\Rightarrow$ *ability for probabilistic inferences, such as likelihoods, MAP*

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***Q*: Can we get the benefits of both ?**

A*: *Probabilistic circuits (PCs) !

Outline

Empirical Evaluation
- Density Estimation
- Principle Component Analysis (PCA)
- Pairwise Correlation

Probabilistic Circuits (PCs)

Conclusions

Empirical Evaluation

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Conclusions

Density Estimation

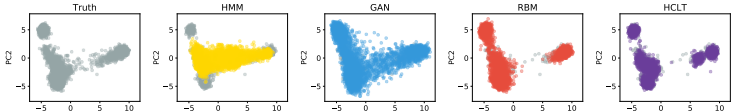
how well the models fit the data

Dataset	Indep	Markov Chain	HMM	HCLT (PC)
805	-491.10	-438.64	-402.50	**-389.20**
10K	-2390.09	-633.14	-1194.72	**-310.93**

Table: **Log-likelihoods results on subsets SNPs from 1000 Genomes Project**

Principle Component Analysis (PCA)

how well the models fit the data



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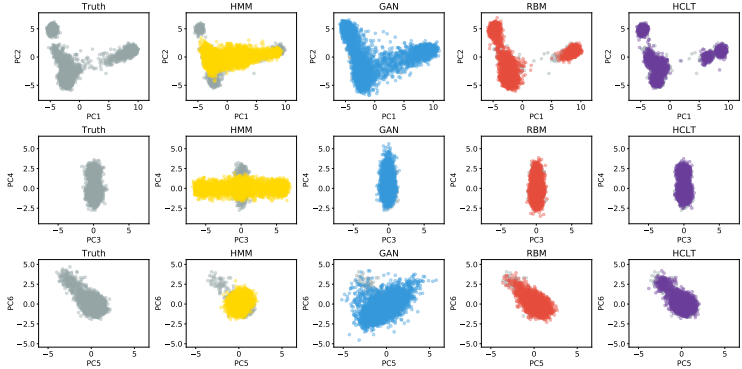
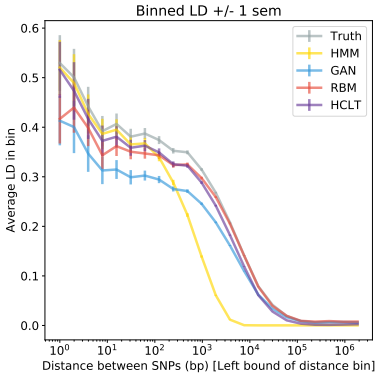
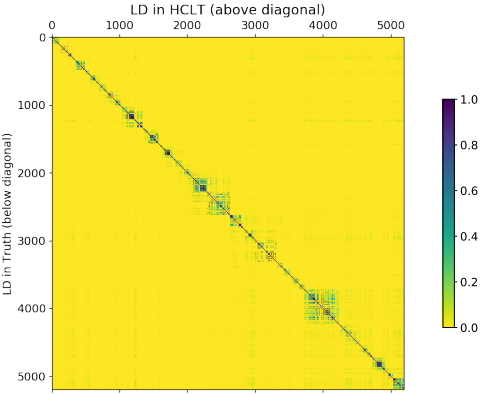


Pairwise Correlation



(a) R^2 as a function of SNP distance



(b) R^2 matrices comparing ground truth and PC

Empirical Evaluation

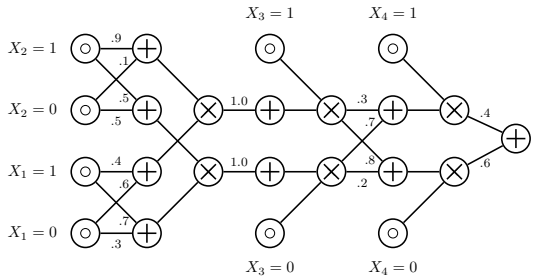
- Density Estimation
- Principle Component Analysis (PCA)
- Pairwise Correlation

Probabilistic Circuits (PCs)

Conclusions

Probabilistic Circuits (semantics)

PCs encode joint distributions via computational graphs, e.g., a PC with 4 SNPs



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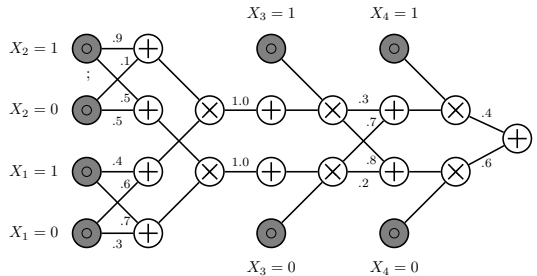

Input nodes are tractable distributions, *e.g., indicator functions* $\mathrm{p}(X_i = 1) = [X_i = 1]$

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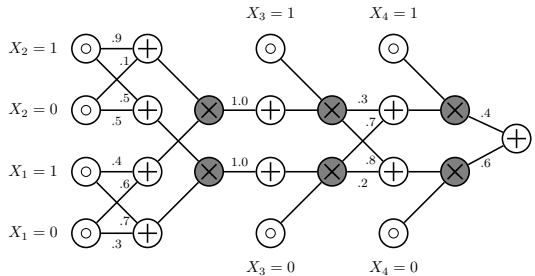

Product nodes are factorizations $\prod_{c \in \mathsf{in}(n)} \mathrm{p}_c(\mathbf{x})$

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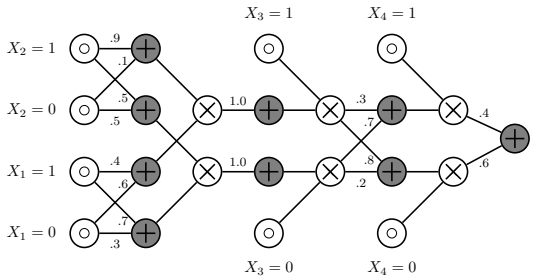
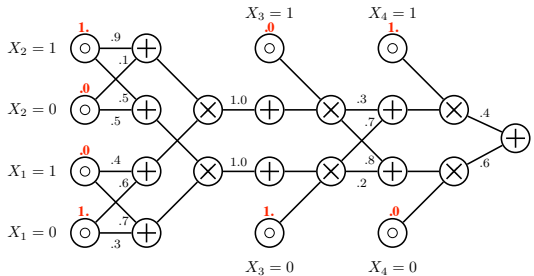


Sum nodes are mixture models $\sum_{c \in \mathsf{in}(n)} \theta_{n,c}\, \mathrm{p}_c(\mathbf{x})$

Probabilistic Circuits (tractability)

Compute likelihood $p(X_1 = 0, X_2 = 1, X_3 = 0, X_4 = 1)$



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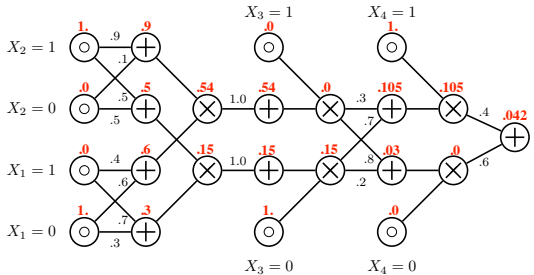

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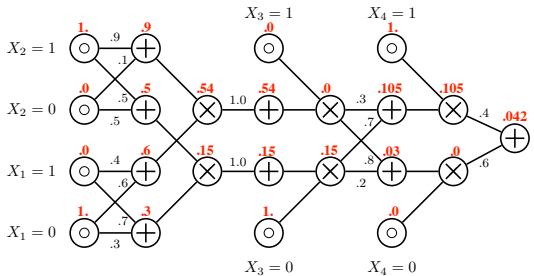
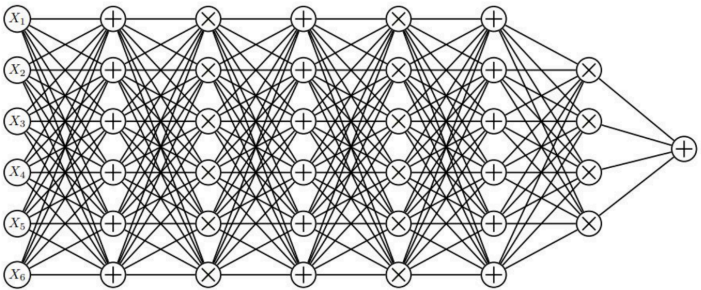


Computing likelihood is time linear in the size of PC

Probabilistic Circuits (expressiveness)

Large scale, a deep architecture, millions of parameters



Efficient learning algorithms

Conclusions

The first attempt to introduce probabilistic circuits to bio-informatics

- comparable or better performance
- tractable, expressive, time-efficient to train
- applicable to different tasks