Hi-C-LSTM: Learning representations of chromatin contacts using a recurrent neural network identifies genomic drivers of 3D genome conformation

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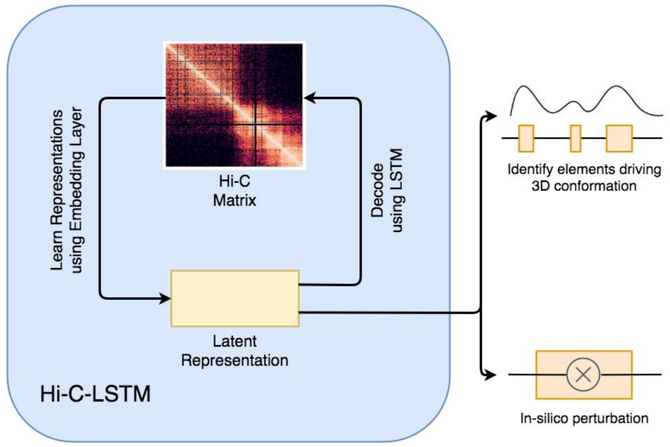
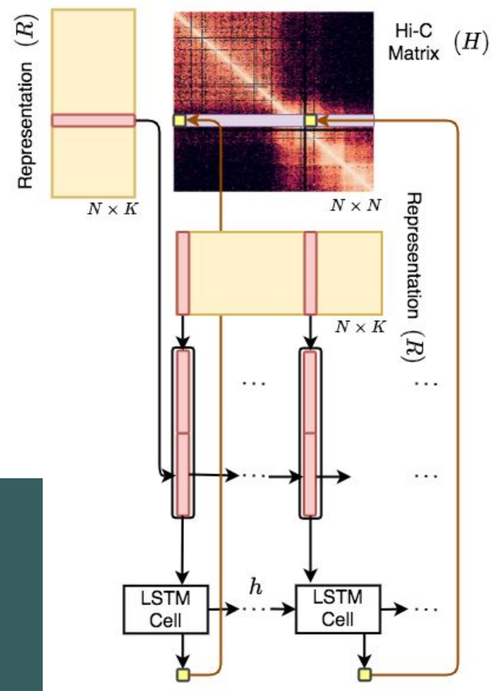
Need for Hi-C Representations



Goal: Understand of how the 1D genome influences 3D conformation

Hi-C-LSTM

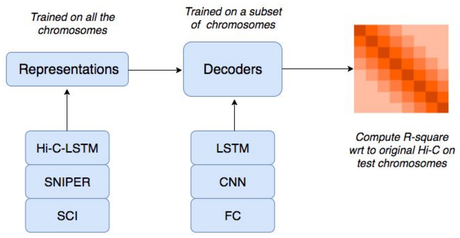


Salient Features of Hi-C-LSTM

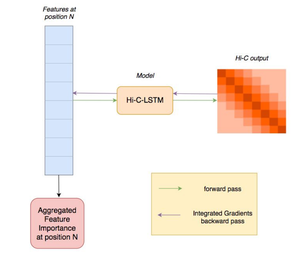
- Works on intrachromosomal contacts in contrast to most existing methods, which were designed for interchromosomal contacts
- Takes into account the sequential nature of the genome
- Representations have information needed to recreate the Hi-C matrix and recreation is more accurate using an LSTM as the decoder
- Captures a variety of genomic phenomena and distinguishes genomic regions that are known to cluster in 3D space
- Feature importance reveals association with transcription factors such as CTCF that are known to mediate chromatin conformation
- Enables us to perform in-silico knockout/insertion experiments as it behaves as a framework for contact-generation
- It can model only cis effects because trans-acting cellular machinery is captured within the Hi-C-LSTM decoder, which cannot be easily modified
- Recapitulates effects of known structural variants seen in certain developmental disorders

Evaluations

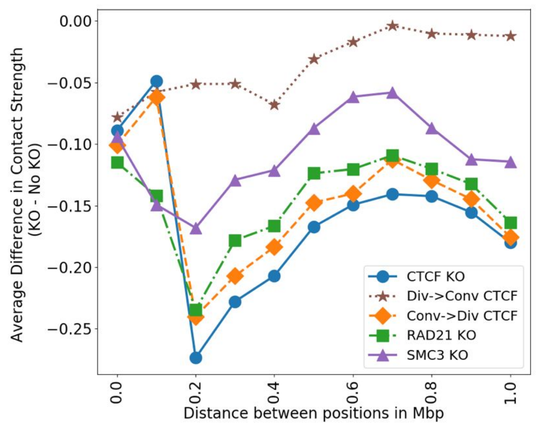
R-squared



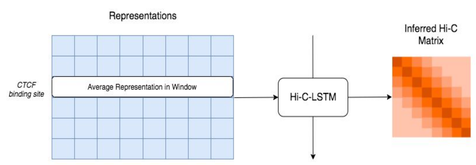
Feature Importance



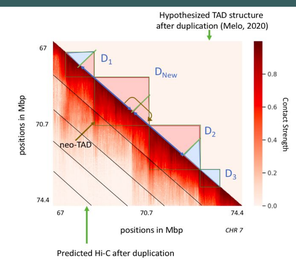
Hi-C-LSTM enables in-silico knockout experiments



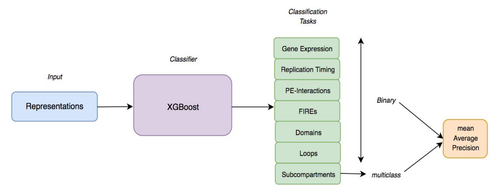
Knockout



Duplication

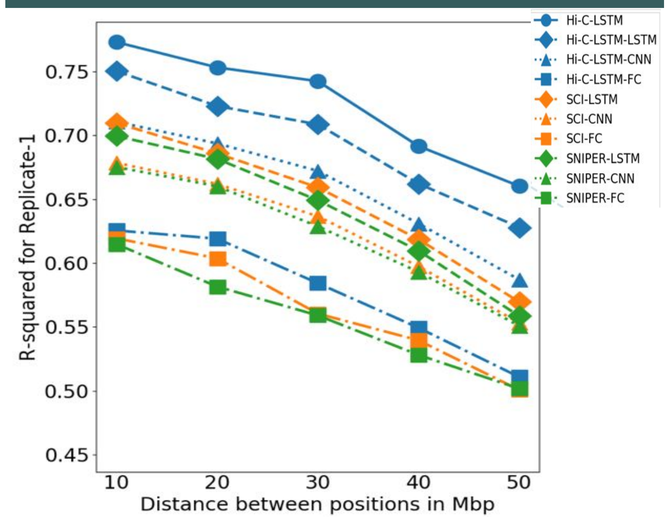


Classification

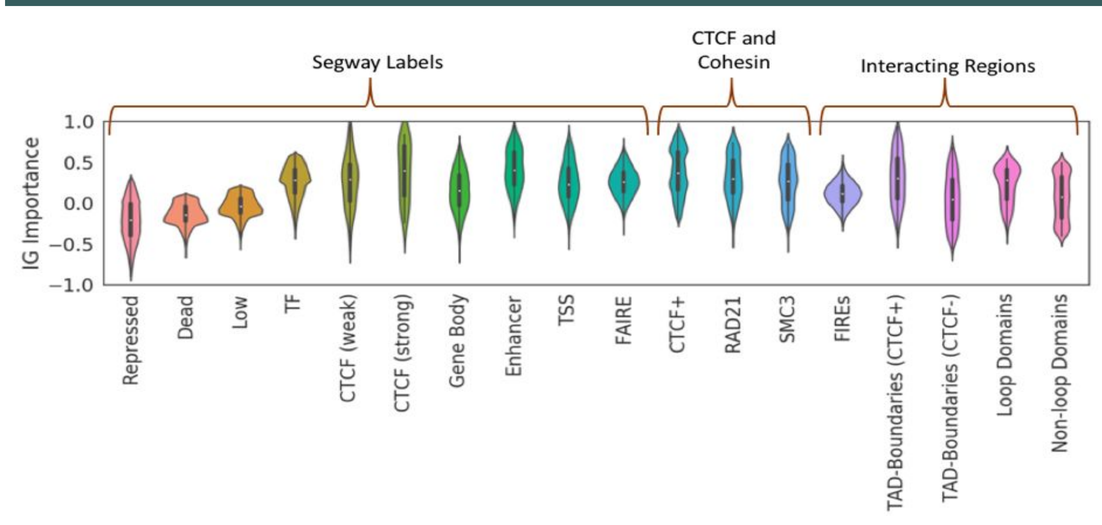


Results

Representations capture information needed to create the Hi-C-matrix



Feature Importance reveals association with genomic elements driving 3D conformation



Representations locate functional activity and regions that drive 3D conformation