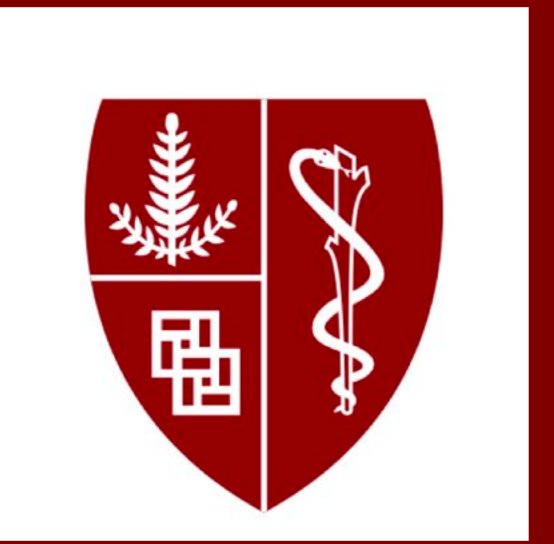# Denoising ATAC-seq with Convolutional Neural Networks
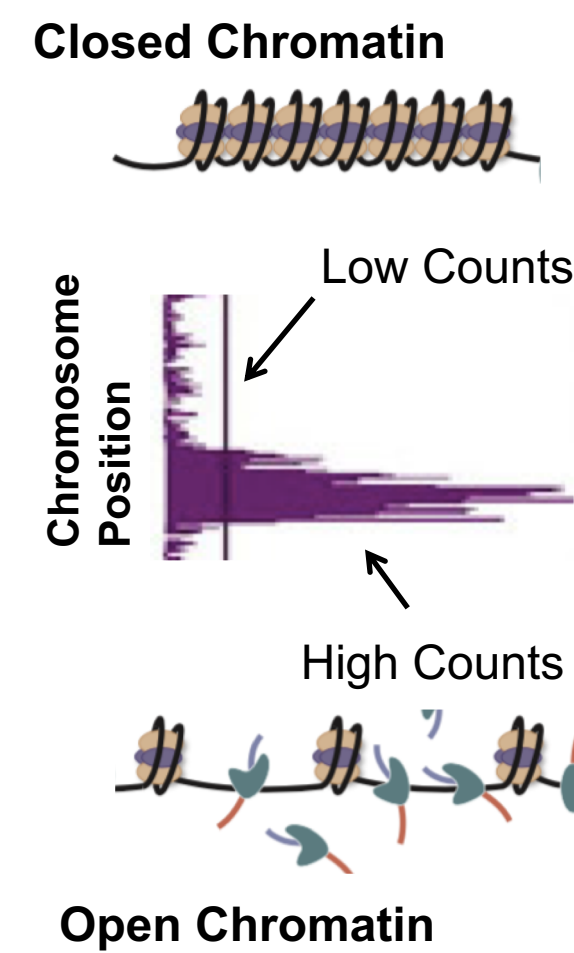
Nic Fishman and Sarah Gurev
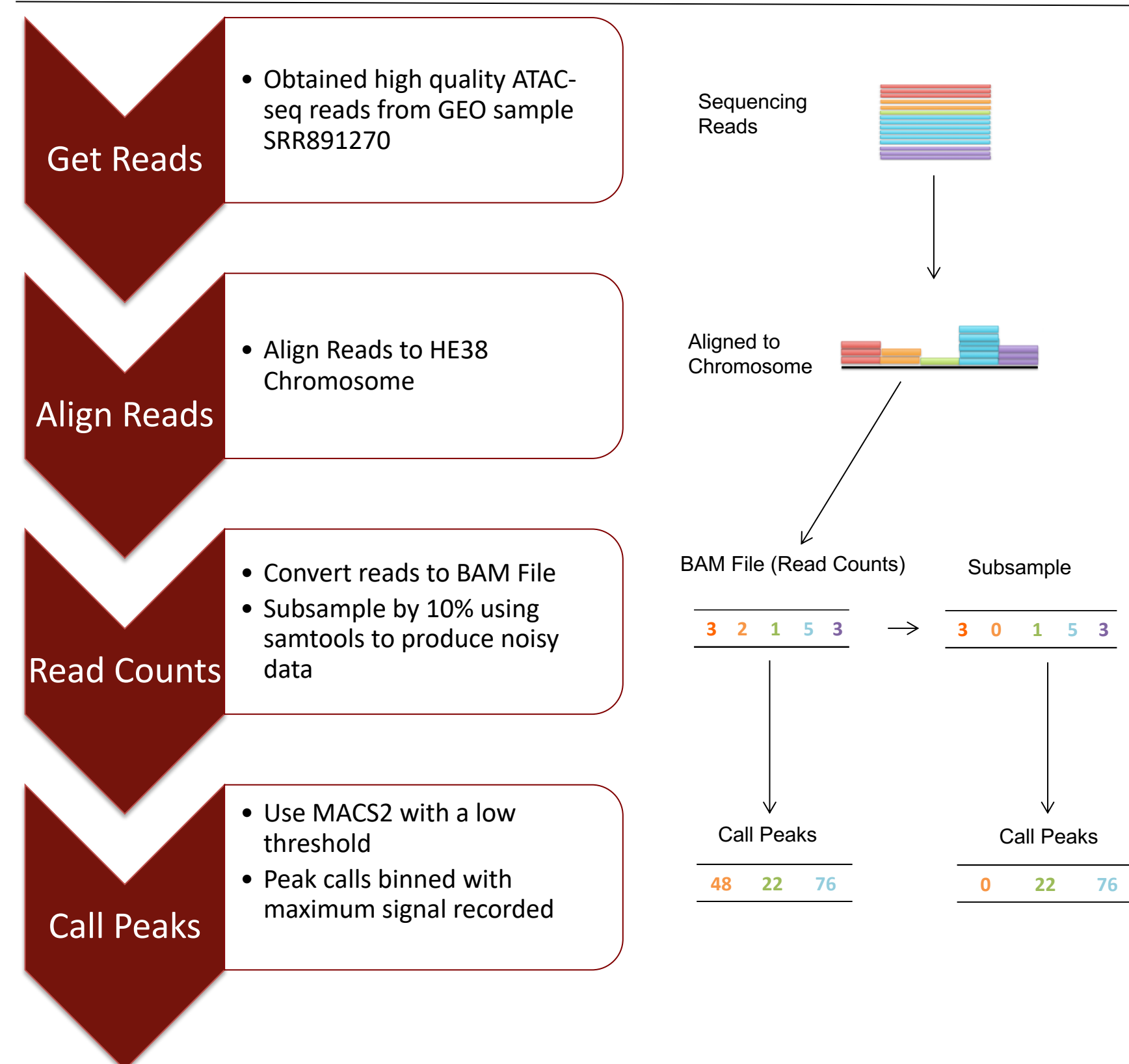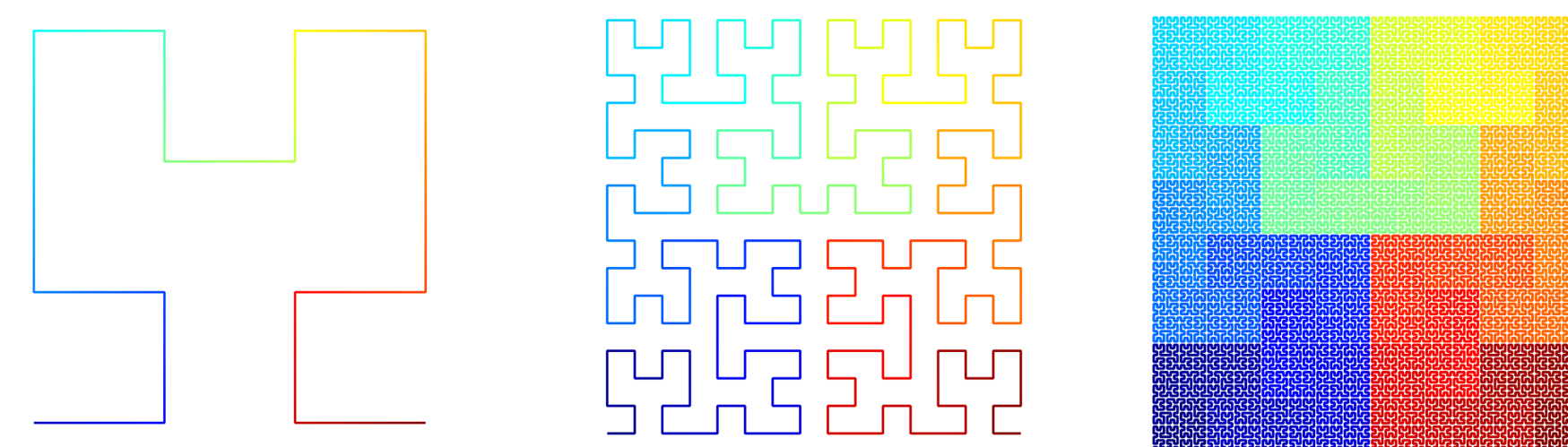{njwfish, sgurev}@stanford.edu

The Problem with ATAC-seq

- Chromatin is a compressed version of DNA. A gene cannot be expressed when it is compressed or closed.
- ATAC-seq is a sequencing technique used to determine what parts of chromatin are open or closed.
- The quality of ATAC-seq data is heavily dependent on many environmental factors, and therefore prone to noisiness

Closed Chromatin

Low Counts

Chromosome Position

High Counts

Open Chromatin

Data Pipeline

Get Reads
- Obtained high quality ATAC-seq reads from GEO sample SRR891270

Align Reads
- Align Reads to HE38 Chromosome

Read Counts
- Convert reads to BAM File
- Subsample by 10% using samtools to produce noisy data

Call Peaks
- Use MACS2 with a low threshold
- Peak calls binned with maximum signal recorded

Sequencing Reads

Aligned to Chromosome

BAM File (Read Counts)   Subsample

3 2 1 5 3 → 3 0 1 5 3

Call Peaks   Call Peaks

48 22 76   0 22 76
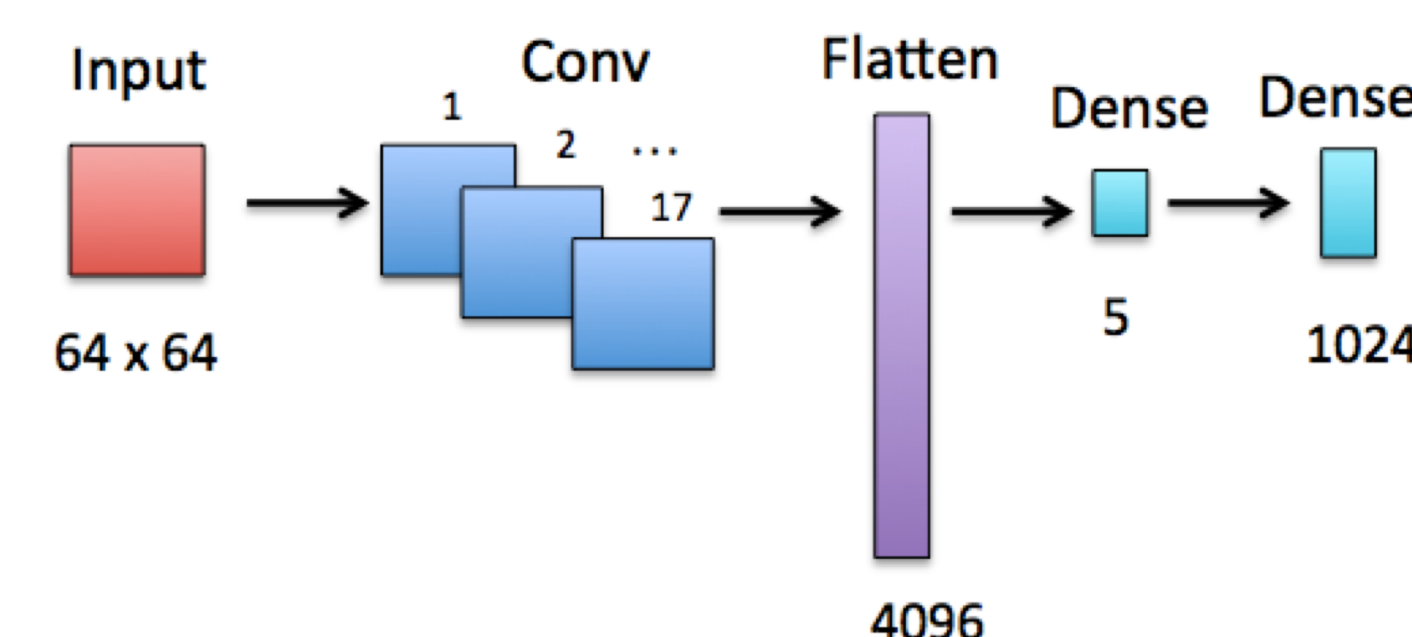
Hilbert Curve

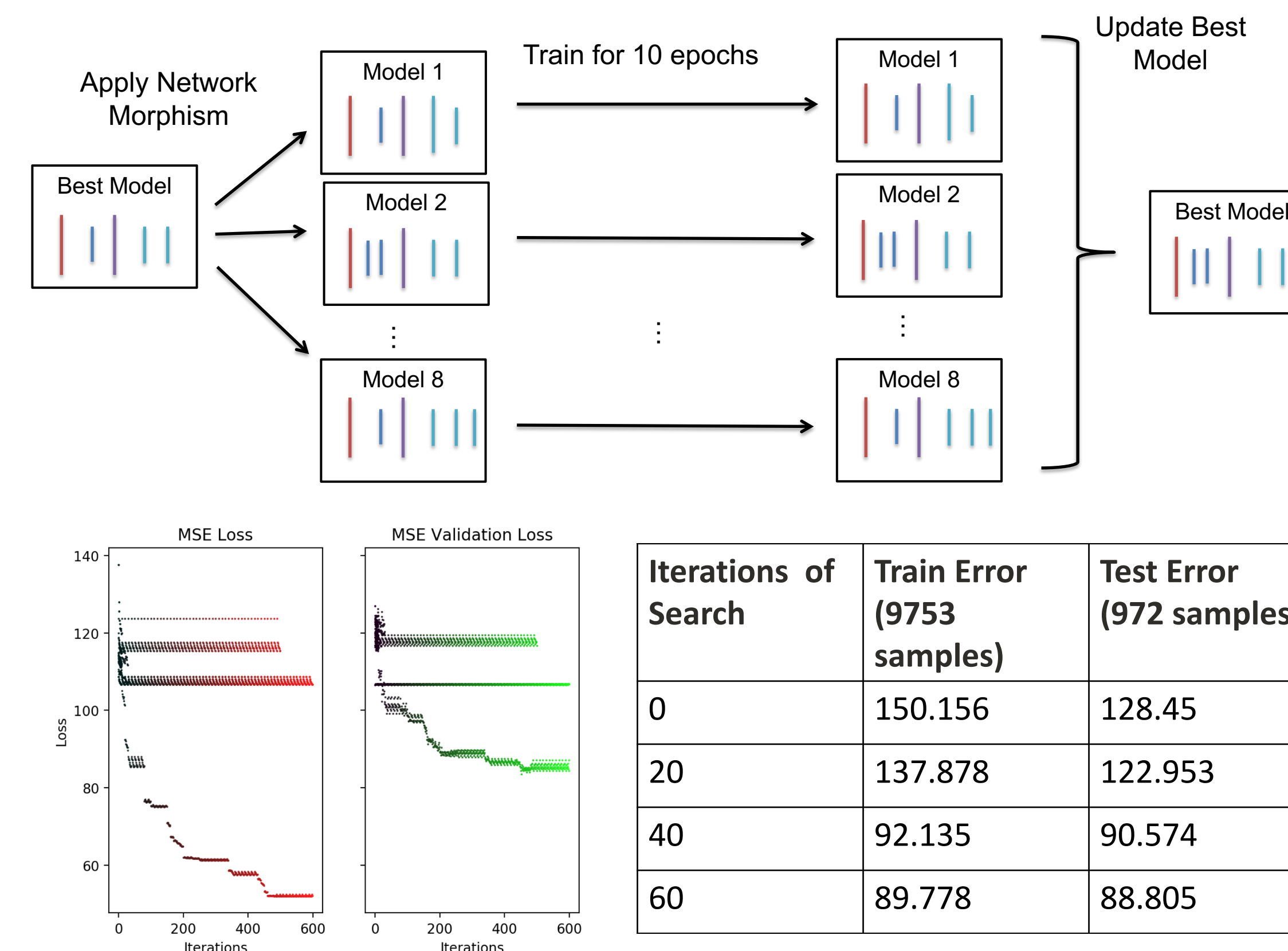## Model Design and Selection

Architecture Search: Random Search

Initial Model:
- Random architecture search
- 1 Conv2D layer into 1 Dense layer
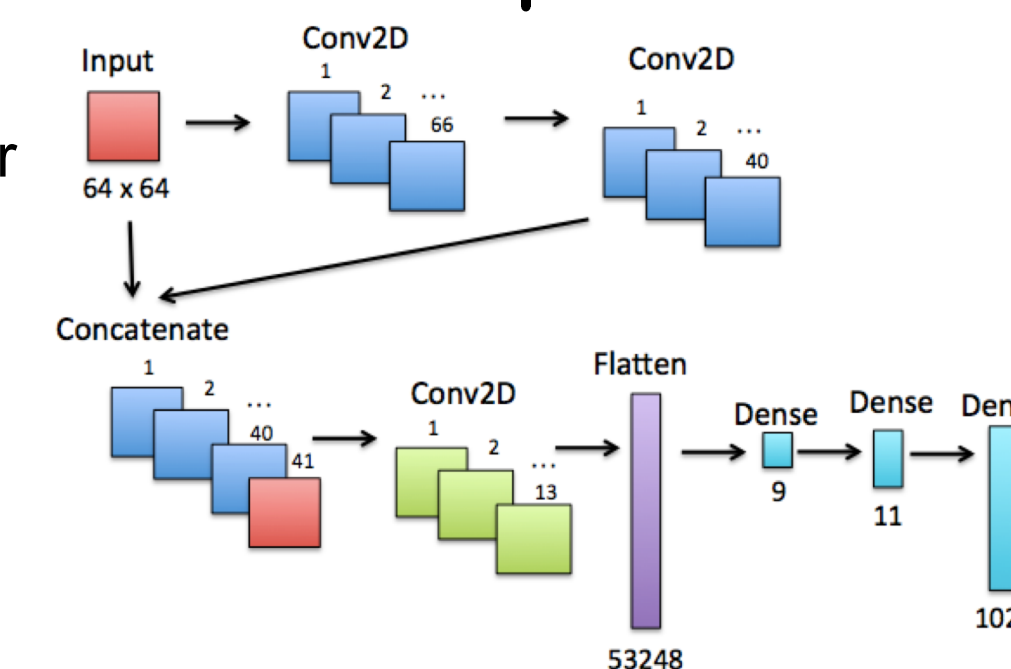- Randomize:
  - Kernel size
  - Filters
  - Hidden units

Input 64 x 64   Conv 1 2 ... 17   Flatten 4096   Dense 5   Dense 1024

Architecture Search: NASH

Apply Network Morphism

Best Model

Model 1   Train for 10 epochs   Model 1   Update Best Model
Model 2   Model 2   Best Model
Model 8   Model 8

MSE Loss   MSE Validation Loss

Iterations of Search	Train Error (9753 samples)	Test Error (972 samples)
0	150.156	128.45
20	137.878	122.953
40	92.135	90.574
60	89.778	88.805

Final Model:
Greedy Hill Search to find a new best model after randomly changing the parent
1. Apply Network Morphisms to develop new model:
2. Train child networks with cosine annealing
3. Move to most promising child of network

Input 64 x 64   Conv2D 1 2 ... 66   Conv2D 1 2 ... 40

Concatenate 1 2 ... 40 41   Conv2D 1 2 ... 13   Flatten 53248   Dense 9   Dense 11   Dense 1024
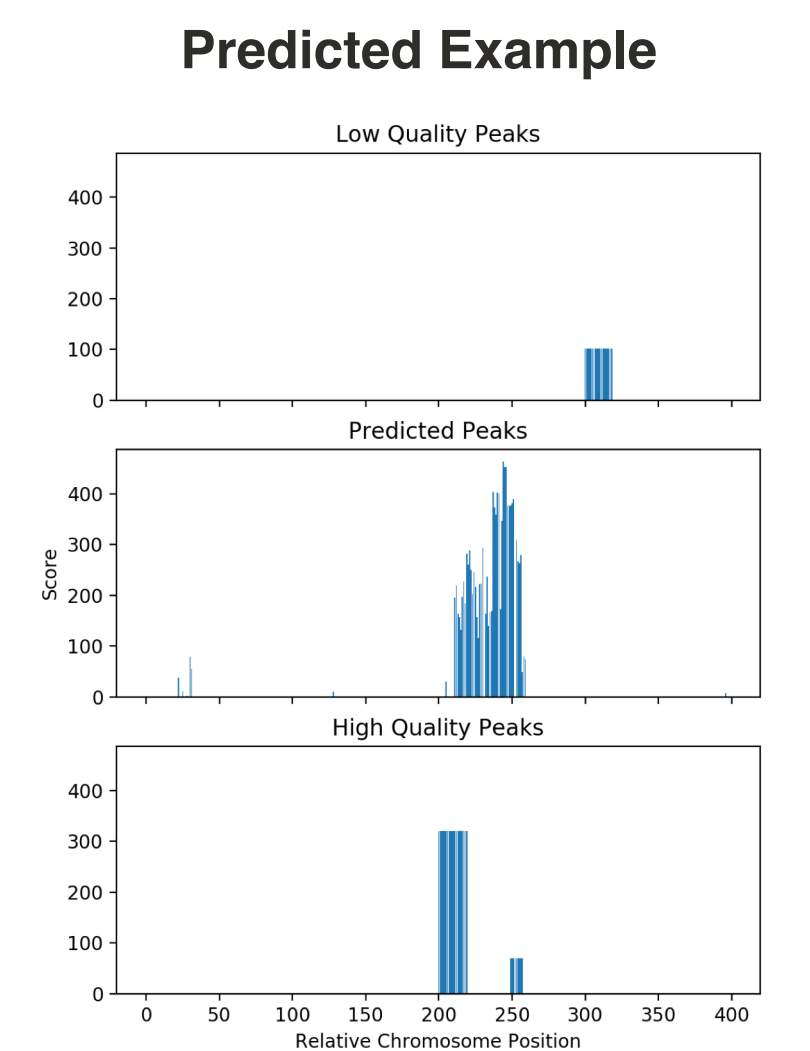
Results

We used an architecture search to develop a CNN architecture that is trained on high quality, low quality pairs of data.

Our model can reliably convert noisy data into high quality data.

An example is to the right, where the subsampled peak is shifted right, and is low score. The model shifts it left, and boosts the peak score.

Predicted Example

Low Quality Peaks

Predicted Peaks

High Quality Peaks

Relative Chromosome Position

Discussion

- Our model is able to map low quality to high quality ATAC-seq data using a CNN developed through an Architecture Search
- The results achieved are good, which is expected given the role of the Architecture Search to build a network with the best possible performance
- Our computationally simulated noise, done via subsampling, is a reasonable estimate of ATAC-seq noise caused by environmental factors like amount of input DNA and sequencing depth, so our model should do a good job of denoising true low-quality data.

Future Work

- Develop pipeline for cell-line specific training
- Confirm biological relevance of denoised data using properties of chromatin accessibility for evaluation
- Replicate work with other sources of noise

References

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