Genome Dreaming
Akshay Maheshwari, Bohan Wu, Öğuz H. Elibol

Introduction and Motivation

- The ability to generate novel genomes and sequences with predictable characteristics would revolutionize synthetic biology
- We build an end-to-end pipeline to:
  1. Learn the properties of unlabeled prokaryotic genomes in an unbiased way
  2. Generate new sequences with predictable properties
  3. Visualize and evaluate learned representations of generated sequences

Data

- 4131 unlabeled prokaryotic genomes and their gene annotations from the KEGG database

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Model & Visualization

Pipeline:

- Learn structure using Recurrent Neural Networks (LSTM)
- Optimize model
- Generate sequence
- Extract hidden layers for all E. coli genes
- Reduce hidden layers into 2D using t-SNE
- Cluster using Mixture of Gaussians
- Extract proportion of points in each cluster
- Create vector embedding for each gene (100-D)
- Reduce gene embeddings to 2D
- Evaluate similarities between genes and generated sequence

Learning and Sequence Generation

\[ L_C(w; y) = - \sum y_i \log p(y_i) \]

LSTM Cells

Sequence Visualization and Evaluation

- Extract hidden layers for all E. coli genes
- Reduce hidden layers into 2D using t-SNE
- Cluster using Mixture of Gaussians
- Extract proportion of points in each cluster
- Create vector embedding for each gene (100-D)
- Reduce gene embeddings to 2D
- Evaluate similarities between genes and generated sequence

Results

Model tuning and optimization

Model Validation

<table>
<thead>
<tr>
<th>Gene</th>
<th>Probability</th>
<th>Distance (MPA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.coli-strain 1</td>
<td>0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>E.coli-strain 2</td>
<td>0.002</td>
<td>0.002</td>
</tr>
<tr>
<td>...</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Sequence Generation and Property Prediction

Generated Protein | grol (Closest Neighbor)

- Build a stronger model: Generative Adversarial Networks, WaveNet, Neural Turing Machines, and Attention Models
- Identify the properties and motifs that the neural network is learning