CSCI2952G Final Project Literature Review
Team Blue Genes
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Deep Learning Models for the Super Resolution Problem

The goal of super resolution (SR) problems is to predict a high-resolution image from a low-resolution input image. We begin with non-DL models. One relatively common benchmark, as seen in [21], is the random forest method. Random forests combine decision tree predictors such that each tree depends on the values of i.i.d. random vectors. In [19], Zhang et al. created HiC-Reg to integrate Hi-C datasets with one-dimensional regulatory genomic datasets such as chromatin marks, architectural and transcription factor proteins, and chromatin accessibility.

Deep learning models are widely used in many fields, such as image processing [1,2,3]. Based on the ability of convolutional neural networks (CNN) to process image data, [4] proposed SRCNN to predict high-resolution images from low-resolution images with the help of end-to-end CNN, which significantly outperforms previous works. However, the pixel-wise mean squared error (MSE) leads to blurry images, making MSE-based models fail on restoring fine texture details. To address such a problem and obtain photo-realistic images, the generative adversarial network (GAN) is utilized to approximate the distribution of realistic images, instead of just learning the pixel-wise projection from low-resolution to high-resolution data. For example, [5] proposed Super Resolution GAN (SRGAN) enhancing image resolutions based on a GAN. SRGAN uses a generator network to generate estimations of high-resolution data and employs a discriminator network for distinguishing generator estimations from true high-resolution samples. Two networks compete against each other to obtain a good distribution approximation. Benefiting from its good performance on generating more visually appealing results, GAN is widely used for SR problems.

After experiencing the benefits of deep learning models, various deep learning techniques and architectures are introduced in this field to make further improvements. Many models [8-12] utilize residual architecture to obtain better stabilization for very deep networks. Using skip connections in networks, residual architecture reuses outputs of previous layers to avoid gradient vanishing problems. In another line of works, researchers propose perceptual-based models to improve the visual quality of estimations and obtain photo-realism. For instance, [13] minimizes the loss in the feature space rather than the pixel space, and [14] integrates semantic prior in an image for improving the recovered textures. Because of rapid developments in deep learning, CNN and RNN-based models have shown promising good performance in SR problems. Considering the Hi-C contact matrix as image-like data, these models can be used for improving Hi-C data resolution in a similar way.

Deep Learning Models for Enhancing Hi-C Data

The current state of the art focuses on two main models: convolutional neural networks (CNNs) and generative adversarial neural networks (GANs). Zhang et al's *HiCPlus* [19] is a CNN that interprets the low resolution HiC matrices as images, applying three layers of convolutions of varying kernel sizes to first extra feature maps from the low-resolution matrices and then using a dense neural network to impute a high-resolution matrix *HiCNN* [16] is a "very deep" CNN that consists of five convolutional layers with a residual block, making it a deep recursive residual network (DRRN). The addition of the residual block and recursive connections allowed HiCNN to outperform HiCPlus in the task of upsampling low-resolution HiC data in terms of both mean squared error (MSE) and the Pearson correlation metric originally used by HiCPlus. *SRHiC* [15] is a recent model that adds a second residual block to its CNN architecture, consisting of three convolution blocks with residual blocks in between toenerate the upscaled HiC matrix.

Another main research direction is the use of GANs. The first GAN used in the HiC task was *HiCGAN* [18], a GAN consisting of a CNN discriminator and a dual-stream residual generator that learns to generate high-resolution data from low-resolution input matrices via adversarial training. Another GAN model, *DeepHiC* [17], takes a similar approach but uses a different loss function and a deeper generator, consisting of 23 residual layers Unfortunately the authors of DeepHiC don't directly compare their results with HiCGAN, so it's impossible to call one the state of the art over the other, although visually DeepHiC's imputed matrices look more accurate.

A final method used is ensemble learning. *HiCNN2* [20] is an extension of HiCNN that considers ensembles of two and three HiCNN CNNs to impute high-resolution HiC data. The addition of the extra models in the ensemble increases performance above that of HiCNN and the other CNN models slightly (excluding SRHiC, which had not yet been released).

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