Predictive Imaging of the Kinetochore Using Machine Learning

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Introduction

Generative deep learning models are relatively recent algorithms that display powerful applications in biological research by allowing for predictive image modeling. This technology can be applied to predictive imaging of the kinetochore, a complex of proteins that is involved in the initiation and control of chromosomal movements during mitosis and is implicated in certain diseases. (Cimini et al., 2008)

Fluorescent images of the kinetochore can be viewed in both red-channel and green-channel modes. By utilizing generative deep learning in the form of a generative adversarial network (GAN), these algorithms can be used to output predictive images of the red channel after being given only the spatial information of the green channel. GANs are a combination algorithm that utilize two adversarial networks that continually improve each other through competition. The discriminatory network and generative network are trained vis-à-vis each other until the desired result is achieved. The discriminator is first trained independently on a training dataset, which makes it proficient at discerning what is a generated image and what is a ground truth image. The generative network then creates simulated images, while the discriminative network evaluates them for accuracy compared to the known dataset (ground truth). Based on how close the generative algorithm was according to the discriminator, the algorithm refines its weights and parses over a different sample from the training dataset.

The end goal of the network is to increase the error rate of the discriminatory network - essentially, to create generated images that are of such high quality that they are indistinguishable from the known dataset (Goodfellow et al., 2014). In the context of this application, the discriminator would be able to discern the accuracy of a generated green-channel image given its training on the green-channel images. The generator would be tasked with creating novel red-channel images based on given green-channel ones. This would allow in the future taking a single-color image and filling in the entire image of the kinetochore. Obtaining full information of the localization of the kinetochore from just one color-channel would be immensely helpful in future endeavors and can be modified to allow for precise protein localization.

Methods

An image generation program (Lawrimore et al., 2019) was used to create a dataset of 40x40 paired image sets (red-channel and green-channel) of the kinetochore. The architecture used was a modified version of the Pix2Pix conditional GAN (Isola et al., 2018), provided by Google's open-source TensorFlow Core. Google Colaboratory software, which allows for cloud computing using high-end hardware, was used for building and training the algorithm. The discriminator was trained by being given a randomized training dataset that allowed it to learn the association between red and green channel images. The generator then made a guess regarding what the associated image to a given green-channel input would look like, and the discriminator returned whether the associated image was "real" or generated. Based on the result, the generator then refined its weights and created another round of images until the loss was sufficiently low.

Results

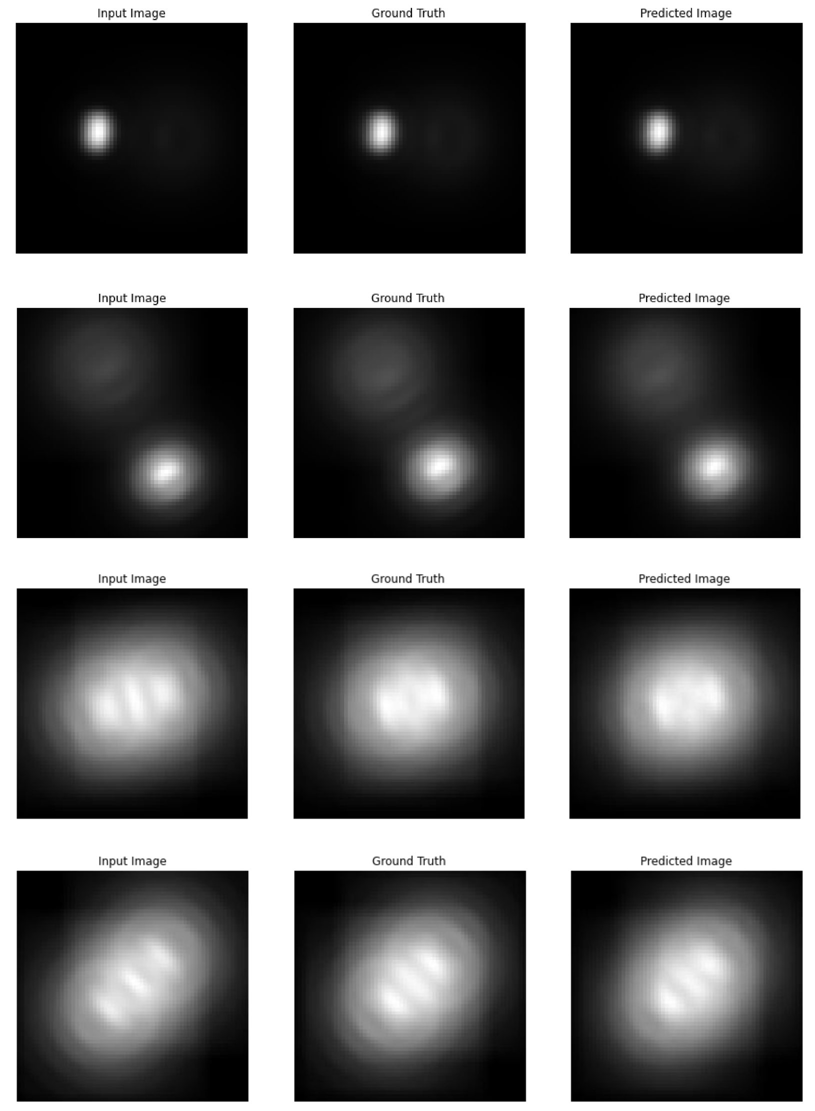

Figure 1. Selected comparison of input images, the ground truth associated image, and the predicted image outputted by the GAN.

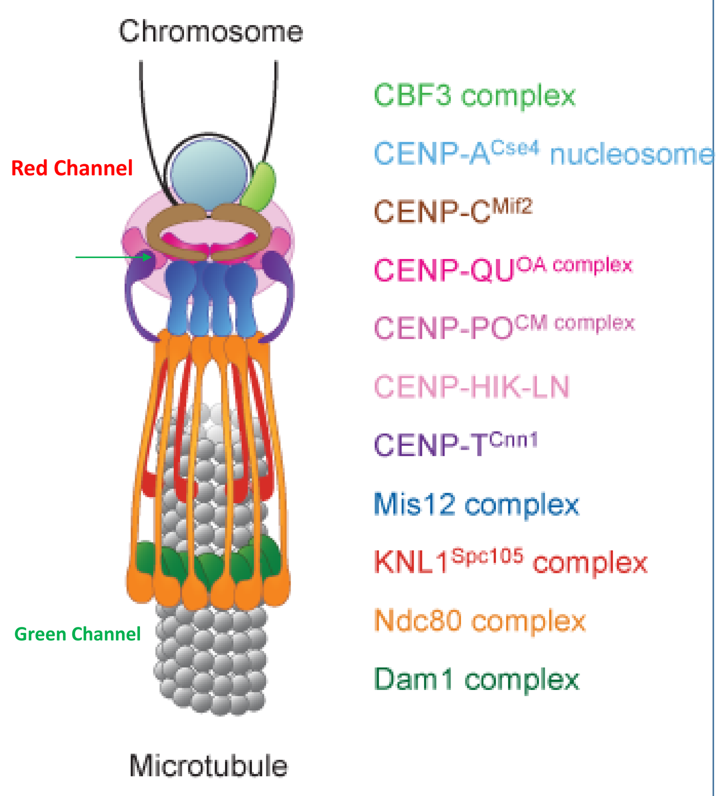

Figure 2. Red and green channel localizations on kinetochore structure.

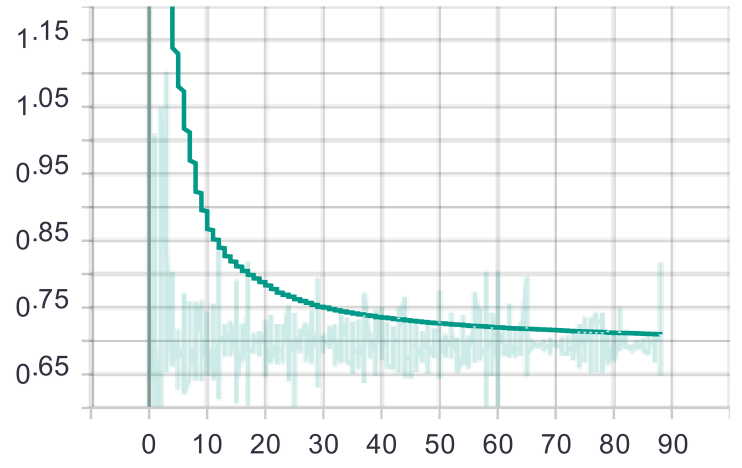

Figure 3. Generator loss over training epochs.

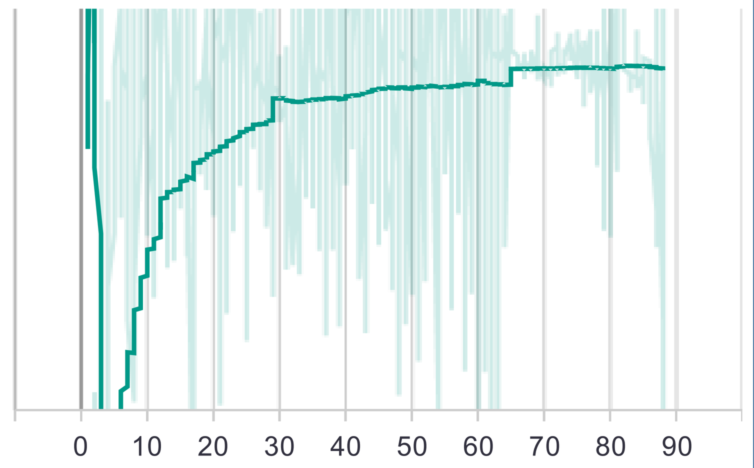

Figure 4. Discriminator loss over training epochs.

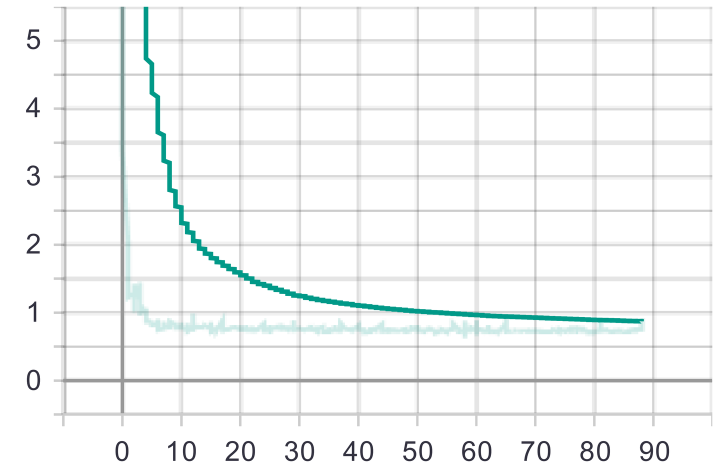

Figure 5. Total GAN loss over training epochs.

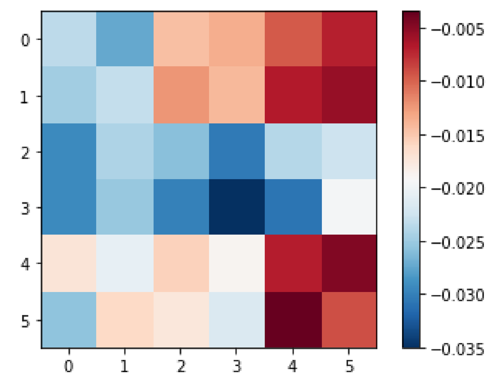

Figure 6. Loss by image region.

Conclusion

The network was reasonably effective at creating images close to the ground truth associated red-channel image when given a green-channel image. (Figure 1) The spatial orientation is excellent, with the borders and location of the predicted image matching nearly exactly with the ground truth. The architecture was also able to pick up on the finer detail of the image and will likely improve in its detail resolution as it is trained and optimized further. The loss for the generator was still decreasing at the end of training, making it highly likely that longer training would produce better results. (Figure 3) The discriminator loss also behaved as expected, as it started low but began to increase as the generator made better images and began to trick the discriminator (Figure 4) Total GAN loss decreased throughout, showing how the algorithm continuously improved its ability to create images that were very close to the ground truth expected images for a given input. (Figure 5) Figure 6 shows loss by image region, illustrating areas the algorithm performed especially well or poorly in and guiding potential improvements.

The immediate next steps will be optimizing the Pix2Pix architecture by allowing for longer training time and allowing training to run for as long as the model continues to significantly improve in performance (shown by generator loss decreasing). Afterwards, the model can be tested on real fluorescent microscopy images of the kinetochore to verify its accuracy in practical applications. The association between the red-channel and green-channel images can also be extended to other parts of the kinetochore, allowing for more in-depth spatial information from only one kinetochore structure.

References

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Goodfellow, IJ, Pouget-Abadie, J, Mirza, M, Xu, B, Warde-Farley, D, Ozair, S, Courville, A, and Bengio, Y (2014). Generative adversarial nets. In: Advances in Neural Information Processing Systems, Neural information processing systems foundation, 2672–2680.

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