CytoGAN: Generative Modeling of Cell Images

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Introduction

Morphological profiling aims to map microscopy images of perturbed cells to salient vector representations that divide the morphological space into clusters of cells with similar properties or function.

Current approaches are divided between **a**) classical image processing, requiring manual fine-tuning and expert knowledge, and **b**) transfer learning with deep CNNs trained on miscellaneous objects, allowing little to no domain-specific adaptation.

Instead, we model cells with *Generative Adversarial Networks* (GANs) for both representation learning and cell image synthesis. Advantages of our approach include:

- **Adaptability** to training data, allowing identification of the intrinsic semantic relationships between biologically meaningful channels,
- **Translation** of learned representations into biological phenotypes.

Code & Data

Code and experiments are available at `github.com/goldsborough/cytogan`. Our data is the BBBC021 dataset from the Broad BioImage Benchmark Collection (`data.broadinstitute.org/bbbc/BBBC021`).

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References

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[3] N. Pawlowski, "Towards Image-Based Morphological Profiling using Deep Learning Techniques," Master's thesis, University of Edinburgh, 2016.

[4] A. Radford *et al.*, "Unsupervised representation learning with deep convolutional generative adversarial networks," *Arxiv preprint arxiv:1511.06434*, 2015.

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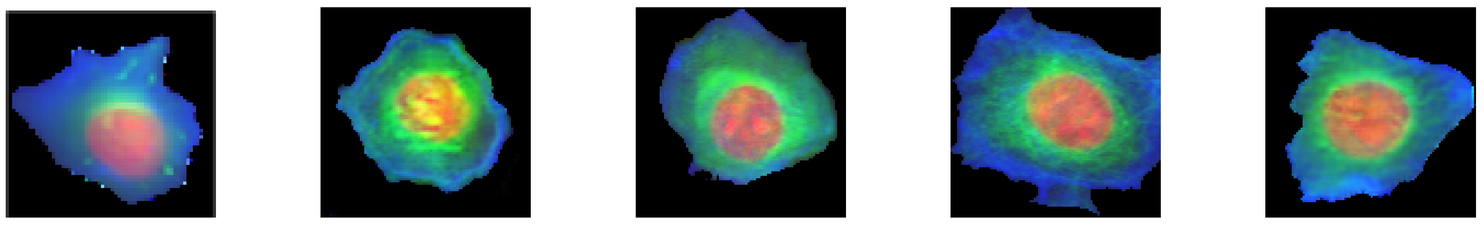
Exploring Biological Phenotypes Using Cell Synthesis

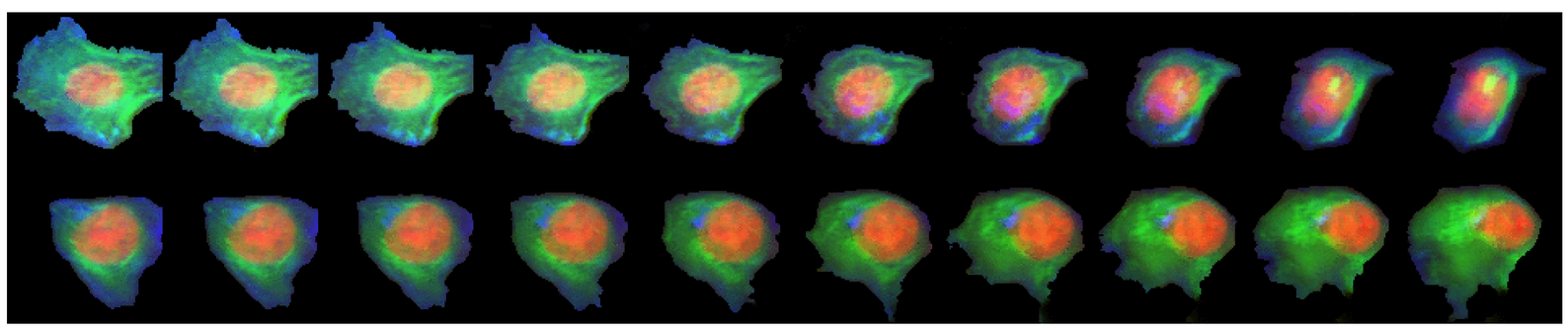
GANs enable us to synthesize cell images and explore variations in the noise and learned latent spaces. This allows biologically meaningful experiments and improves interpretability of our method.



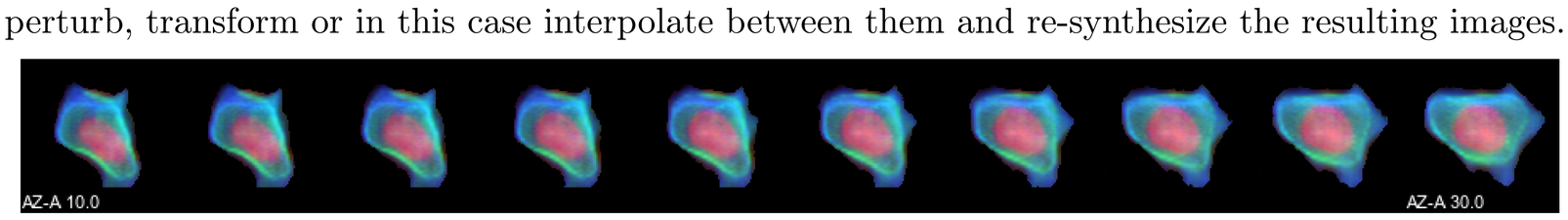
Shown above are cells synthesized with LSGAN, WGAN, BEGAN and BiGAN architectures alongside a real cell. The synthesized images are not only highly detailed and realistic, but also consistent with their biological nature. For example, it is characteristic that β-Tubulin (green channel) forms a circular halo cradling the nucleus. This property is maintained clearly in most generated images.

Interpolating Cell Images in Noise and Latent Space

GANs are known to learn low manifolds of their input priors, such that interpolation between two points $\mathbf{z}_1, \mathbf{z}_2$ drawn from the noise space P_{noise} results in visually smooth transitions in generated images [4]. We confirm that this property holds for microscopy cell images.

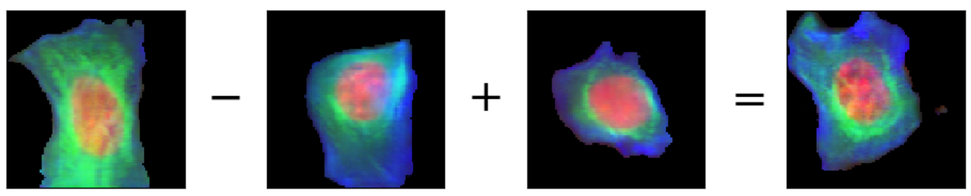


Bidirectional GANs (BiGANs) [2] extend the vanilla DCGAN [4] architecture with an explicit encoder network that enables both synthesis of images from noise *and* inference of latent representations, in such a way that the noise and latent space are fused. This means we can encode real cell images, perturb, transform or in this case interpolate between them and re-synthesize the resulting images.



Vector Algebra for Biological Interpretability

We find that GANs partition the noise space into regions capturing different semantic properties of cells, allowing biologically meaningful algebra on noise vectors.



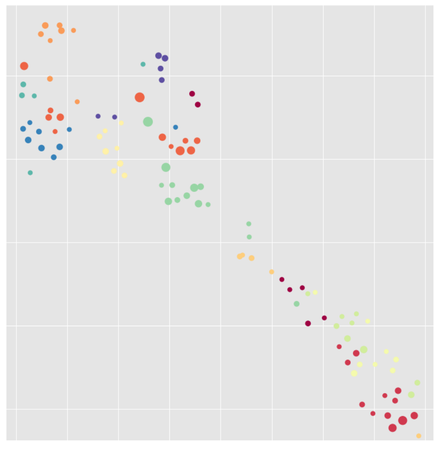
Much β-Tubulin Little β-Tubulin Any Cell More β-Tubulin

When the noise and learned latent space are fused (BiGAN), algebra on real cell images becomes possible. This opens the door to discovery of a whole new class of highly interpretable and biologically valuable relationships, such as:

- $\text{emetine}_{1.0} - \text{emetine}_{0.3} + \text{taxol}_{0.3} \stackrel{?}{=} \text{taxol}_{1.0}$
- $\text{Protein Synthesis} - \text{Protein Degradation} \stackrel{?}{=} \text{DMSO}$
- $\text{Kinase Inhibitor} - \text{DMSO} + \text{DMSO}' \stackrel{?}{=} \text{Kinase Inhibitor}'$

Representation Learning for Morphological Profiling

We investigate the ability of GANs to learn high quality vector representations of cells perturbed with particular drug compounds. We want chemicals with similar effects on cells to have short distances in feature space. We train a variety of GAN models on 1.3 million cell images, average signatures across treatments, and predict the effect of unseen chemicals via nearest-neighbor classification.



Prediction Accuracy

LSGAN	BiGAN	VAE [3]	CP [5]	Transfer Learning [1]
68%/76%†	70%/72%†	49%	90%	91%/96%†

† Whitening Transform