COVID Information Commons (CIC) Research Lightning Talk

Transcript of a Presentation by Ilya Goldberg (ViQi Inc.), October 4, 2022

Title: *Machine Learning for Early Detection of COVID-19 Plaques in Cells*

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Youtube Recording with Slides

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Transcript

Ilya Goldberg:

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Thank you. Is my audio all right? Slides ok?
Thanks. So, this is our work that we did in the training of AI to detect infected cells.

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The NSF made call in 2020 for developing innovative technologies to address the COVID pandemic. Our company, ViQi has a cloud based imaging and analysis platform. And so we have a lot of expertise in developing cell based assays for microscopy and other kinds of imaging, especially using AIs and to deploy this in the cloud so that we have little impact on local storage and equipment and software requirements. The reason - so the basis of the grant was to answer the question: can we detect virus infection in brightfield microscopy images? The reason this is important is that measuring the infectivity of a virus or viral infectivity assay - critical workhorses in the drug development industry - evaluating vaccines, monitoring how vaccinated people respond to variants. They all rely on measuring how infectious particular viruses that's either been treated both in antiviral or with serum from vaccinated individual etc. So they're key [to the] assay and virology field. And if you can do this, using images of brightfield microscopy - brightfield microscopy is very easy to arrange - it plugs in easily into a lot of automation equipment that's already used in a drug industry. So that was the basis for proposing this question that we would answer.

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The reason why we thought we had a good shot at being able to detect these infections is because when people look at infected cells in electron microscopes, which we're looking at here, you see the development of these fairly large structures. The key thing, really, is the size. Because electron microscopes are not a practical instrument for doing an assay, because they're extremely expensive and finicky. But if you can detect things that are large enough, then you should be able to see them in a standard light microscope. And even if you can't really see them and image them, they should have an impact on the images from a regular microscope that you should be able to train an AI to detect. Even if you can't see them, we can see them ourselves.

So all these different viruses have formed these structures when they infect cells. This is important because different viruses have different lifestyles of how their infection proceeds depending on their genome and whether or not they have an envelope. So viruses either come with an RNA genome or a DNA genome, and they either have a membrane envelope or not. And this effect seems to be universal across these different lifestyles.

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So if can we can do this, the benefits would be that we would be looking at a first round of infection in cells, it's a contrast. And with other ways of doing infectivity assays there are fewer processing steps, because we would be doing some large cells. That we would also because the assay is read out by a machine, there will be - it would eliminate person to person variation. We produce quantified numerical results about the assay. And because of the way it's deployed, it would be automated and scalable, which would allow us to more easily plug into the drug discovery industry

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To compare to current assays that are used to measure infectivity, they essentially - all of them - rely on a very long incubation period, because the detection is to detect dead cells. And as those cells accumulate, you count that as a positive infection. In contrast, we're detecting individual infected cells before they die. So number one, the incubation time's, much shorter. And number two, a lot of viruses that are pretty important, they don't actually kill cells. A good example of that is HIV, which produces what's called a latent infection where cells kick out viruses at a certain rate, and they die of natural causes, let's say. So compared to all these different current assays, this would be a much, much faster turnaround time for the results, which of course lets you iterate faster over, let's say, testing new drugs.

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So the way this works is fairly easy to set up we have - because of our experience and automatically training AIs and doing this with relatively small amount of data. You can do this on a common format plate. This is called a microtiter plate. Each well on here contains cells and varying amounts of virus using twofold dilutions. So there are also machines that will image these plates. So it's like a robot microscope that lives in a box, it produces a bunch of images, these get uploaded, and all of this stuff happens automatically in the cloud. There's importantly, there's nothing for the user to adjust in terms of how the

AIs are to be trained. And then the result of that is a report of all this work, which is sent back to the researcher by email.

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So an important thing here about AIs interpreting images is that - so on the left, we can see microscopy image of cells that are uninfected and then much later in infection. And you can see that eventually, in this case, at least, cells begin to die. And you can very obviously see that and that's what most existing infectivity assays rely on. Whereas if you use an AI and you compare in the upper right, on uninfected versus infected cells at two hours, you can see by eye there's not a lot of difference, but the AI that's trained to recognize infected cells can discriminate them fairly accurately. Later on, at eight hours, the accuracy increases, you start to maybe see some effects. In this case, this is influenza - one of the effects it has is it causes cells to fuse. And you might be seeing some events here. The other thing to recognize is that we haven't told the AI what to look for, we just presented with images of infected and uninfected cells and it figured out what the difference between those images is on its own. We don't really know what is looking at. I mean, we can kind of guess or figure that out, sometimes, usually not, actually. So that's kind of how a lot of AIs work, we don't really need to tell them what to look for.

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This is what you get back. It's a auto generated report that explains how the AI training went and what its ultimate accuracy was. But the really important thing is this calibration curve. So the dilutions provided by the researcher is on the x axis here. And then the response of the AI - the response of the AI is on the y axis. And you can see that as you dilute out the virus, eventually, the assay stops working. And that's its detection limit out here. And then at the high end, there's not going to be a lot of difference infecting a cell once or twice or ten times. And so eventually, you will saturate the infection and that's the upper bound of the range of the assay, which is reported to the users - this green bar. So this tells the user the target dilution that they should use in order to get a reliable result from the AI.

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So like I said, different viruses have different lifestyles. Very importantly, dependent on their, what their genome is, and whether or not they have a membrane. We have examples now of every kind of virus, about 10 different viruses, including Corona 229E, which is a cousin of SARS-CoV-2 which causes COVID-19. We haven't actually tried COVID-19. That's a high isolation virus. Those facilities are growing in number, but they're very highly oversubscribed still. But we do have on deck, a couple of collaborators that will collect data on SARS-CoV-2 soon. But there's a lot of other important viruses here that are of interest in for vaccines, drug discovery, etc. And they all work fairly well in our assay.

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So just to summarize, being able to detect infected cells with brightfield lets you have very fast assay that has few processing steps. It's cheap and it has a very fast turnaround. It's objective and it produces numerical results that don't vary from person to person. And it's scalable to automated drug discovery systems that are prevalent in industry. If you're interested in more about ViQior about this assay there's some links down here to contact us or visit our websites.

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Lastly, I'd like to thank our collaborators. We jokingly say that we don't have a lab, we don't even have computers, that everything's in the cloud. So we rely heavily on all of our wonderful collaborators in academia and industry to provide us with the grow cells and infect them provide us with images. Thank you.