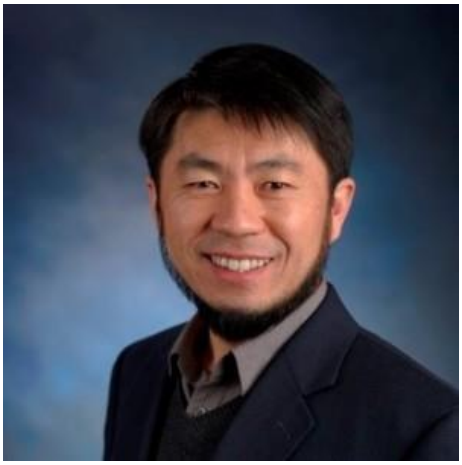
COVID Information Commons (CIC) Research Lightning Talk

Transcript of a Presentation by Gangli Wang (Georgia State University), June 19, 2021



Title: RAPID: Microelectrode Array Sensors for SARS-CoV-2 and Other RNA Viruses

Gangli Wang CIC Database Profile

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YouTube Recording with Slides

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Transcript

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Hello everyone. I want to start by thanking CIC [COVID Information Commons] for offering this amazing platform, you know, for ours from very different fields to share our progress and our research on this common theme motivated by the COVID pandemic. So, this is a product supported by chemistry- NSF [National Science Foundation] Chemistry Chemical Measurement and Imaging.

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So, we are relatively late. We started around June or July to work on this project, because at the beginning I thought the existing tools and PCR-based methods which is a live analysis technology would be more than adequate to offer a good yes or no answer to for this qualitative testing needs. It was not until all the false positive and false negative results being reported of all those tools being used under emergency usage we realize there are fundamental things we can contribute. So, our goal is to develop a measure that can be further developed into a tool that it needs to be highly accurate. In the meanwhile, it needs to be low cost, easy to operate, and offer results quick instead of taking multiple steps and you know from how whatever sample you take, many steps down the road you'd get a readout. We really want to simplify this procedure to speed up the process.

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Researchers have been working on developing better tools for analysis basically, non-stop way before this pandemic hit us. There are fundamental reasons why these are very- such a challenging task. For this specific project, the utmost sensitivity we want to, we need, or we can achieve we'll be detecting a single virus. And we really want the detection to be specific. The more specific to the virus would be the genetic material, in this case is RNA sequences, specific to the virus. Right, so fundamentally there are problems to achieve this kind of a goal. One is the signals associated with single molecules. They are generally very very very weak and because every measurement there is noise associated with it, it can be random noise meaning there's nothing we can control of and there can be sampling errors especially when handling the samples with very low quantity of the target. Of course, there will be human mistakes and more or less, it is going to occur especially when you handle the sample multiple times, like what happens down here. So, to avoid and to overcome the signal to noise limitations all the [inaudible] currently adopted tools are almost exclusively based on sample amplification. These include lab tools like PCR and almost all the fast testing tools that I'm aware of. Right, so you just need it to amplify- grow the signal sample more so that the signal is strong enough to be measured. So, what we decided to do, is we want to tackle the problem from another angle is called signal amplification. So instead of grow this samples, we try to improve or amplify the signal.

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So, this is the core of the method or concept. Hopefully my explanation makes sense. So, you look at this faucet and remember water flows through when you switch this one on. So that's the principle we operated we designed this tool. What you are seeing is down here is an electrode. We can read a signal out and there are DNA aptamers in here, folded in a way that this molecule is far away from the electrode so there's no signal. You do not see a signal. Now in this loop structure, there's a segment that is the imperfect complementary to the specific RNA sequences, and in this case the SARS COV-2. Right so when this viral RNA is present in the sample is going to bind to this thermodynamically favorable and then it's going to unfold it so that you know after the unfolding, this molecule is going to be close enough to the electrosurface that turns the signal on. So, this is a principle that has been used for many years and here has a credit to the earlier work, but the signal associated with the single probe is not strong enough for us to read the signal out directly. And if you only have one, or a handful of variety in that, that's just not going to give you enough signal. So, our contribution is to introduce this redux cycling mechanism. It's basically when this molecule is undergoing electron transfer reactions, in the meantime, there's some secondary reaction going on in the solution so you can turn this molecule back so that this molecule works as a tunnel or mediator. So, it allows the signal to go from all of this here just through here. It's almost like you are using the wearer [inaudible] as a handle to switch the signal on and then water flow and that gives you the signal.

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And in case you are interested, here are how the- what the data looks like. I'm going to skip all the details on how to read them and understand them exactly from the earlier work when we work on

micro nAs. So, these are published. Basically, you see a quantum correlation from the matter signal to the sample of target concentrations. In different zones, there are different correlation profiles that allows you to do a quantitation. And here are the results we have so far. We already pushed the detection limit down to atom molar this is 10 to -18 and that translates into a few thousand molecules in a few minutes and then, remember, we amplify the signal directly so this is a one-step detection exactly directly read the signal out down to this level. And there are rooms to improve. We are actually having some success to push it down to zeta molar concentration range or we are seeing signals from tens of hundreds of molecules in tens of minutes. Okay, so that's being wrapped up and hopefully we will be ready to report that soon.

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This is a fundamental product that generally takes many years to develop. Although this one year project is approaching an end, we surely will continue to work on this direction because the method and this technology can be quite versatile to tackle other type of hardware errors or micro RNAs. So currently, we are trying to improve the results through modern simulation, and experimentally we need to establish parameters to work on to be ready for to tackle real life samples. And this is a prototype device we made in-house. Obviously, we cannot make a million of them and so we need to- or someone need to figure out the engineering aspect for mass production. But at least the benchmark number you saw in the last page, I would say that's pretty impressive. That's way beyond my initial expectations. So, these are not trivial and the very technical challenging products. I need to give credit to my team and my collaborator Dr. Kumar, and this is Jonathan he is a Ph.D. with me. Currently, he's working as a postdoc and Sarah just started. She'll be working on some modeling and simulations and the Meijun worked on this project at the beginning and then he took an offer that she could not resist. Again, I want to thank NSF Chemical Environment Imaging for the support of this product and thank you for your attention.