SAND2022-14546C

Sandia National Laboratories

Rapid Detection of Viruses via Metal Organic Frameworks (MOFs)

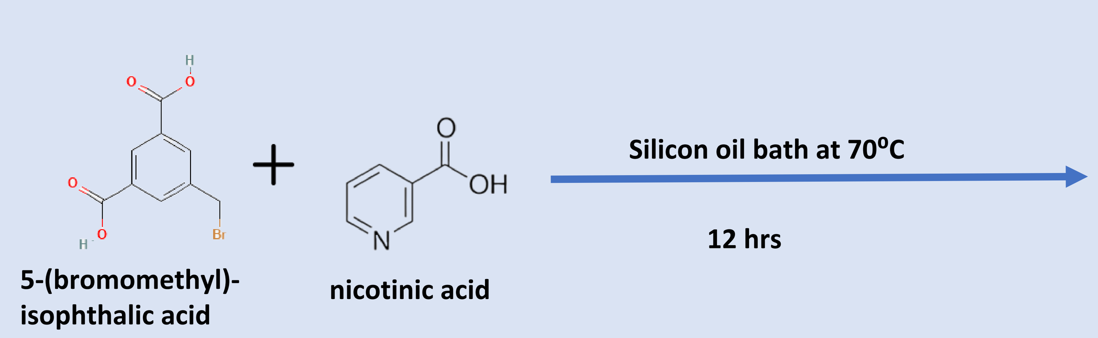
Elizabeth M. Zapien,, Elizabeth A. Nail, Andreana M. Nourie, Leah N. Appelhans*, Kimberly S. Butler* Sandia National Laboratories, Albuquerque, NM

*lappelh@sandia.gov
*kimbutl@sandia.gov

Synthesis of MOFs

Metal Organic Frameworks (MOFs) are crystalline porous materials that consist of positively charged metal ions surrounded by organic linker molecules. They have been of interest to many as they have unique properties such as a uniform pore structure. MOFs have also been used for a wide range of applications including sensing. We wanted to investigate if MOFs could be used for Viral Detection Platforms. We synthesized a variety of different MOFs using different methods such as heating in an oven or microwave, or performing the reaction at room temperature.

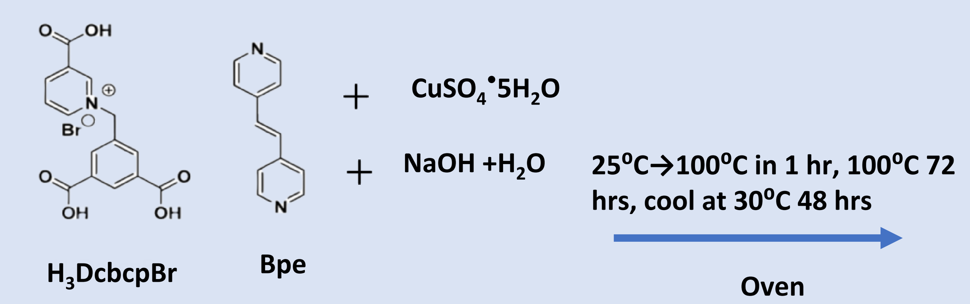
Synthesis of ligand N-(4-carboxybenzyl) -(3,5-dicarboxyl) pyridinium bromide ($H_3DcbcpBr$)



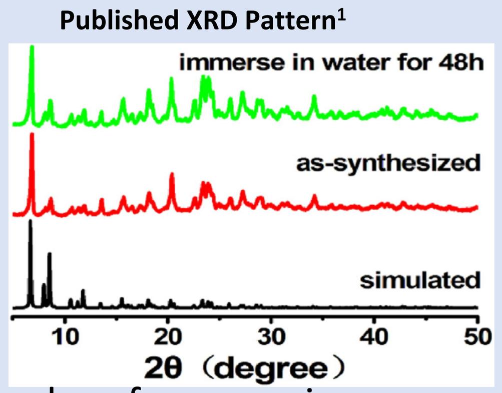
$H_3DcbcpBr$ Synthesis Methods

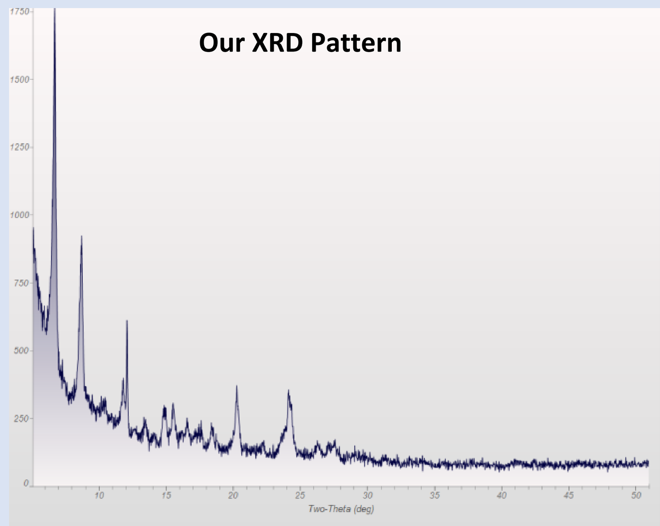
Run	Method	Yield
1	Stir overnight @RT	0.0 mg
2	Stir @ RT for 1 hr, leave out for 24 hrs	0.0 mg
3	Microwave @70°C 10 mins	0.06 mg
4	Microwave @ 70°C for 2 hrs	193 mg
5	Microwave @ 70°C for 2 hrs., rest, +6 hrs.	130.9 mg
6	Silicon oil bath @ 70°C overnight	168.9 mg
7	Silicon oil bath @ 70°C overnight	224.0 mg

Synthesis of copper 1,2-bis(4-pyridyl) ethylene MOF using ramped heating



Published XRD Pattern[1]

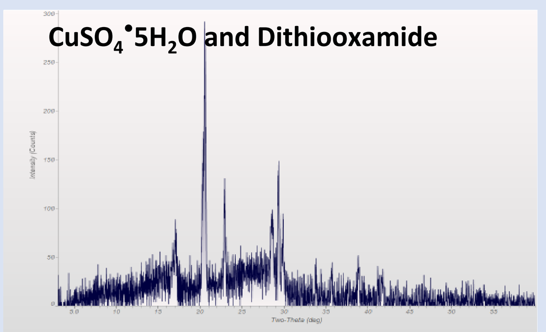




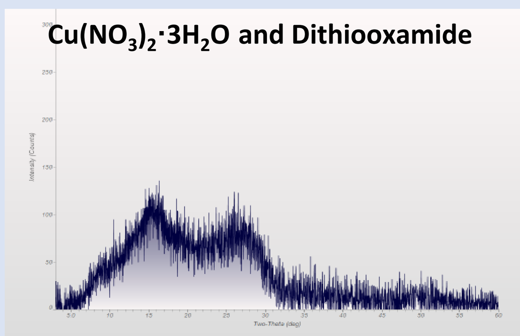
The sharp peaks in the graph indicate that crystalline product was formed

We discovered that following the ramped heating procedure from previous research[1] gives us the highest yield of crystalline product. Our sample's XRD pattern looks very similar to that of the published sample. We can conclude we obtained the targeted crystalline Cu MOF.

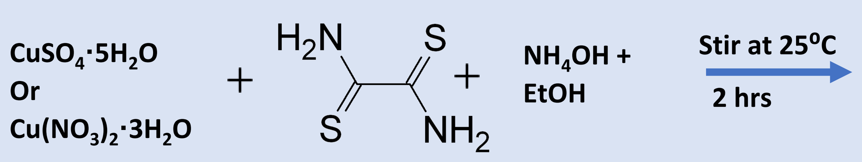
Synthesis of Copper and Dithiooxamide at Room Temperature



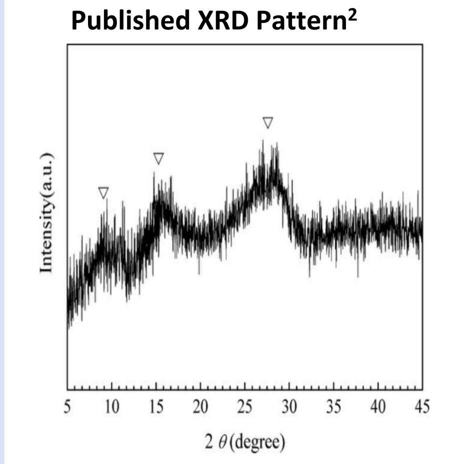
Crystalline XRD



Amorphous XRD

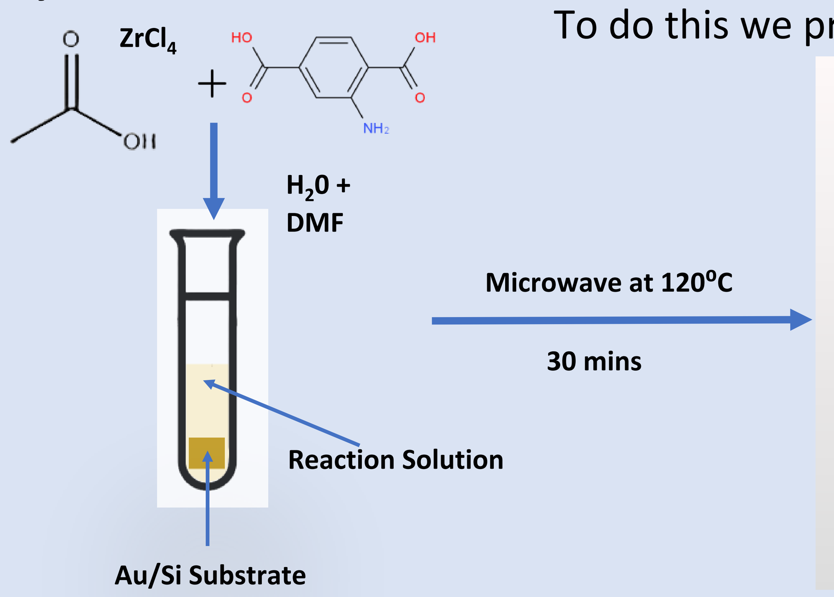


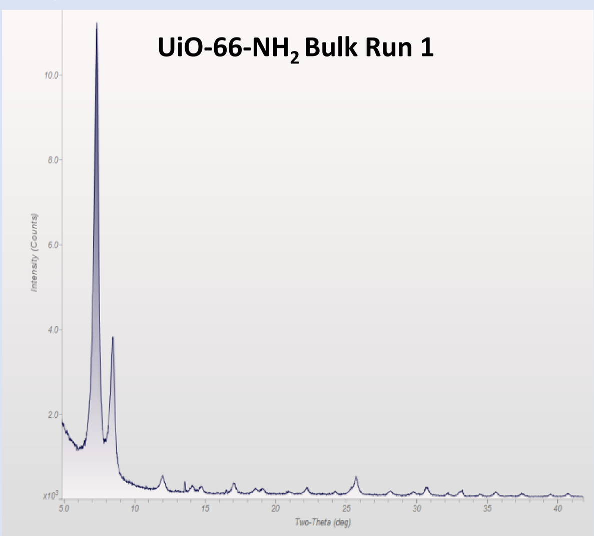
Published XRD Pattern[2]

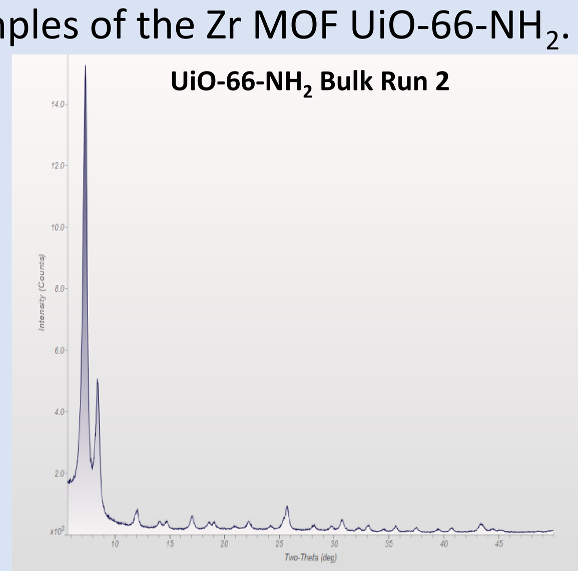


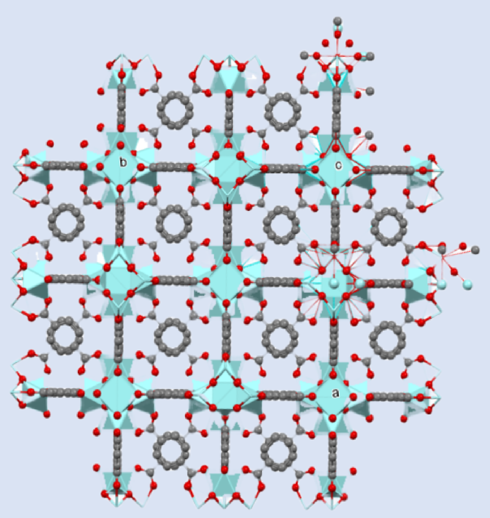
This synthesis yielded a crystalline and amorphous product. We followed an experiment from previous research[3] and performed this synthesis at room temperature while stirring. Black precipitate formed and that is what we collected as our product. The difference between the 2 samples is the type of copper that was used.

Synthesis of UiO-66-NH2: We also want to compare the performance of thin film MOFs with bulk MOFs for virus detection. To do this we prepared both thin film and bulk samples of the Zr MOF UiO-66-NH_2.







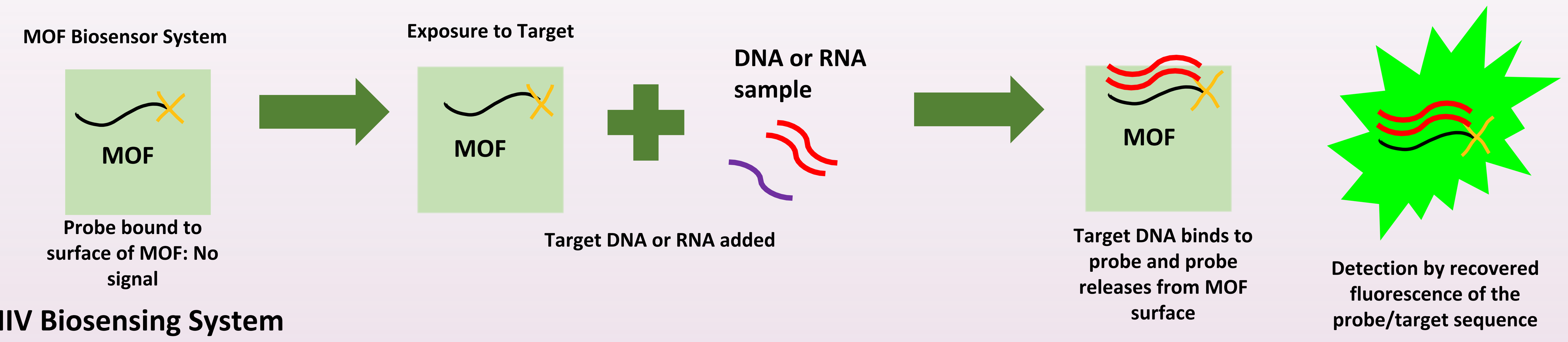


This reaction synthesized zirconium and 2-aminoterephthalic acid. The synthesis of UiO-66-NH_2 yields two products, a thin film and the bulk product.[4] A substrate consisting of a silicon substrate with a gold coating is placed in the vial and a thin film of UiO-66-NH_2 forms on the substrate. The bulk product is formed in a microwave vial along with the thin film. We set the temperature for 120°C for 30 mins and the synthesis is run in the microwave.

RESULTS: We were able to synthesize our MOFs and successfully generate an XRD pattern for each MOF. The sharp peaks on the graph indicate that that the copper and bpe, one copper dithiooxamide, and MOF UiO-66-NH_2 MOFs are crystalline. The other copper dithiooxamide MOF is amorphous.

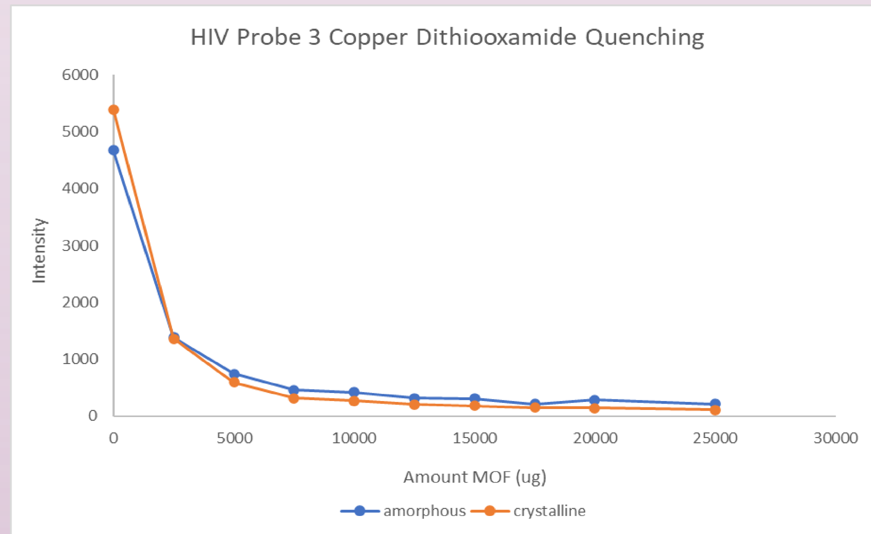
MOFs as a Viral Detection Platform

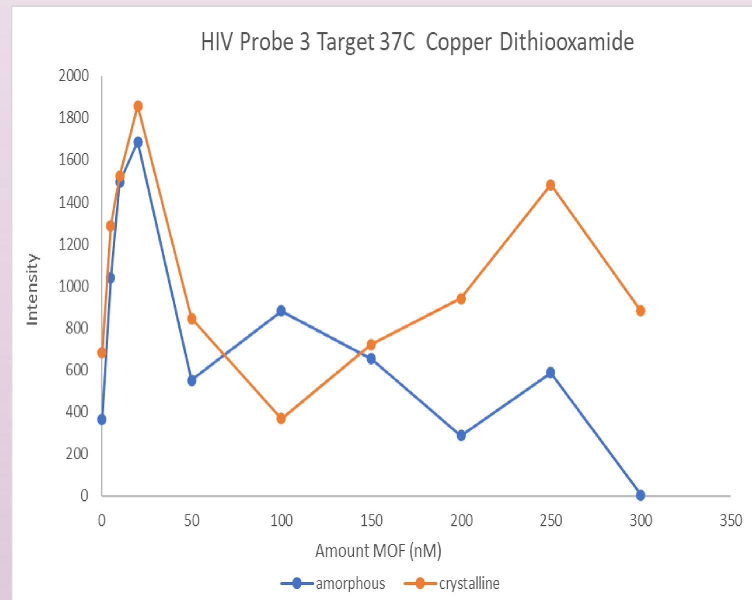
In this study, we tested to see if rapid, accurate viral detection was possible by using MOFs as a detection platform. The MOF biosensor system consists of a fluorescent DNA probe, which is sequence specific to the virus we want to detect. The MOF quenches the probe fluorescence and when the system is exposed to the virus, the probe preferentially binds to the DNA and will be released from the MOF which causes the fluorescence to be recovered. We are also investigating if the MOF needs to be crystalline or amorphous for the biosensor to be able to function.



HIV Biosensing System

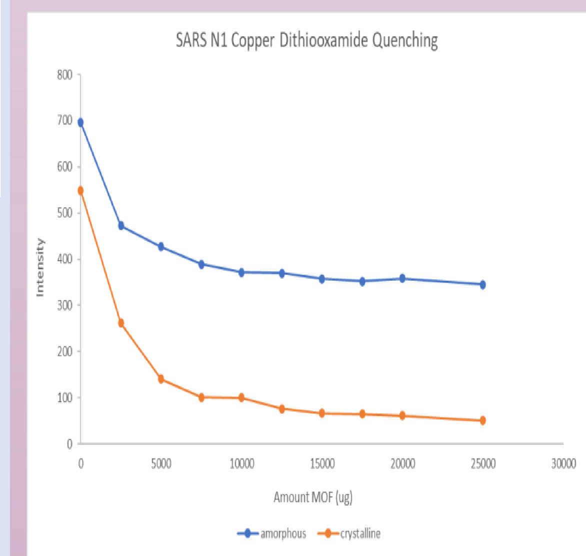
We tested both the quenching efficiency and fluorescence recovery using copper dithiooxamide as the MOF sensing platform and an HIV-virus specific sequence the target. Increasing amounts of MOF are added to different samples to determine the amount of MOF necessary to quench the probe. We then add the target virus-specific DNA sequence to look at the recovery of the fluorescence.

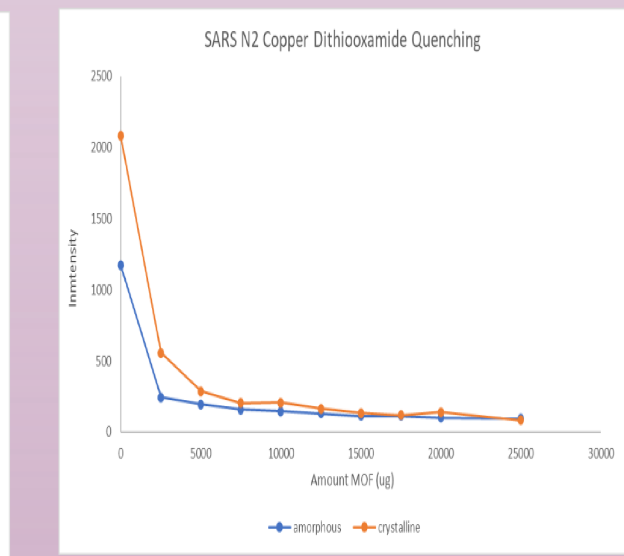


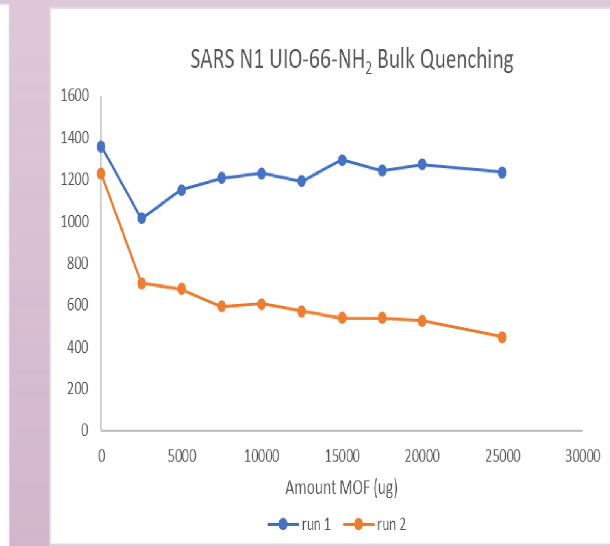


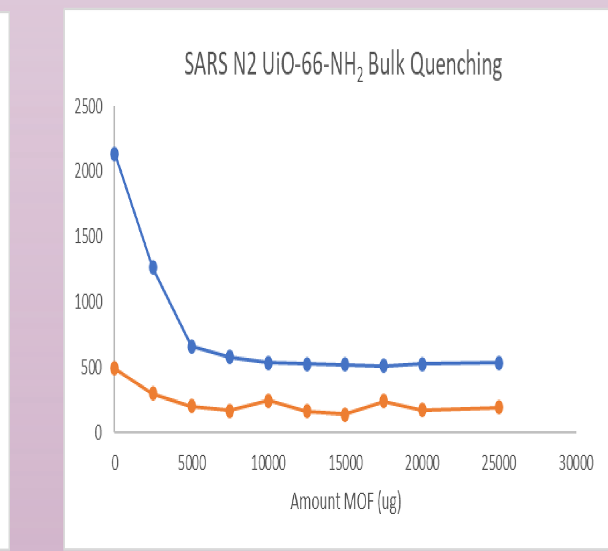
RESULTS: the copper dithiooxamide MOFs successfully quenched the HIV probe. There is not much difference in the quenching efficiency between the crystalline and amorphous sample. When adding the target viral sequence we found that crystalline more efficient at fluorescence recovery.

SARS N1 and SARS N2 Biosensing System









We investigated the use of the copper dithiooxamide and UiO-66-NH_2 MOFs for SARS probes. We found that the crystalline copper dithiooxamide MOF was more effective at quenching SARS N1 probe than the amorphous sample. While quenching still occurs in the amorphous sample it is not as efficient as the crystalline sample. While looking at SARS N2 probe the quenching efficiency was similar between both crystalline and amorphous samples. We next tested the UiO-66-NH_2 MOFs on both SARS probes. Run 1 and run 2 are composed of the same materials, and have very similar XRD patterns, but we see run 1 being more effective in quenching SARS N1 and SARS N2 probes. We are not sure why there is a difference between the samples, but that is something that we will continue to study with future experiments.

Conclusions and Future Work

Our goal was to synthesize a MOF that can be used as a biosensing platform. We tested a few different MOFs and tested to see if we need a highly crystalline MOF for the biosensing system to be successful. The crystalline MOF does perform significantly better for some probes. Future work includes more testing of the copper dithiooxamide MOFs and well as the UiO-66-NH_2 MOFs to determine reproducibility with both quenching and fluorescence recovery with each MOF and viral sequence pair. We will also develop a protocol to test the thin film UiO-66-NH_2 MOFs. Finally, additional future work includes synthesizing additional different MOFs and then testing them to see if they can be used as a detection platform. The use of additional virus-specific sequences is also included.

Sandia National Laboratories is a multimission laboratory managed and operated by National Technology &Engineering Solutions of Sandia, LLC, a wholly owned subsidiary of Honeywell International Inc., for the U.S. Department of Energy's National Nuclear Security Administration under contract DE-NA0003525.
SAND No. ___________

(1) J.-X. Chen, B.-P. Xie, P.-P. Hu, Z. Liang, Y.-M. Laing, B. Sun, L.-P. Bai, Z.-H. Jiang,. *Sensors and Actuators B 254 (2018) 1133–1140*
(2) X. Li, L. Zheng, L. Huang, O. Zheng, Z. Lin, L. Guo, B. Qui, G. Chen, J. Appl. Polym. Sci., 129: 2857-2864
(3) R. Guatam, S. Banerjee, M. Sanroman, M. Chattopadhyaya, Journal of Environmental Chemical Engineering 5 (2017) 328–340
(4) L. Appelhans, L. Hughes, B. McKenzie, M. Rodriguez, J. Griego, J. Briscoe, M. Moorman, E. Frederick, J. Wright., *Microporous and Mesoporous Materials 323 (2021) 111133*