Automating Workflows in *Stanford's Brain Stimulation Lab*

At Stanford Medicine's Brain Stimulation Lab, researchers are working toward solutions for a problem that affects 5 percent of adults around the world—depression. As the number of people living with this condition grows, so too does the number of people whose depression is classified as "treatment resistant"—that is, it does not respond to traditional pharmacology options.

A potential recourse for these patients is brain stimulation—a therapy that involves activating or inhibiting the brain directly with electromagnetic fields. Brain stimulation has shown promise for treating some neuropsychiatric disorders that do not respond to traditional treatments. At Stanford, researchers are studying the use of Repetitive Transcranial Magnetic Stimulation (rTMS), which uses magnetic induction to direct targeted electrical stimulation to a specific brain region.

The Stanford team is looking for ways to improve this promising treatment, which is already approved by the FDA for treatment of depression, OCD, smoking, and migraines. One potential improvement being studied is a personalized TMS approach pioneered by Nolan Williams, MD, and his team at the School of Medicine—Stanford Neuromodulation Therapy (SNT).

Dr. Azeezat Azeez, a postdoctoral scholar with Stanford Psychiatry and Behavioral Sciences, is one of the researchers collaborating with Dr. Williams. As Dr. Azeez explains the process, SNT delivers an accelerated high-dose intermittent theta-burst stimulation (iTBS) treatment over the course of five days. The team plans the treatment by first capturing a baseline Resting State Functional Magnetic Resonance Imaging Scan (rs-fMRI), then selecting the optimal target in the patient's brain using a proprietary algorithm. After the

care team reviews and validates a patient's personalized target, they begin the five-day treatment course.

"As you can imagine, it is quite a labor-intensive process from start to finish," says Dr. Azeez. "We really want to make sure that every subject is getting the best personalized target that we can generate for them."

For many patients, the team's care and rigor are paying off—results published in 2020 showed a remission rate of 78.5% among subjects in the four weeks following treatment. With this promising foundation, the Stanford team's work is growing, and so is their need for smart data management.

"As we're growing, we're realizing that if we're going to do this sort of process for each subject, we have to scale up," says Dr. Azeez. "We're getting new grants. We have multi-site collaborations across the nation, and it's requiring a lot more patient data to be input. This is where the Flywheel platform comes in, because at the end of the day, there is a human being at the end of this pipeline and we want to provide them the best possible treatment that we can."

A Need to Move Beyond *"Skimming the Surface"*

Dr. Azeez was well positioned at Stanford—the birthplace of Flywheel—to scale up her research. The lab collaborates with the Stanford Center for Cognitive and Neurobiological Imaging (CNI) to obtain its scans, and Flywheel was already in use to help manage the data flowing from the 3T scanner at the CNI to researchers within the university.

But in the case of the Brain Stimulation Lab, "we were formerly just skimming the surface" in applying Flywheel, according to Dr. Azeez. The lab originally used the platform to store raw and reconstructed data and applied its basic tools for reconstruction and quality control. But when they wanted to perform analysis, researchers were still downloading data to a static lab PC.

With this process, it typically took the team days following a patient's baseline MRI to begin delivering treatment. The process also demanded significant time from lab staff, and made it difficult to track data provenance.

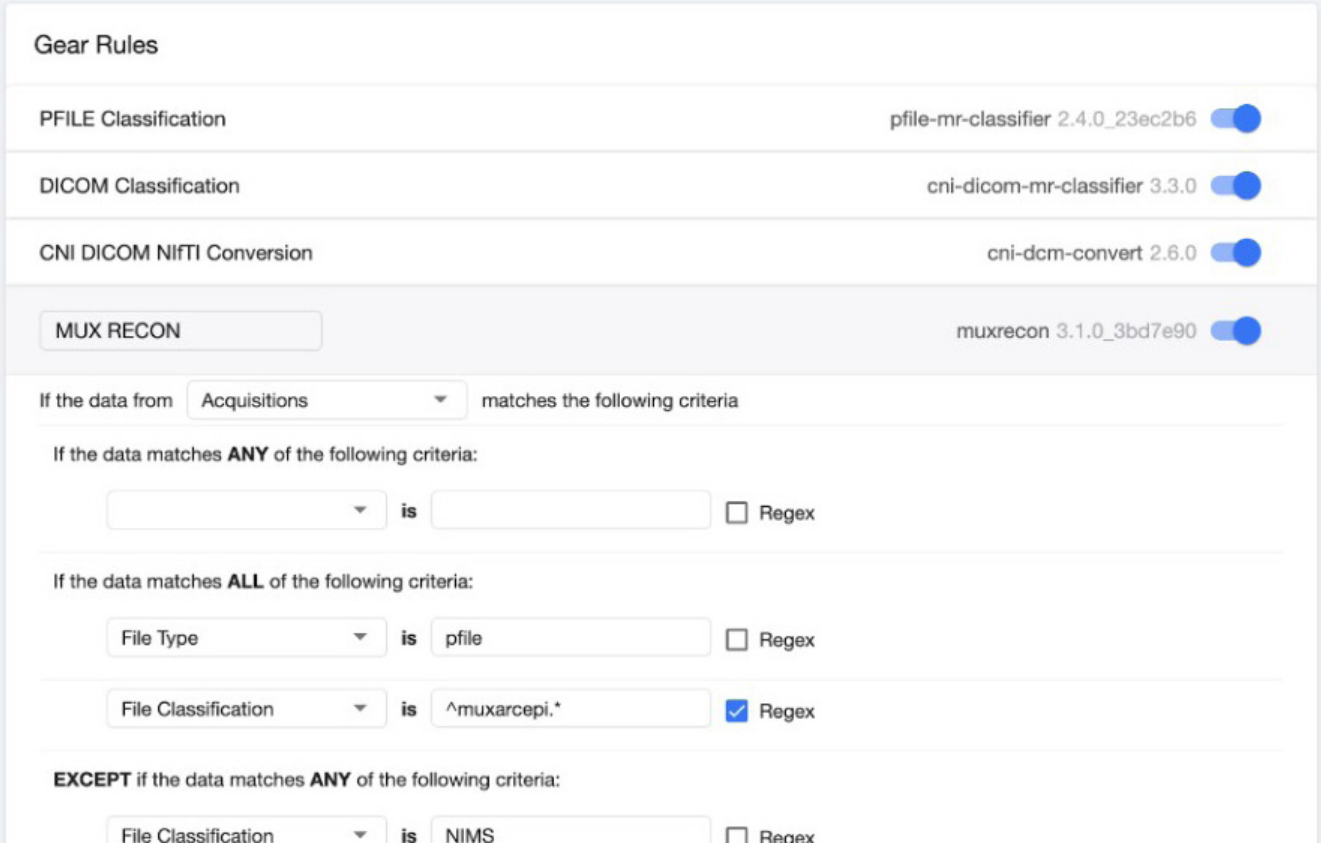
Scaling Up with *Flywheel Gears*

As part of her initiative to improve the lab's workflow, Dr. Azeez began leveraging more of Flywheel's capabilities. Most importantly, she dedicated time to building custom Flywheel Gears—containerized algorithms that are run and managed within the platform. Flywheel provides an ever-expanding library of ready-to-use Gears, for everything from routine data processing tasks like metadata extraction and classification, to more complicated processes like independent component analysis and structural segmentation. Users also have the ability to develop their own custom Gears, which they can choose to keep private within their institution, or publish to share with the larger Flywheel user community.

Gears give Flywheel users a number of benefits:

- Gears have mandatory versioning & image persistence, which assist in reproducibility
- Provenance is streamlined with automated capture of inputs, configuration parameters, logs, and outputs
- Execution of Gears can be automated via rules
- Computation with Gears is configurable and cloud-scalable, which allows for massive parallelization to meet time critical workflow demands

This screenshot shows an example of rule-based execution of Gears within Flywheel



By better utilizing existing Flywheel Gears and developing her own, Dr. Azeez and her collaborators have been able to dramatically streamline their workflows. Flywheel also provides an SDK (software development kit) library, a powerful suite of tools and utilities that allows users to programmatically interface with the platform. Using these tools, Dr. Azeez has daisy-chained Gears together so that once a patient's baseline scan is received, the platform automatically runs Gears in sequence for reconstruction, quality control, fMRIprep pre-processing, and the lab's custom targeting algorithm.

Having now created two custom Gears, Dr. Azeez says the process is, "really just packaging what you've already written on your local computer into scripts with a few additional files." In her questions during the process, she relied on IT support from Flywheel's Scientific Solutions team, "who I've been really grateful for," she says. "The Flywheel team is really good at answering whatever questions we have and making sure that the Gears function the way they're supposed to."

"It gives us the ability to be really smart with our time."

Andrew Geoly, a research analyst at the Brain Stimulation Lab, works closely with Dr. Azeez

"The Gears are all daisy-chained really easily from the SDK," says Geoly. "I can run them and go and do something else while they're running. That's really, really convenient and it frees up a lot of time."

and has seen the benefit of the new workflow. Describing a typical process for a patient of the lab, Geoly notes that within an hour or two of the patient's scan, Flywheel has enabled full reconstruction, quality assurance, and BIDS (Brain Imaging Data Structure) curation. The data then continues an automated workflow over the next several hours, with Gears running back-to-back for additional pre-processing and TMS targeting. The targets are then reviewed and finalized by a committee of clinical and data team members. "The Gears are all daisy-chained really easily from the SDK," says Geoly. "I can run them and go and do something else while they're running. That's really, really convenient and it frees up a lot of time."

The new process is enabling the lab to complete its pre-treatment work in under two days, while simultaneously collecting important data to calibrate the stimulation level and position of the TMS coil for each patient. For inpatient studies that require an expedited process, the lab can accelerate its prep work to

under 12 hours.

"A patient can be at the hospital; they can get scanned in the afternoon, and the target is ready for them the next morning," says Geoly.

Summarizing how Flywheel has impacted the lab, Geoly says, "We're able to improve our efficiency, and this gives us the ability to be really smart with our time. We can run multiple targets simultaneously; we can multitask and have different teams working with the data all at the same time; and we're able to do something with our targeting algorithm that is fairly new—we can run iterative processes of it that allow us to have a more advanced target for treatment."

Dr. Azeez enthusiastically agrees with Geoly on the importance of freeing up staff time, noting, "We are working in a lab where we have loads of intelligent people. So if we can save human resources, that's always a plus."

Expanding Research to *Provide the Best Care*

To date, the team's work has been published in high-impact journals and has even attracted mainstream media attention from outlets like CBS and NPR. Looking to the future, Dr. Azeez foresees more randomized control clinical trials; incorporating more data such as ASL, DTI, EEG and HRV; new collaborations across institutions; and varying analytical techniques—all of which will require a data platform that can power the team's increasingly sophisticated work.

"Again, these are folks with treatment-resistant depression; the traditional approaches have already failed them. So it is imperative for us to provide them the best possible treatment that we can," says Dr. Azeez. "The Flywheel platform allows us to accelerate this clinical research and free up a lot of time so that we can meet our goal of providing the best possible care to these patients."

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Stanford Brain Stimulation Lab:
Before and After Leveraging Flywheel

	Pre-Flywheel (manual)	Flywheel (semi-automated)
Time to Deliver Treatment	Estimated: 1-2 days	8-12 hrs
Computational Resource	Static Lab PC	On-demand cloud scaling with custom configured resources
Quality Assurance	Yes	Yes: Standardized, configurable workflow
Standardized Scripts	Yes	Yes: Tested, validated, versioned, and implemented as Flywheel Gears
Data Provenance	N/A	Yes: Flywheel logs + analysis tracking = reproducibility
Human Resources	Time-consuming	Visual inspection, Initiating Gears with Python SDK

*Visit **flywheel.io** for more on how Flywheel is enabling research in high gear.*