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Process Intensification: PAT, AI, ML to Support Intensified Bioprocessing

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ABOUT

Arthi Narayanan is Senior Leader Innovation, Pharma Technical Operation at Roche-Genentech USA. Arthi and John Bonham-Carter, Vice President of Business Development and Product Management of Erbi Biosystems discuss how artificial intelligence (Ai) and machine learning (ML) can improve efficiencies in bioprocessing.

**Arthi Narayanan,
Senior Leader Innovation,
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**John Bonham-Carter, VP Business Development and Product Management,
Erbi Biosystems (now part of MilliporeSigma)**

John Bonham-Carter: I'm very happy to be here with Arthi Narayanan, an innovation leader at Genentech. We're going to be talking about PAT, artificial intelligence, machine learning in bio processing to intensify processes. To level set where we are, what has happened in the last 20 years? Can you give a status of these technologies?

Arthi Narayanan: Artificial intelligence, machine learning, and modeling are all different tools. In the biopharma industry, we're still barely scratching the surface in terms of maturation. It is far ahead in enterprise learning, as well as the hospital industry. So, it's a novel technology that we can use as a predictive tool and that's why it falls under the PAT realm.

JBC: We may be a little late to the party, but what is the eventual goal? What kind of outcomes are you expecting in the next five, or 10 years?

AN: Maybe we should just take a step back and establish some common context, but you have to dream big. We gravitated from small molecules into antibody production—somebody dreamed big. Now, in the field of PAT, we've come a long way from having manual counting. We proceeded to using offline instruments and

then online sensors. Over the last the 20 to 30 years now we built a lot of data. Data is your goldmine.

Now that we have so many molecules in the pipeline, and we have rich data generated by development and manufacturing sites, this is the time you start investigating these novel technologies, to see if you can use all these data to build models and predict the future.

The current state is you have pilot plants where you run studies for tech transfer, but can we get to a zero-study tech transfer? Building, maintaining, and sustaining these models will take a lot of infrastructure. The end goal is to build these predictive models. But how do you get there? We need a roadmap.

JBC: Do you think these models will be predictive enough that you can get to a real-time release, or use it in some closed-loop automation? Is that the near term, or still far away?

AN: I think that is near term. It's not your moonshot. If you have a robust model that can do a good job predicting your product quality attributes, or your key process parameters, and key process indicators, then real-time release is not too far out there.

JBC: When is the right time to start implementing AI? Is it right at discovery? Is it early stage, or is it really when you have a pile of data from Phase III and later that you can properly leverage?

AN: Right now, we are in the proof-of-concept stage. So where would I want to invest? I say put it in the manufacturing environment, because that's where you have the power of data. In development, you're still talking about batches that you can count on your fingers, as opposed to sitting on thousands of batches of data. I think to go from the proof-of-concept to the pilot stage and to build confidence in the robustness of these models and their consistency, you have to ask: How can I predict across molecules? Can I predict across sites? There's a lot of questions that we need to answer.

JBC: So you think you can build that model of manufacturing and develop your process? You know how it is going to fit to shorten tech transfer?

AN: Correct. If you have N number of days that it takes you right now for tech transfer, can you cut that by half or cut it by one-third by developing these predictive models? You won't have to do studies, just model-based tech transfer.

JBC: You will still have humans involved in this process. How do you train them and get them to trust and accept this technology?

AN: It's not easy. It takes a shift in the mindset because you now have to start thinking differently in terms of the talent that you're hiring. In the past, if you had your lab full of technicians and technical specialists. Now you need people that can build models, who understand programming, and understand the nuances of machine learning and deep learning. That industry is rapidly evolving. The model that I used three months

ago, has now become something else. The biggest scouting we're doing is where is the model that can get us the best accuracy with minimum data? We're not gathering data from millions. We do have thousands of batches, but can we have a more powerful model with less data?

JBC: You are talking about people who were historically biologists in these roles and now you need people who are more mathematical who may lack that biological capacity. How do you go about integrating these two teams?

AN: You're right. We do need a good mix of people that have process knowledge, as well as those modeling skills. I'm happy to see that schools are offering majors where you can do chemical engineering, data science, computer science with a bioinformatics as minors so they can have a balance of both. In the meantime, we will have to manage it through our workforce, to have a good hybrid of programmers and traditional chemical engineers, so that one can teach the other.

JBC: Why is it that suppliers don't exist here that can come with an off the shelf model, say I built a digital twin, or I built an intensification strategy for your tech transfer. Or is there a reason these suppliers won't exist?

AN: I think they're starting to exist, but we'll have to give it some time. Part of the problem is the suppliers don't know what the end user wants. These small companies in AI and ML don't quite understand our business. I think it's a two-way street. As much as we want to gather their expertise, it's also a matter of teaching them what we're looking for.

JBC: You said earlier that data is the goldmine. But how will it work if you're involving suppliers, where they need to get into that data to start building and validating these models? Is that required? Are you going to get their tools off the shelf, or will you have to open up to the supplier and share the data?

AN: We have confidentiality disclosure agreements that we can sign with suppliers, and we can definitely get them to start building models with our data. There are ways to protect data. I'm not saying we will completely outsource—that's where I use the terminology of buy, build, and borrow. In the short term, you leverage external vendors or smaller companies to build models for you. Development and manufacturing is biopharma's bread and butter, and the end goal should be to integrate the AI/ML into our bread and butter as well.

JBC: We spoke about tech transfer in manufacturing, but what do regulators think about this? What transparency do they need to feel confident with this and how do you go about interacting with them to make this a reality?

AN: Again, this is a process of evolution. Thirty years ago, when we launched our antibodies, we were counting cells manually. Now, you have inline Raman probes and regulatory agencies are also evolving with these technologies. With AI/ML it's about us proving the robustness of this technology, to show that these models are promising, they are accurate, and they have good specificity. I don't see why they will not accept it. But there's work to be done.

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This case study was presented at Evaluating Biopharma's Process Intensification: Improving the Process Status Quo virtual networking and educational event which included two additional presentations and two interactive networking sessions.

Details of future events can be found here.

You can watch Arthi 's presentation in full and on-demand here.

Process Intensification:
Improving the Process Status Quo

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Moderator:
John Bonham-Carter, VP Business Development and Product Management,
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ABOUT EVALUATING BIOPHARMA

Evaluating Biopharma is a convener of knowledge, data, and industry leaders within the biopharma and bioprocessing industries. Built upon the foundation of BioPlan Associates decades of data collection and analysis, Evaluating Biopharma brings together top industry experts, innovators, decision-makers, and leading providers so that together they can share, evaluate and discuss critical topics that will help biopharma and bioprocessing leaders advance life sciences.

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