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### The Razor's Edge

June 24, 2014

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*“The power of high throughput quantitative biology is taking biology from a very slow manual process and bringing it into what I consider to be a real science, a real engineering practice, by allowing you to work with things that are digital.”*

TODD HUFFMAN

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#### SPEAKERS

- + **Ryan Bethencourt**  
CEO and Co-founder, Berkeley Biolabs  
Program Director and Venture Partner, Indie.Bio
- + **Stewart Brand**  
Co-founder, Global Business Network  
President, The Long Now Foundation

In this video, Todd Huffman of 3Scan explores how knife-edge scanning helps drive biodiscovery.

#### SPEAKER

**Todd Huffman**  
Chief Executive Officer, 3Scan

**Kirkpatrick:** Todd Huffman is the CEO of a company called 3Scan that has a very interesting technology that's being applied in biodiscovery, so we're going to give him a chance to tell us about it.

**Huffman:** Thank you. And actually, before I start, I want to thank Lindy and Breakout Labs. They were our first money in and I can tell you that if you're starting a bio company, you should absolutely talk to them, because it's the best deal you'll ever get and it's the most help you'll ever get. The stuff that I'm showing you wouldn't be possible without her.

My company is called 3Scan and we're an automation and information company and we focus in on tissues. Now most of the time when you hear about bioinformatics, people are talking about DNA, RNA, proteins. Well, as you move up through the scales, there are some things that really can't be reduced down to that level—so things like cancer, Alzheimer's disease. As we get into the 3D printing of tissues and organs, you're going to need tissue-scale digitization, automation.

Now things are currently done—when you're looking at tissues—they're done by pathologists. And so that's my favorite pathologist over there in black and white, Ramón y Cajal, in 1887, in his lab and this is a modern pathologist I pulled off Google image search. You'll notice that they're sitting in the exact same position relative to the microscope. The workflow really hasn't changed since the 1880s. So what we've done at 3Scan, we've taken the microscopy workflow, where you start with a tissue block, you



slice it up, you put it onto a piece of glass, you put it into a microscope, you look through the microscope—we've taken that process and we've automated it.

Now in the span of five minutes, I can't really get into a satisfactory technical description but if you're a microscopist, we've taken the microtome and the microscope, we've put them into one robot. We're imaging continuously while we slice. For those of you who aren't microscopists, the thing that allows us to do, is instead of doing twelve slices an hour, that a human can do, we're doing 3,600 slices an hour, because we remove all the human hands from that process.

And so that speedup of orders of magnitude allows us to think about microscopy in a very different way. So if you get cancer, the pathologist who examines it will look at a half-dozen slices. And they'll be looking at them in two dimensions and they'll be making qualitative decisions on what they see.

This is the microvasculature in a mouse brain, this is raw data coming out of our microscope. It's actually not fully raw, because this is a terabyte of imagery. It's 50,000 slices that we did over the course of fourteen hours. And so instead of taking six or seven slices out of a sample, we can do thousands. And that allows us to look at things in 3D; it also allows us to look at things digitally. A human can't look at a terabyte of imagery, so we write algorithms that go through and trace the structures.

So this is out of the previous dataset that I showed you. We're zoomed in and we're looking at the capillaries. And so we've done a 3D visualization of the capillaries, where the capillaries are in red and it changes colors as it moves up the size scales. So this helps the biologists or the medical researchers that are looking at the tissue to understand what's going on, because 3D is a complex space to understand.

What actually matters more to me is the quantitative analysis that we can do off of it. If you look at the top, we've taken three areas of interest from that sample and we can just calculate the number of vascular segments, the total length of the vasculature, surface area, volume, volume as a percentage of total, fractal dimensions. And it allows us to take a manual qualitative process and make it high throughput and quantitative. And I think that really the power of high throughput quantitative biology is taking biology from a very slow manual process and bringing it into what I consider to be a real science, a real engineering practice, by allowing you to work with things that are digital.

I've shown you vasculature partially because people know what blood vessels look like and so you can intuitively understand what this looks like, but we do this to lots of other kinds of cells and have a bunch of variations on a technique.

We're a small company in San Francisco. I love giving lab tours, so if you're ever near 7th and Mission, send me a note and I'll give you a tour of our lab. So this is our company. Thank you.

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