Diagnostics for the Rest of Us

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Jana Care

Low-cost, point-of-care (POC) diagnostics are a Holy Grail of healthcare.[1,2] Many initiatives and much funding have focused on this area but, with a handful of notable exceptions, few have been able to deliver on the promise of accessible and affordable blood tests.[3,4] By studying past efforts and learning from experience, a few key principles stand out to help those working to develop medical diagnostic platforms that truly are “for the rest of us.”

01

Don’t Hunt Zebras

The idea of an easy to use device that can do everything, like the Tricorder from Star Trek, captures the imagination because it literally brings healthcare to your fingertips. Well-funded companies have been launched with the promise of performing hundreds of blood tests from a single drop of blood or with no blood at all. Such a device may be possible, but will likely be incredibly expensive at first. And how often would anyone actually need to run a panel of 100 or 200 blood tests?

In medicine, there is a well-known aphorism that states, “When you hear hoof beats, think of horses, not zebras.” Rather than building a test for an esoteric diagnosis, or “zebra,” first see if there are everyday “horses” you can improve access to and end up serving a much larger global need.

An affordable, connected ecosystem of technologies that can perform 10-20 key blood tests, while providing actionable lifestyle feedback to empower patients and healthcare providers, can offer greater value than an expensive box that tests for 100 analytes.

02

Only Reinvent the Wheel When You Need To

The key to building a cost effective, easy to use diagnostic platform is to leverage existing, pervasive technologies whenever possible.

For instance, colorimetric test strips already exist for many of the most critical biomarkers of chronic disease, such as glucose and lipids. Building a diagnostic reader that can read multiple existing strips and provide quantitative, cloud-connected results in minutes adds value without requiring substantial assay development. R&D funds, then, can focus on tests that are not readily available at the cost and performance required for global markets, such as POC HbA1c or electrolyte tests.

03

Affordability Requires Manufacturability

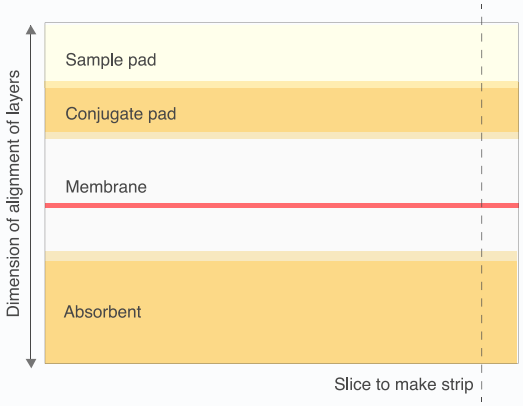
A focus on affordability can sometimes lead to an obsession with a low bill of materials (BOM). While important, a low BOM must be matched with a low cost of manufacturing to achieve affordability.

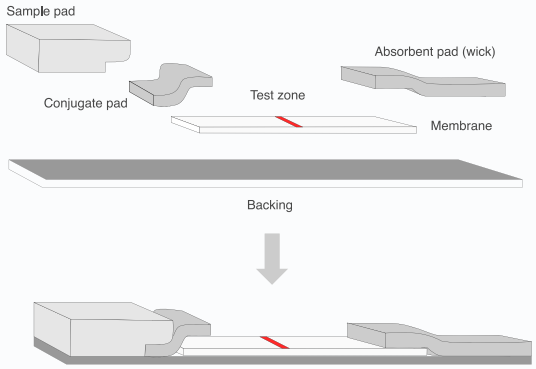
For example manufacturing a test strip that only requires registration of layers along one dimension (e.g. a traditional lateral flow immunoassay) allows easy integration with high-speed guillotine cutters and roll-to-roll manufacturing. Features that require registration in additional dimensions (e.g., adding a hole in a test strip) would require vision systems to ensure alignment during assembly.

Sometimes complex features are necessary for an assay to work, but the choices to include them must be made with the manufacturing repercussions in mind.

Example A

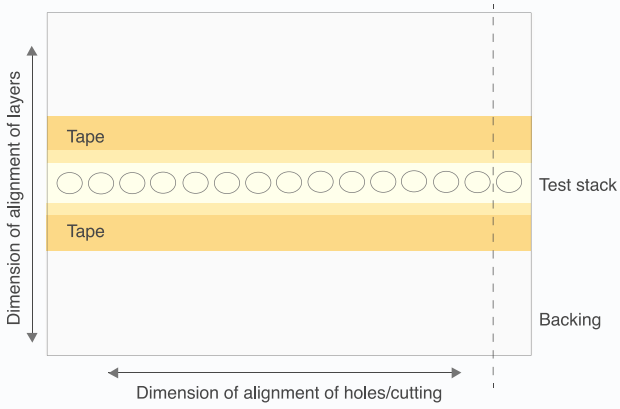
Test strip design that only requires alignment in one direction for greatest ease of manufacturing.

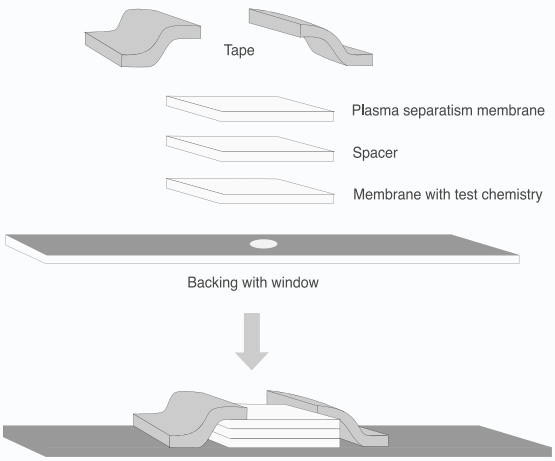




Example B

Test strip design that requires alignment in two directions for functionality. Manufacturing method to cut the strip requires more sophistication than in (A).





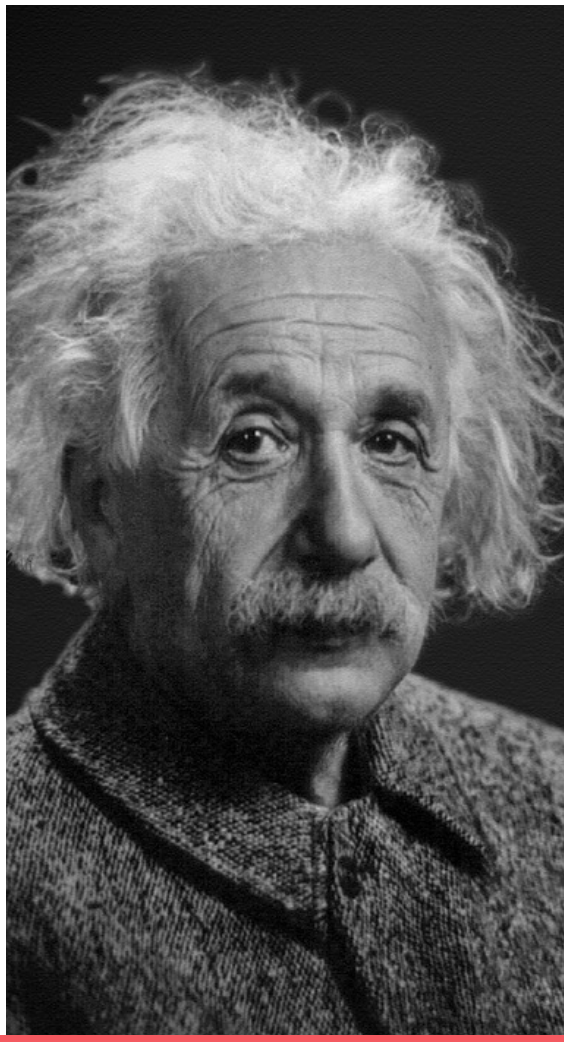
04

Simple, But Not Too Simple

Simplicity goes hand in hand with affordability and manufacturability. Achieving simplicity requires a deep understanding of a biomarker.

When beginning to design new assays, first think about the analyte you are trying to measure. What fluids is it in? What's the typical quantity? What is an abnormal amount? How is it formed or secreted? How is it broken down or filtered out of the body? Once you have a handle on these questions you can choose the right detection method.

Sometimes an enzymatic reaction resulting in a chromophore may be the simplest solution. At other times, an immunoassay or an electrochemical assay may be a more direct route to detection. Don't be afraid to build on well-tested methods with creative additions or modifications, but only if the added complexity is required to achieve an outcome like sensitivity or room temperature stability.



As the aphorism, often attributed to Einstein goes, *"Everything should be as simple as possible, but no simpler."*

05

The Human as a Design Factor

Simplicity in technical design interweaves with simplicity in human design: the design of the way in which a person performs a test, experiences it, and receives the results.

When determining whether a biomarker is relevant to managing chronic disease, it is important to talk with physicians, patients, caretakers, and others to imagine who would benefit from a point-of-care test and at what frequency they would perform the test.

Human-centered design techniques require thinking of a human as a necessary part of the device. In some cases, designing a “sample-to-answer” solution, where the user does very little besides provide a sample, may be appropriate but this operational simplicity often comes at a cost either in accuracy or in affordability. In some cases, a lower-cost assay that requires a few steps and is intended for point-of-care use by healthcare workers is a more appropriate solution than an expensive test that is amenable to home-use.

06

Connectivity and Quality Control

One of the reasons that a “sample-to-answer” solution is appealing is that it potentially ensures quality by removing human error. Connectivity provides another way to minimize human error and reduces the burden on the assay itself.

By integrating a diagnostic device with a smartphone or tablet, the familiar touch screen interacts with a user and provides instructions, warnings, and errors.

The connectivity of these devices means they can be remotely monitored to determine whether they are being used properly, quality control materials have been run, a device has been damaged, or a user is frequently encountering an error. Remote monitoring enables proactive intervention to repair or replace a faulty device or provide follow-up training or clarification to a user.

07

Above All, Accuracy

No matter the cost, the simplicity, or the elegance, the most important aspect of a diagnostic test is whether it can be trusted to make a decision. This requirement is not always identical with the absolute accuracy of the measurement of a specific biomarker.

Sometimes it means, “Does this device give a repeatable enough result so that I am certain that a value is either increasing or decreasing?”

Affordability, manufacturability, simplicity, and human-centered design are all parts of the puzzle to achieve a reliable test. The balance for any particular test will likely be different.

Healthcare can leverage many of the lessons from technology companies to enable cost effective, easy to use, accurate diagnosis of chronic diseases. But, unlike some of the more well-known philosophies of many tech startups-- *“move fast and break things,”* and, *“f--- it, ship it”*-- our essential conviction must be, “would we be comfortable letting our loved ones use it.”

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Previously, Dr Kumar was Postdoctoral Fellow and teaching consultant at Harvard University. He served in the Peace Corps in rural South Africa from 2007-2009. Dr Kumar holds multiple patents. His work has been published in a range of leading industry and academic publications. He holds PhD and M.S. degrees in applied physics from Harvard University and a B.S. degree in physics from Stanford University.

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