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Science Behind the Strip: Key Considerations for Scaling Microfluidic Devices

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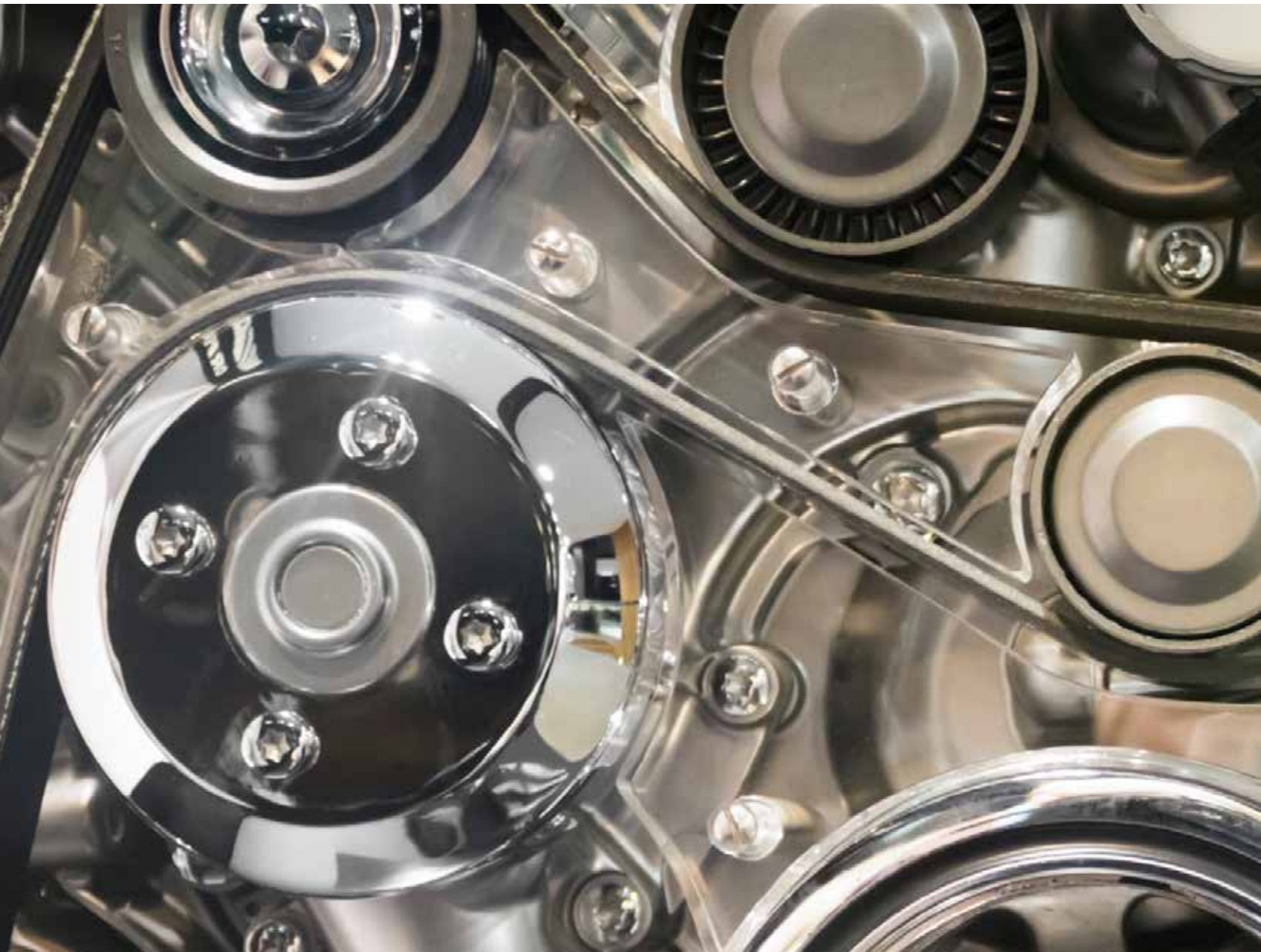

Science Behind the Strip: Key Considerations for Scaling Microfluidic Devices

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Introduction

Microfluidic devices transform lives. Thanks to modern technology and miniaturization of diagnostic tests it's possible to diagnose from almost anywhere—right at the point of care. This ability to get answers and explore treatment options, immediately, has incredible implications for patients and providers around the globe.

Developing A Miniaturized Test: No Small Feat

While miniaturized tests are an increasingly common diagnostic tool used all around the world, engineers face a mounting design challenge: how do you scale production of the miniaturized test while ensuring test accuracy and effectiveness? A miniaturized test should demonstrate an ability to be mass produced and maintain reliable functioning before it can be brought to market.

Not enough work has been done to accelerate the step between proof of concept, shrinking a laboratory test onto a credit card size device and product commercialization.[1] To bridge the gap, engineers must take scalability into account during the design process. This paper will explore three critical considerations for scalability: materials utilized, development parameters, and manufacturing techniques.

Key Consideration #1: Materials Utilized

From prototype to production—materials matter. Preferably, the material for prototyping should be the material for mass manufacture.

Otherwise, a costly and time-consuming redesign is possible.[2]

Accurate functioning of the miniaturized test is often considered the most difficult part of development. This is why miniaturization is frequently carried out using custom prototype chips, handmade with great care and attention. The prototypes are commonly created with glass, PMMA, Polycarbonate (PC), Polystyrene (PS), COP or COC. Out of all these materials, glass has the best chemical resistance and is usually readily available in an academic lab.[2] However, glass may not be the best material of choice if the microfluidic device is to be mass produced and used at the point of care.

Materials such as polymeric films and sheets may be preferable, because they enable a scalable manufacturing process. Parts or whole devices can be machined and/or cut from blocks of material, injection molded, micro injection molded or laminated and die cut from film and sheet stock with high accuracy.[3] Using polymeric materials during the prototype phase, in turn, may accelerate the transition from research and proof of concept to commercial product because injection molding and die cutting are scalable processes.

There are more material considerations—like compatibility and temperature. The surface-to-volume ratio of the miniaturized test is higher than conventional laboratory equipment, which results in stronger interactions of the sample material and reagents with the substrate. Therefore, compatibility of the polymer material may affect the diagnostic integrity of the device. The device may also be subject to extreme storage temperatures, so thermal-transition properties of polymer materials should be considered as well.[3]

Often, the high cost of specialized manufacturing technologies and materials can't be justified. Given the versatility and cost-effectiveness of polymer materials, devices can be manufactured with a competitive cost of ownership per test.[3]

Key Consideration #2: Development Parameters

Right from the beginning, it is important to consider the end-user and end-user environment for the intended application. These variables will inform design and development and, subsequently, scale. Asking questions and getting answers enables engineers to create a catalogue of parameters—critical to the reliable and accurate functioning of the mass-produced diagnostic device—to be monitored and controlled during development.

Consider the following questions.

User/environment-related questions may include:[4]

- Is the device to be used by health care professionals or patients?
- Is the device safe to be used by non-professionals in a home environment?
- What size should it be to make it easy to handle for the user?
- What size does it need to be to efficiently fit required features such as reagent vessels, chemistry deposits, mixing features, reaction zones, detection zones, etc.?

How these relate to scale: The answers to these questions play a pivotal role in scaling devices. For example, if the device will be used or stored in hostile temperatures or environments, the materials must exhibit resilience and versatility—and be able to deliver accurate results independent of extreme conditions. The final device may need to exhibit longer shelf life or better reproducibility. It will be important to choose a material that accounts for these variables and factors following device production.

Application-related questions may include:[4]

- Can the analysis be reduced in complexity; the analysis protocol be simplified? E.g., can mixing of reagent be done prior to storing reagent on a device to minimize the steps for reagent addition?
- How should reagents and chemistries be deposited on the device to enable good stability and a reliable and scalable deposition process?
- What fluids need to be moved and how can these be moved?
- How can the device be sealed without damaging or reacting with deposited chemistries on the device?
- Which materials are compatible with a deposited chemistry and reagents?
- What detection mode is used? Is a material required which does not interfere with optical (UV/VIS, Fluorescence, imaging) detection?
- What sensitivity is required for the application to function reliably?

How these relate to scale: The selection of a suitable material for a miniaturized test is highly dependent on the intended application. Harshness of the chemistries, and detection process as well as the design complexity of the device due to sample preparation requirements. Almost every bioanalytical application will introduce specific technical demands for the chosen material; therefore, required test accuracy and manufacturing technology may impact the scalability of the process.

Key Consideration #3: Manufacturing Techniques

Manufacturing technology plays a pivotal role in the cost-effective production of microfluidic devices. According to the guidelines published by The Microfluidic Consortium (2014), it's important to consider application requirements such as harshness of environment, required test accuracy, device throughput and number of devices produced when deciding which material and/or manufacturing technology to use for a microfluidic device.[2]

Materials and Environment

There are many factors to consider in terms of materials and fabrication environment. Manufacturing techniques vary—some utilize chemicals (i.e. hydrofluoric acid) or thermal transitions to fabricate devices. These environmental variables will impact materials. Material properties to consider, in relationship to the environment, include:

- Optical properties
- Chemical inertness
- Surface properties
- Thermal stability
- Compatibility
- Hydrophilicity

Manufacturing Processes and Device Throughput

There are a variety of manufacturing techniques for producing microfluidic devices. Some techniques are relatively new or an adaptation of other processes, others are already established. The low material cost and great structural resolution of polymers makes for a highly cost-effective approach to designing and fabricating complex devices. Careful attention must be paid to the way the manufacturing process is scaled in volume—but low cost, great design flexibility, and the ability to cost-effectively achieve high production volumes means more microfluidic devices can be brought to market with polymer materials.[3] As evidenced by the various techniques below, volumes, setup costs, batch sizes and more must be considered.

The following manufacturing processes are available:

Roll-to-roll laminate processing (scalable very small to very large volumes)

Laminate manufacturing methods are compatible with a wide variety of materials. For laminate microfluidic devices, each layer is cut individually. A device is designed using CAD software, the device geometry is cut, the inner portion is cleaned (weeding), and the layers of the device are bonded together to form a closed channel. The accuracy of the process is dependent on chosen cutting method, materials and layer thickness.[9,5]

Hot embossing (large volume)

Hot embossing is a popular replication process since it is relatively easy to tool-up for and is a comparatively easy process to execute. It can achieve excellent replication of high-aspect-ratio microstructure.

Molding (large volumes)

Injection molding is a highly developed process for macroreplication and is now increasingly available for microscale thermoplastic replication; it has the advantage of extremely fast cycle times, of the order of a few seconds per cycle—but requires more costly, complex molding tools.

Laser (small to medium volumes)

Laser micromachining systems are non-contact tools that can be rapidly reprogrammed to produce varied patterns, making them particularly suitable for the design and development phase of the microfluidic biosensor.

Planar processing (large volumes)

Planar processing of silicon or glass includes wet chemical etching, dry etching, and powder blasting. Setup, costs, processes and volumes are all impacted by the specific approach.

Xerography (small to large volumes)

Corona charging of a photoconductor, exposure to and development of latent image to be transferred and fixed on a target substrate. Many xerographic "inks" are made from copolymers of styrene and acrylate.[7]

Powderblasting (small to large volumes)

A particle jet is directed towards a target for mechanical material removal. Powder blasting creates fluidic channels and interconnections.

Casting (small volumes)

Creation of a mold to be used a template for a microfluidic device. The mold is the "negative" of the device. The actual device is created by

pouring (casting) PDMS into the mold and curing the material. PDMS is an elastomer known for its low shrinkage during cure and excellent elastic properties.[6]

Etching (small volumes)

Dry etching creates deep, high density and high aspect ratio structures in glass and silicon substrates. Wet chemical etching uses chemicals (i.e., hydrofluoric acid) to create channel structures in glass and silicon.

Three Stages to Scale

Mass-manufacturing a microfluidic device is an iterative process. The device must be designed and developed—and prove its performance every step of the way. Making smart choices regarding materials and manufacturing techniques, as well as identifying parameters for development, helps ensure success. It's important to consider these factors in the beginning. A change in materials from Stage 1 to Stage 3 is likely to create considerable cost, as well as significant time delays, in any development project. It is important the device continues to perform accurately and consistently—as the margin for performance variability decreases as development advances.[3]

Stage 1

Each individual component is joined to show a working assay. Sensitivity, selectivity, specificity and performance variation are evaluated—and likely compared to laboratory performance. Design improvements are often necessary, based on sources of manufacturing variation that are identified.

Stage 2

The manufacturing process must incorporate some element of batch or volume manufacturing with critical parameters identified and controlled there should now be less variability in performance. Ideally, there is less need for design change at this stage and high-speed replication processes can be used.

Stage 3

Stage 3 must be able to produce runs of up to 10,000 devices in a few months. If the developer aims for a low-cost disposable polymer chip, there should be a clear manufacturing path to achieve production volumes of 10^5–10^7 devices per year; clearly only achievable with high-speed replication, minimal assembly, and considerable process automation. This is best achieved using a highly integrated polymer device.

Conclusion

Miniaturized tests are critical tools capable of transforming and helping to save lives around the globe. These devices enable point-of-care testing, which helps patients and providers find answers and seek treatment sooner. Scalability plays a pivotal role in bringing reliable miniaturised tests to market faster. Choosing the right materials and manufacturing techniques and asking the right questions in the initial stages can help speed the process and ensure the device goes from lab—to life.

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