Hybrid Structures for Complex Analytical Instruments

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The use of microfluidic metal structures in complex integrated analytical systems that are mostly composed of conventional elements, brought with it a vast number of interfaces. This introduced challenges regarding reproducibility, dwell volumes, variances, method compatibility and standardisations. Hybrid structures drastically reduce the number of interfaces while increasing the proximity between the electronic and fluidic realm, thus providing a solution to complex integrated assemblies, requiring fewer external interfaces, and offering new possibilities regarding integration depth, allowing for entirely new arrangements of parts impossible by means of conventional technologies such as capillaries, machined parts, and separate electronic components.

Introduction

This article outlines the basics of hybrid structures (HS) in their current state along with the implementations as well as the implications. Hybrid structures are based on the fundamental building blocks of multi-layer circuit boards (MLCB) and metal microfluidic (MMF) structures. MMF structures are the counterpart to multi-layer circuit boards in the fluidic realm. While circuit boards allow for the precise manipulation of electrons, MMF devices make it possible to precisely manipulate solvents, or the molecules solvents are composed of. MMF devices and the related technology are already in use in applications that require high temperatures and high pressures, or both, such are aerospace equipment, high power propulsion systems and high precision analytical equipment such as chromatographs. The integration of MMF devices and circuit boards into one integrated assembly does however introduce new possibilities, such as combining multiple components into one compact, complex precise device, that have not been utilised before. This is in part due to the unique setting that an ultrahigh-performance liquid chromatograph ((U)HPLC) system provides for those technologies, e.g. the low flow rates (between 0 and 10 ml/min), the high pressure (up to 1500 bar), and the absence of temperatures above 150°C.

Some modern (U)HPLC systems already use MMF devices for different applications such as heat exchangers, mixers, and manifolds.

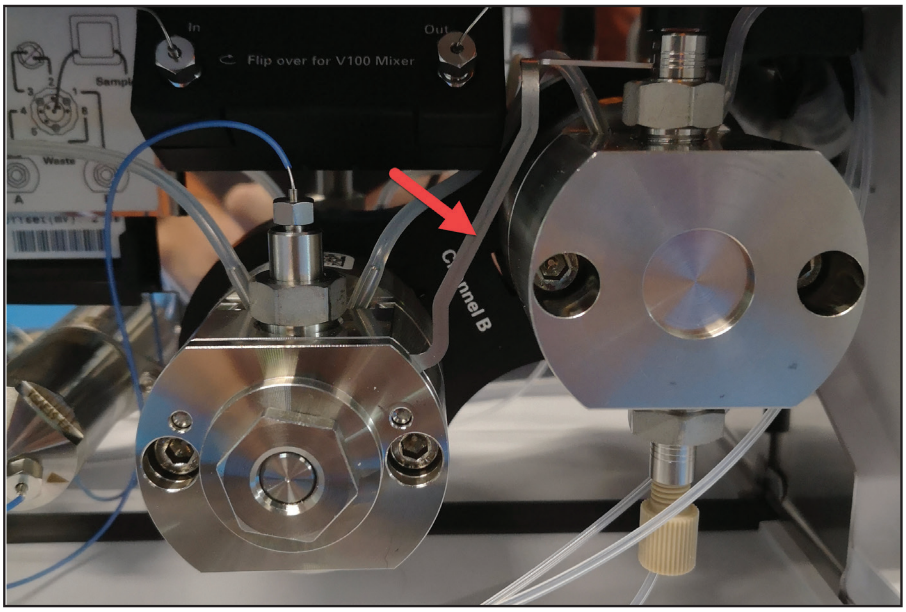

Figure 1. Example of a current application for MMF devices. Conventional pump head that is equipped with an MMF heat exchanger.

Those devices are generally surrounded by conventional capillary tubing, machined parts such as pump heads, valves, and circuit boards [1, 2]. Figure 1 shows a conventional pump head that is equipped with an MMF heat exchanger. The heat exchanger is used to connect the primary and the secondary pump head via a heat transfer element to reduce the impact of thermal contraction in the secondary head, which can impact the flow rate accuracy. While the devices themselves already bring value to the current configurations by serving the use case they are designed for with minimal overhead, maximum reliability, and a high performance, they do remain islands in a 'sea of capillaries and interfaces'. They are much like the first integrated components that were introduced into phones, radios, TVs, and other electronic equipment as more complex integrated components in a 'sea of wires and plugs' [3]. To fully leverage the advantages of MMF, a migration of capillaries and interfaces is required. Radios and phones only started to shrink in size and grow in performance when the functional blocks were combined into fewer main circuit boards. To improve the performance and reliability, it is necessary to reduce the failure modes and performance limiters in the system. Failure modes in (U)HPLC systems are often caused by interfaces and

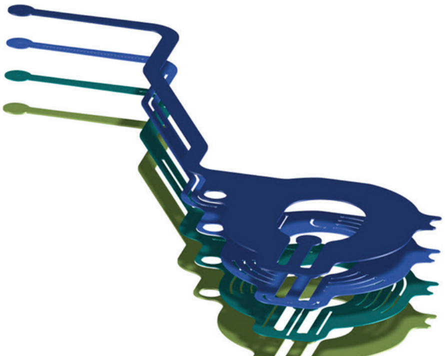

Figure 2. Individual layers of the high pressure heat exchanger prior to bonding the individual layers. Each layer has a sub-set of channels which, when combined, result in the complete flow channel for the device.

connections. Leaks, blockages, restriction and dwell volume variances and others are just a few of the failure modes that can be introduced. In addition, the flow path complexity that can be handled by means of capillaries, or wires for the MLCB example, is limited. This is the gap that hybrid structures can fill. Not only do they make it possible to combine several components in one domain, such as the fluidic realm, into one main component, but they also allow us to bridge the gap to other domains, such as the gap between the electronic and fluidic realm, into one device. This opens new possibilities for the use of complex integrated devices that boost performance while providing a much easier use and reliability. This is very similar to the development progression with electronics [4], but this time in combination with fluidics. Having a counterpart to a circuit board for fluidic applications facilitates similar technological leaps that was seen for electronic components regarding performance, reliability, cost, and serviceability. It does, however, require other technologies such as sensors, actuators, and coatings to make this technological leap a reality [5]. Those technologies are largely available, both for the electronic and fluidic side of things, and can now be utilised in combination with MMF to a hybrid structure, making it possible to challenge the previously impossible [6].

Implementation

Existing solutions implement the solvent and sample handling separately from the evaluation and actuator electronics. Those configurations are not only error prone, but they also introduce challenges regarding method reproducibility and compatibility from system to system and over time [7]. In addition, the conventional setup introduces physical limitations that translate directly to performance limitations.

MMF devices as well as circuit boards are composed of multiple layers. An MMF device consists of thin layers of different metals, the number of layers dependent on the application. The layers carry patterns like the circuit boards, only inverted. While circuit boards keep or add material in places where electron flow should occur, the MMF layers require the removal of material in locations where molecules are transported to create a channel. Each layer can be used to implement a sub-set of functionalities into the final device. Figure 2 shows a simple heat exchanger prior to bonding the individual layers. The layers are subsequently combined to compose the entire MMF device with multiple functionalities, inlets, outlets, and other interfaces. Figure 3 shows an example of a flow path within an MMF device that is utilised to split flows in a mixer evenly into various dwell channels. For a hybrid structure the multilayer circuit board is printed directly onto the MMF device resulting in one assembly for the fluidic and electronic functions of this component.

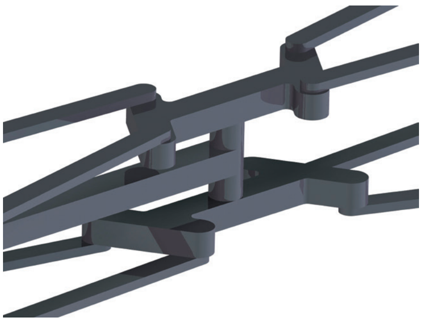

Figure 3. Flow channel example of a splitter in a mixer. The channel height is 80µm.

In some versions, depending on the nature and complexity, the circuit board is only attached to the MMF part. Due to the similar form factors (flat and thin), the combination of the MMF device and the MLCB, whether printed or glued, does not pose a problem. Part of this assembly are the sensors, the actuators, and the evaluation electronics needed to run the device. The proximity of the elements, in combination with the well-controlled manufacturing process and low tolerances, allow for a uniquely precise part that replaces several individual assemblies in a conventional setup. In turn, this reduces the tolerances and performance variations for one and the same functional element. Figure 4 shows an example of such an assembly.

Printing the circuit board directly on the MMF device also makes it possible to utilise existing volumes from mixers, filters, heat exchangers, manifolds, valves etc. for more than one purpose. The volume can simultaneously be used to detect the pressure or the flow, to heat or cool solvent, etc. This allows for a significant reduction in dwell volume of a functional group. What used to be separate elements, such as a heat exchanger (V_x), a filter (V_f), a valve (V_v), a pressure sensor (V_s) and a mixer (V_m) with a dwell volume of $V_{xfvsm}=V_x+V_f+V_v+V_s+V_m$, where $V_v<V_s<V_f<V_x<V_m$, can now be reduced to a integrated hybrid structure on the basis of the heat exchanger. This allows for an integration of the heat exchanger, the filter, the valve, the pressure sensor, and the mixer into one structure composed of the fluidic part (MMF) and the electronic part (MLCB). For the volume of the resulting new structure, the following would be true: $V_{HS}\leq V_m<<V_{xfvsm}$. The resulting proximity between the electronic and fluidic realm also aids the sensor and actuator applications, e.g. flow sensing, heating, and cooling, etc. Figure 5 shows a magnification of one of those applications with a strain gauge used as a pressure sensor on an MMF flow channel.

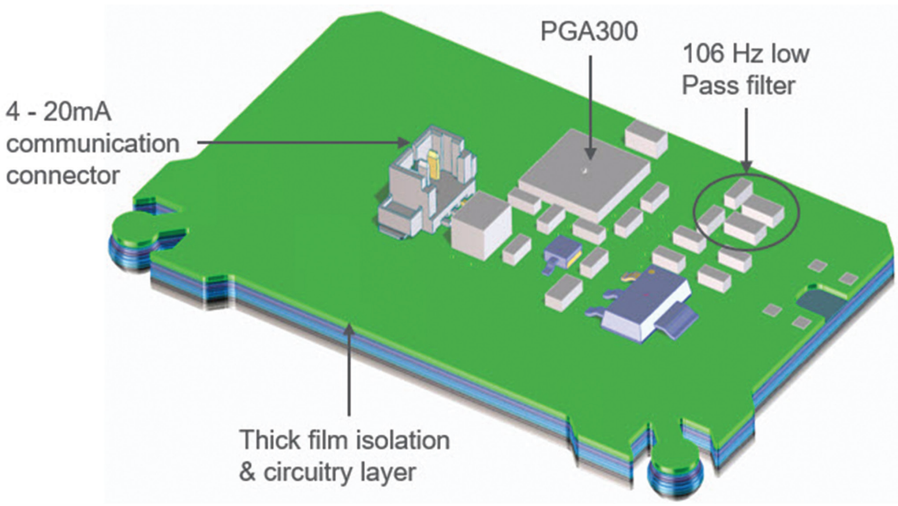

Figure 4. Example of a hybrid structure.
The MMF device (a V380Mixer for high-pressure applications) is outfitted with various sensors.

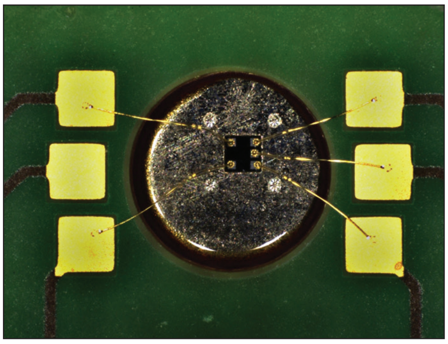

Figure 5. Magnification of a strain gauge sensor. The strain gauge is attached to the surface of the MMF structure and the board of the hybrid structure.

Implication and Discussion

The use of hybrid structures facilitates a significant reduction of dwell volume and interfaces in the system, both fluidic and electronic. The proximity greatly simplifies sensing of and acting on the solvents and the integration makes it possible to combine the boards currently spread across several components. In addition, the ability to specify the performance of the entire functional element precisely, allows for significant improvements regarding system robustness and reproducibility. This technology reduces the number of interfaces significantly enough (often just one in and outlet) to allow for a precise specification of those interfaces. The narrow specification with the ability to monitor those interfaces by means of inbuilt sensors, in turn allows for a swift qualification of the component at any point in time. This leads to improved predictive maintenance and a significant simplification of service operations.

One use case for such an element is a heat exchanger manifold with an inbuilt low- and high-pressure mixer and a pressure sensor. This device is used before, between and after the primary and secondary pump head of a (U)HPLC quaternary pump and serves as a connecting manifold. In such a setup the device connects a gradient valve to the primary via a low pressure mixer and a passive inlet valve, the primary to the secondary via a heat exchanger and the secondary to the sampler via a mixer and a pressure sensor. In total, the device does not exceed the dimensions of 80x40x5mm (length x height x depth). As far as interfaces go, it has three inlets and three outlets (one low pressure inlet, two high pressure pump interfaces with one in and outlet each as well as one high pressure outlet to the system) as shown in Figure 6. The advantage of such a setup is the small form factor, which leads to a low dwell volume, the simple connection mechanism as well as the ability to detect malfunctions in this sub-assembly. This also brings with it the ability to test a sub-assembly for adherence to specifications.

Additionally, the MMF technology provides an easy way to add functionality by adding steps to the manufacturing process, much like circuit boards. For example, the same design can be used for the standard system and the bio-compatible system by simply adding a thin and highly conformal coating of bio-compatible material to the structure. The base design remains the same and will therefore not introduce performance variations, but the added coating turns the design into a bio-compatible element. This has been shown to work and is already in use, for example, in microfluidic high pressure mixers for (U)HPLCs. A system that is mainly composed of MMF and hybrid structures does not only introduce significant advantages regarding performance and reliability, but it also introduces a new standard for usability, serviceability, and user friendliness in general. This is achieved by means of re-thinking the overall configuration, producing channels and flow path geometries with very low tolerances, qualifying the performance for components rather than modules or entire systems and by using a modular approach with standardised interfaces for all functional groups.

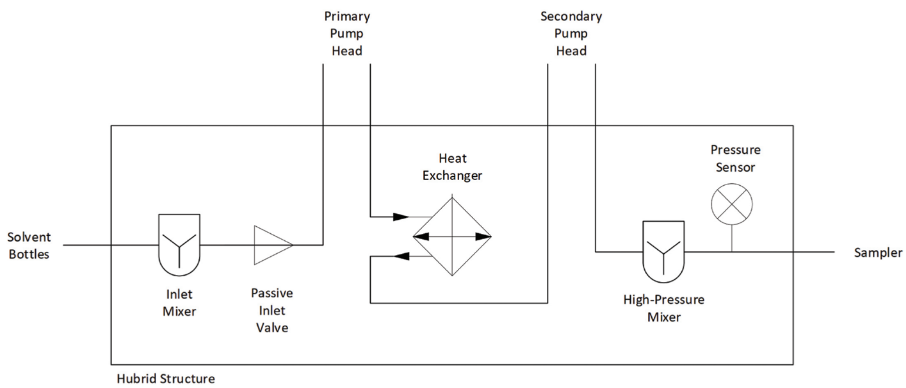

Figure 6. Diagram of pump head manifold. This hybrid structure is used before, between, and after the primary and secondary pump head of an HPLC quaternary pump and serves as a connecting manifold. In this setup, the device connects a gradient valve to the primary via a low pressure mixer and a passive inlet valve; the primary to the secondary via a heat exchanger and the secondary to the system via a mixer and a pressure sensor.

Conclusion

A hybrid structure allows for the combination of solvent manipulation and the required electronics in one inseparable assembly. This technology not only reduces the number of fluidic and electronic interfaces, but it allows for entirely new arrangements of parts impossible by means of conventional technologies such as capillaries, machined parts, and separate electronic components. The ability to use pre-existing features such as dwell volumes for second or third applications like sensing (pressure or temperature) or actuating (variable restrictors), allows for significant optimisations in the overall performance of a device (e.g. dwell volumes). The ability to control, adjust and fix the interfaces during the manufacturing process significantly increases the reproducibility of assembly performances as well as the number of possible error modes. In addition, this process facilitates standardisation and design re-use because the cost of the device does not scale with complexity, but only with size. The building blocks of this technology (e.g. the MMF devices mentioned above, as well as the ability to use a highly conformal coating to turn a non-bio-compatible microfluidic device into a bio-compatible device, the new interfaces for microfluidic elements and others) are already in use in some (U)HPLC systems and are readily available. Hybrid structures composed of those building blocks show great promise in evaluations and tests. Looking at the above outlined possibilities and the maturity of this technology, MMF and hybrid structures have the potential to fundamentally change the possibilities of (U)HPLC systems.

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