Development of a high-performance and low-cost fraction collector

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Abstract

Preparative high-performance liquid chromatography is a chemical procedure in which a components mixture is separated into its components. In this procedure, fraction collectors are used to fill the separated components of a mixture into their dedicated vials. Fraction collectors available on the marked are usually made of a multiplicity of custom-made parts, which results in high manufacturing costs. A wide used drive concept for fraction collectors is the spindle drive, which is slow due to its gear ration. In this work, we propose an approach of building a fraction collector using a fast timing belt drive, which has performed well for 3D-Printers in practice. The result of a first prototype showed, that this drive-concept can be adapted also for fraction collectors. Thereby, the material and manufacturing costs can be kept low using a manufacturing aware part design.

Contents

1 Introduction **3**

2 Material and Methods **5**

2.1 Movement Concept 5

2.2 Bearing 5

2.3 Form Finding Process 7

3 Results and Discussion **7**

4 Conclusion **9**

5 References **11**

1 Introduction

Preparative high-performance liquid chromatography (HPLC) is a chemical procedure in which a component mixture is separated into its components. While analytical HPLC is used to analyze the amount of a component in a mixture, the main goal of preparative HPLC is to extract the desired components from the mixture. Thus, preparative HPLC is done with much higher flowrates and higher sample volumes compared to analytical HPLC. Preparative HPLC is used, for example, in pharmaceutical small batch production for research purposes. Another application example is the caffeine extraction from coffee..

The topic of this paper is the construction of a fraction collector (collector) for HPLC. The collector itself is a laboratory device which is used during the separation process to fill each separated component from the component mixture (also called fractions) into a dedicated vial. The vial selection is usually done by a xy-portal which moves the drop former over a vial. For a better understanding of the collector's function and requirements, we start by giving a short overview of the HPLC process:

Fig. 1 shows the basic component of a HPLC system and an example process signal (also called Chromatogram). An HPLC system is a combination of different devices. The pump is used to deliver a solvent composition through the system. Behind the pump, the Autosampler is used to inject a sample into the system. The sample as well as the solvent composition (also called mobile phase or eluent) flow through the column (stationary phase) under high pressure, which separates the different components in the sample due to interactions between the mobile and the stationary phase. In a well-adjusted process, each component from the mixture will leave the column at different times.

A detector (e.g. light absorption) after the column is used to detect the signal. If a substance, different from the solvent, flows through the detector cell, the measured signal rises. For each separated component a peak is measured (see Fig. 1 (9)). At the end of the HPLC process the Collector is used to fill each separated component into its dedicated vial or into waste. Whether the current volume is delivered into the collector or into the waste vial is controlled by the waste/fraction valve, whose position usually corresponds to a chromatogram peak (e.g. in Fig. 1 (9): a peak-start corresponds to the valve's fraction position) [1].

The fraction collector must fulfill certain requirements to be used. Often the

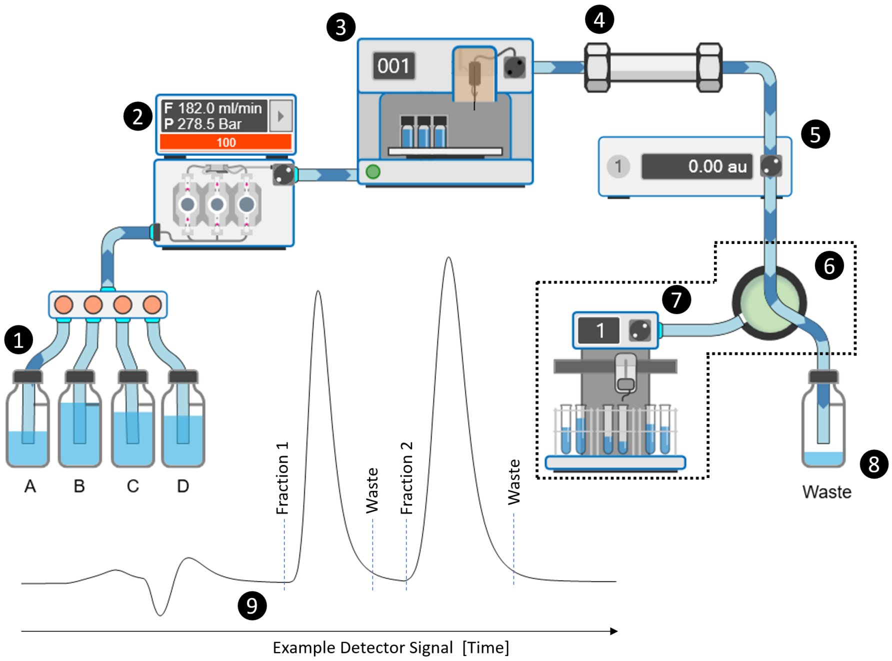

Figure 1: The basic components of a preparative HPLC are shown: (1) Solvents composition; (2) Pump; (3) Autosampler; (4) Column; (5) Detector; (6) Waste/Fraction-Valve; (7) Collector; (8) Waste; (9) Example Chromatogram, which contains two separated components. The dashed lines inside the Chromatogram indicate a collected value-fraction. The dotted line which surrounds (6) and (7) highlights the topic of this work.

separated components are valuable, so a high efficiency is needed to recover the maximum of the desired component. The efficiency can be improved by reducing the pipe volume from the waste/fraction-valve to the collector's output, which is also called the dead volume. A fast movement speed also increases the efficiency by reducing the time the waste/fraction-valve is set to waste during a fraction switch, which i.e. occurs when a vial was filled and thus the collector moves to the next vial. Other requirements result from the laboratory environment itself. Device parts which are likely to be exposed to solvents should not react in a way that affects the functioning of the device (i.e. corrosion). The device should be high enough that litre-vials can fit in, but it should also handle smaller vials as well. The useable area inside the collector must be at least 410 mm x 240 mm.

There are already collectors available on the market, see e.g. [7],[8]. Many of them are quite expensive due to small series and complex parts. Therefore, the main aim is to create a design which allows a cost-efficient manufacturing. Thus, research institutes with low budgets can profit from this design.

2 Material and Methods

The collector was planned and designed using the CAD-Software Solidworks 2018. In order to create a cost-efficient design, as many standard parts as possible were used. To get an idea of movement concepts, other devices with a xy-drive were examined. Among other things, 3D-printers have a similar dimension and also use a xy-drive. Due to the latest market developments, there is a wide range of 3D-printers which are custom-made or open source (i.e. the Ultimaker) – therefore also the drive systems and components are available on the market.

2.1 Movement Concept

A wide used drive concept for xy-portals are spindle drives, where each axis is driven by a rotating spindle. The axis torque is provided by a motor which is mounted along the axis. Disadvantages of the spindle drive are on the one hand a higher rest mass, because a motor is mounted along an axis, and slower movement speeds due to the spindle gear ratio.
To create a fast economic xy-drive one must minimize the moving mass. XY-driving concepts where the motors are not being moved with one axis result in a lighter moving mass. Another advantage of fixed mounted motors is that one does not need flexible supply cables. In order to work well, a 3D-printer xy-drive requires exact positioning and a fast travelling speed. A standard drive concept for 3D-printers is the timing belt portal drive, which shows a good performance in practice. Thus, it is obvious to test this drive concept in the context of a HPLC collector.
Fig. 2 shows the adapted movement concept. The sliders are connected to the timing belt to provide the movement force. Along one movement axis two sliders are driven synchronous to prevent canting in the sliding bearings. Each outer driving shaft is mounted using miniature ball bearings. Optical positioning switches are used to determine the home position.

2.2 Bearing

To move an axis, the motor must overcome all counteracting torques caused by the friction of the bearings. The torque which is then left is used for acceleration. Thus, reducing the countering forces results in a more effective drive. The main countering force in the used drive concept is the friction in the slide

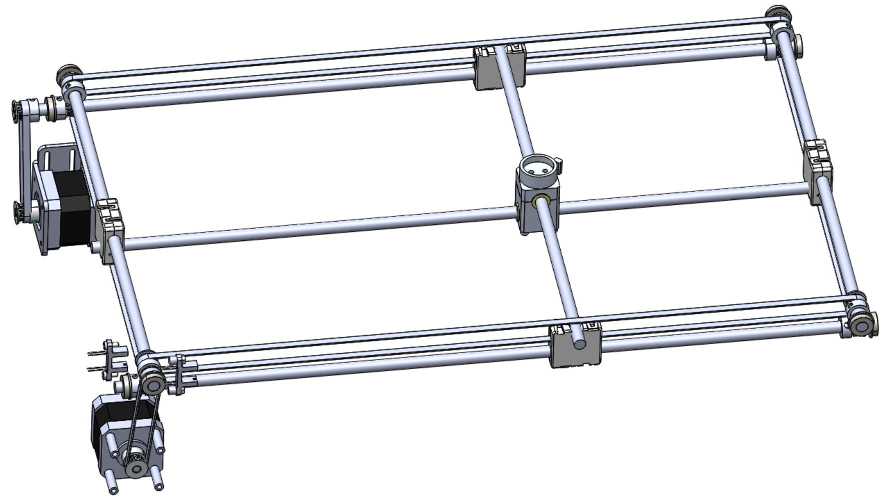

Figure 2: The used timing belt driving concept, which is also used by some 3D-printers (i.e. the Ultimaker). The xy-portal dimensions are 350 mm x 530 mm.

bearings along the axis (see Fig. 2). Due to the friction law $F = \mu \cdot N$ the friction can be reduced by reducing the normal force N (i.e. the weight) as well as optimizing the friction coefficient μ using a smart material coupling [4]. The drive concept shown in Fig. 2 is a static overdetermined system (along one axis) due to the fixed connection of the movement axis. Thus, if the drive shafts are deformed or not parallel enough, additional friction in the bearing is created which results in an overall drive stiffness.

A low manufacturing tolerance as well as a precise part connection is needed for a precise drive shaft positioning. Thus, the normal force inside the slide bearing and the resulting friction can be optimized. The overall required manufacturing tolerance can be estimated using the fit specification from the drive shaft and the slide bearings. Assumed a E7/h8 fit, the slide bearing tolerance would be $-25\,\mu\text{m}$ to $-40\,\mu\text{m}$ and the drive shaft tolerance from $0\,\mu\text{m}$ to $-22\,\mu\text{m}$ using a diameter of $8\,\text{mm}$ [5]. Thus, the slide bearing clearance would be $25\,\mu\text{m}$ in the tightest case. So if the parallelism of two drive shafts deviates in the tightest case more than $25\,\mu\text{m}$, additional friction is being created due to the statically overdetermined system by the cross table axis.

One cross table axis is held by two parallel gliders each. If one slider fixes bearing (which holds one cross-axis) is replaced by a slide bearing, the system is statically determined again, which allows higher manufacturing tolerances to be compensated.

2.3 Form Finding Process

In order to find a appropriate device form and design, the ideas can systematically lead along the requirements and decisions that have already been made. The liquid which is filled into the vial is driven by the portal from above. The vial should be placed inside the collector, not on the table itself. The user needs easy access to the vials during the laboratory routine, so an open construction is preferred. The xy-drive itself needs to be rigid enough that only negligible deformation occurs and must allow a precise manufacturing. To fulfill these requirements, an open device with two connected side parts had been chosen. There are many other forms in which the device can be constructed, but this form has many advantages which will be discussed in the next section.

3 Results and Discussion

The construction design considering the above determined requirements is shown in Fig. 3. The side parts (8mm thick) are connected through the front panel and two hidden panels inside the back. In order to achieve a precise connection of the side panels, which is necessary for axis parallelism, we use a shaped form connection due to the tolerance of the screw connection in addition to the screws [2]. Fig. 4 illustrates the connection between the front panel and side panel by showing the tongue and groove shaped connection. The side parts, the front panel, the hidden panels in the back as well as the top and rear panel are made of aluminum, which must be anodized or powder-coated to create a chemical resistant surface. The ball bearings for the drive shafts are mounted in the side panels through a press fit.

The vial racks are placed into the floor pan, which is made of stainless-steel sheet metal (X5CrNi18-10), and the edges are welded and electropolished for easy cleaning. Due to mechanical stress from the vial racks, which are being slided inside the floor pan, one cannot use anodized or power- coating materials, because the surface coating would be damaged during the regular usage. Another important feature of the floor pan is a drainage, to safely handle overflowing liquids from the vials. One has to keep in mind that metal sheet parts have a high manufacturing tolerance, thus those parts should not be used for a precise part connection. To compensate these manufacturing tolerances, larger bore holes in the floor pan have been planned to connect the side parts.

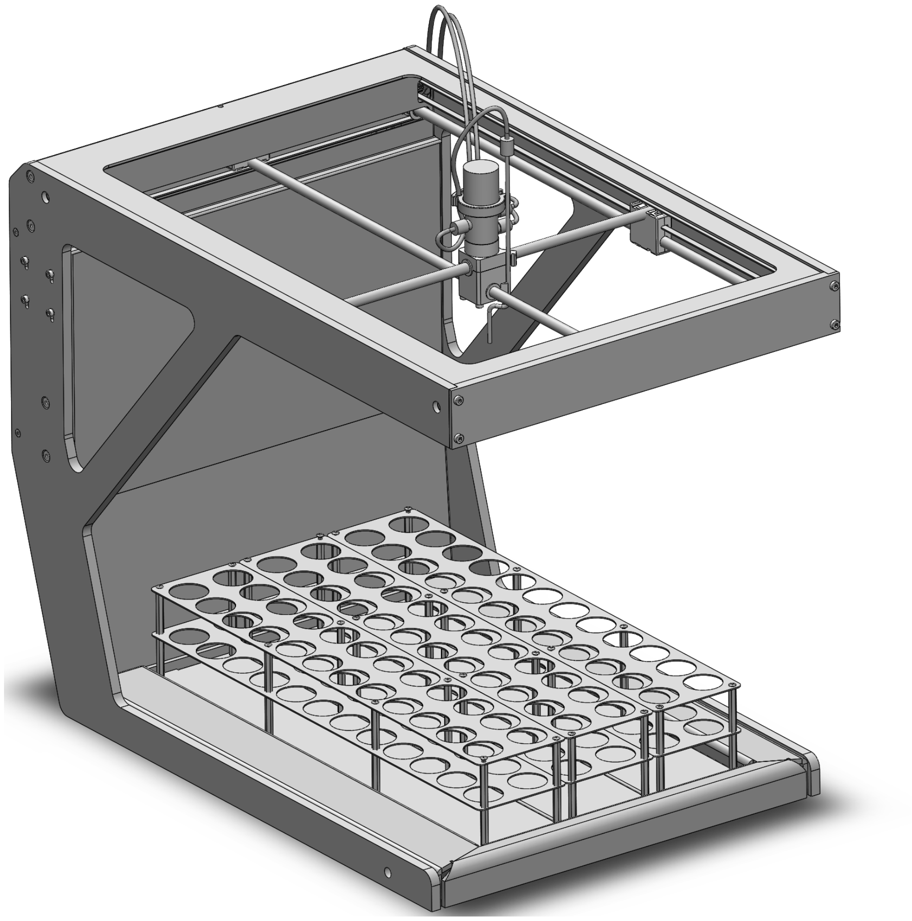

Figure 3: Illustration of the construction result with three empty vial racks in the floor pan. The rack size can vary with the vial size.

The timing pulley xy-drive, which was shown in detail in Fig. 2, is built using 8mm high precision linear hard anodized aluminum drive shafts. Hard anodized material is specified to be chemical resistant. On each of the four outer drive shafts a linear slide bronze (Cu Zn25Al5) bearing with graphite deposits is used to mount the slide blocks. The two cross-table axes are mounted on the sliding blocks. The linear bronze bearings are specified with a surface hardness from 190 HB to 220 HB. To get good tribological properties, the drive shaft must be at least 100 HB harder than the slide bearing and should have a depth of roughness smaller than $R_z < 6.3$ [3], which is given here, because hard anodized aluminum is specified with a surface hardness of 523 HB [6]. After an initial lubrication using lithium saponified grease, no further lubrication is needed during the slide bearing's lifetime [3]. All timing belt pulleys have 12 teeth, resulting in a motor-to-axis gear ratio of 1:1.The 12-tooth pulleys used have an outer diameter of $12.44\,\mathrm{mm}$, which results in a motion length of $200\,\mu\mathrm{m}$ per step when using a 200-step stepper motor in

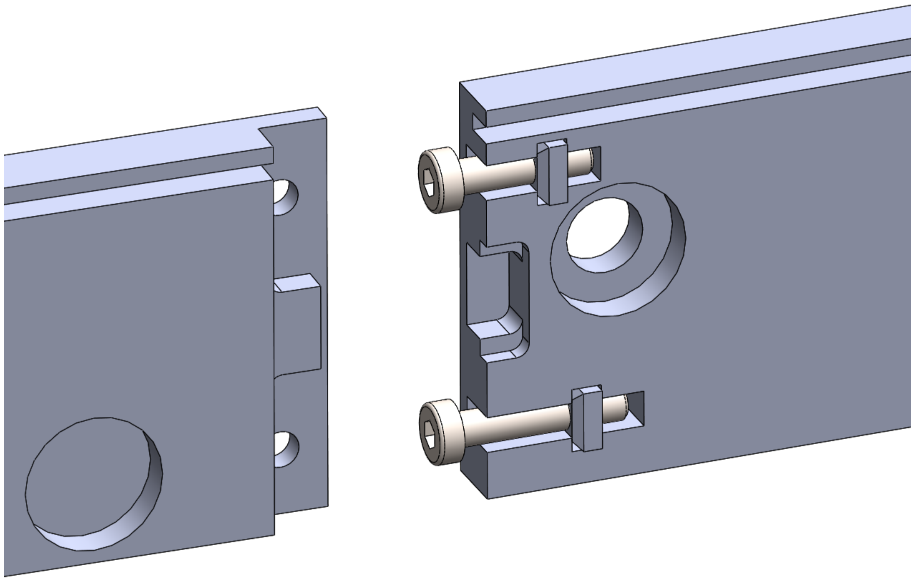

Figure 4: Illustration of the shaped connection between the front panel and the side panel. A square nut is used as screw thread. Thus, these parts can be manufactured using only a 3 axis CNC-Mill. The axis ball bearings are mounted inside the hole using a press fit.

full-step mode.

At the axis intersection from the cross-table the head is arranged using dry sliding bearing bushings (see Fig. 5). To reduce the pipe dead volume from the waste/fraction-valve to the mouthpiece, the waste/fraction-valve is mounted on top of the head. There are four connections to the valve: The input tube, the electrical supply wires for position switching, the fraction output as well as the waste output. While the fraction output is directly connected to the head's mouthpiece, all other head connections come from outside and will be grouped into one tube to create a cable guide. The clamp cable ring around the valve is used to guide the valve connection to the top.

4 Conclusion

The goal of this work was to create a cost-efficient fraction collector for HPLC which can handle dynamic vial sizes and which performance is comparable to other products in this segment. The main idea to achieve this goal was to use as many standard components as possible, but also in line with the goal to build a ready-to-use laboratory device. Researches has shown that similar devices are 3D-printers and that their movements components of the xy-drive

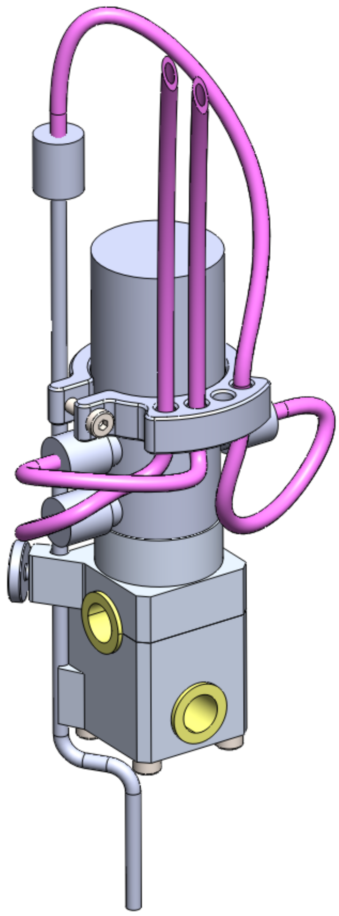

Figure 5: External view of the collector's head which is mounted on the cross-table axes using dry slide bearing bushings. The bushings are mounted using a fit connection. The head itself is made of two parts (top and bottom), which were connected using four screws on the bottom. The waste/fraction-valve is mounted on top to minimize the dead volume from the valve output to the drop former. The valve is fixtured using two screws from the inside of the top part.

are easy to obtain and in the same dimension range as needed for this project.

All components required for this construction can be grouped in three categories: 'standard Components', 'metal sheet parts' and 'manufacturable parts using a 3-Axis CNC mill'. With exception of the two head parts, all other milling parts can be manufactured from a single 8 mm thick 850 mm x 500 mm aluminum sheet. Prototypes of the xy-portal showed that this movement concept can be adapted to the needed dimension, speed and load. But a low manufacturing tolerance and a precise part connection is crucial to create a precise axis parallelism to reduce the countering forces in the sliding bearings.

This design concept is beneficial for those who are in need of a high-performance fraction collector but are on a low budget.

Acknowledgement

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