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(54) **Sampling arrangement**

(57) The invention provides a sampling arrangement (105) for sampling from a reactor (50), the sampling arrangement (105) comprising a gas inlet (110), a solvent inlet (120), a solvent compartment (130), one or more multiple-position valves (140), a sampling compartment (150), and an outlet, wherein in a first operational mode (10) the one or more multiple-position valves (140) are configured to provide: fluid contact between the solvent inlet (120) and the solvent compartment (130); fluid contact between the reactor (50) and the sampling compartment (150); and fluid separation between the solvent compartment (130) and the sampling compartment (150); and wherein in a second operational mode (20) the one or more multiple-position valves (140) are configured to provide: fluid contact between the gas inlet (110), the solvent compartment (130), the sampling compartment (150), and the outlet (160).

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Sampling arrangement

FIELD OF THE INVENTION

The invention relates to a sampling arrangement. The method further relates to a system comprising the sampling arrangement. The method further relates to a method for sampling.

BACKGROUND OF THE INVENTION

Systems for sampling are known in the art. For example, US2011318243A1 describes an in situ sampling device for capturing a material sample from a vessel. It describes devices with elongate probes having extendable sample capture elements. A sample capture element of such a device may include a concave sample capture pocket located near a distal end thereof. The sample capture pocket is adapted to capture a volume of material when the sample capture element is extended into said material. The material sample remains trapped in the sample capture pocket upon sample capture element retraction. The sample capture pocket may be provided with a port for receiving material therein and a port for expelling material therefrom. These ports may be placed in communication with corresponding material transfer channels extending through the sample capture element.

SUMMARY OF THE INVENTION

The development of new chemistry as well as the scale-up of established chemistry may benefit from detailed insight in the ongoing processes in a reactor, especially on a molecular level, for kinetic analysis. Kinetic analysis may require successively collecting a plurality of samples within a short timeframe. Therefore, there may be a need for automated and accurate sampling at predetermined time-intervals.

The prior art may describe sampling systems. However, these systems may suffer from various drawbacks. In particular, the prior art systems may, among others: (i) perturb conditions in a reactor, especially via the introduction of one or more (gaseous) compounds, which may be particularly detrimental for reactors with a low volume, (ii) be unsuitable for oxygen-sensitive processes, (iii) be unsuitable for sampling from hazardous conditions, such as especially high-pressure processes, high-temperature processes, or processes involving dangerous chemicals, (iv) be inflexible with regards to sampling volume, (v) have an insufficient sampling rate and may therefore be unsuitable to probe fast processes, (vi) may be prohibitively expensive, especially with regards to consumables, (vii) may be inaccurate with respect to sampling volumes of sample and/or solvent, and (viii) may provide the samples in a container/condition unsuitable for direct further analysis.

Hence, it is an aspect of the invention to provide an alternative sampling arrangement, which preferably further at least partly obviates one or more of above-described drawbacks. The present invention may have as object to overcome or ameliorate at least one of the disadvantages of the prior art, or to provide a useful alternative.

Hence, in a first aspect, the invention provides a sampling arrangement for sampling from a reactor. The sampling arrangement may comprise a solvent compartment, one or more multiple-position valves (also: “multi-position valves”), and a sampling compartment. In embodiments, the one or more multiple-position valves may be configured to provide in a first operational mode (also: “first operation mode”): (i) fluid contact between a solvent inlet and the solvent compartment; (ii) fluid contact between the reactor and the sampling compartment; and/or (iii) fluid separation between the solvent compartment and the sampling compartment. In further embodiments, the one or more multiple-position valves may be configured to provide in a second operational mode (also: “second operation mode”): fluid contact between (successively) a gas inlet, the solvent compartment, the sampling compartment, and an outlet.

During the first operational mode, the sampling compartment may be filled with a sample from the reactor, especially due to a higher pressure in the reactor relative to the sampling compartment. Similarly, during the first operational mode, the solvent compartment may be filled with a solvent portion from the solvent inlet. During the second operational mode, an inlet gas (also: “gas”) from the gas inlet may push the contents of the solvent compartment and the sampling compartment to the outlet, especially thereby providing the sample for further analysis. Hence, during the second operational mode, a gas may be provided from the gas inlet to successively the solvent compartment, the sampling compartment and the outlet, *i.e.*, the gas may be provided from the gas inlet to the outlet via the solvent compartment and the sampling compartment, wherein the solvent compartment is arranged upstream of the sampling compartment, and wherein the sampling compartment is arranged upstream of the outlet. In particular, the (successive) arrangement of solvent compartment and sampling compartment provides that the solvent portion may essentially wash the sampling compartment as it travels through, thereby reducing, especially preventing, the presence of any residual sample in the sampling compartment, which may be beneficial both by facilitating providing the entire sample to the outlet, and by removing the need for a washing step to remove residual sample from the sampling compartment prior to sampling again. Hence, due to the (successive) arrangement, the second operational mode may be directly followed by the first operational mode without the need of an intermediate washing step, thereby simplifying, improving and/or accelerating the sampling procedure.

The sampling arrangement may enable accurate sampling of fast reactions, as well as of reaction mixtures that continue to react at room temperature and/or atmospheric pressure (see below). In particular, the sampling arrangement may facilitate sampling with sampling frequencies ≥ 6/min, such as ≥ 5/min, especially ≥ 2/min. In further embodiments, the sampling arrangement may have a fastest sampling rate ≤ 2/min, such as ≤ 3/min, especially ≤ 4/min, such as ≤ 5/min.

Thereby, the invention may provide a sampling arrangement that may be simple in use, while facilitating obtaining well-defined samples in quick succession. In particular, the sampling arrangement may be suitable for sampling from hazardous conditions, and may be essentially non-invasive with respect to the reactor conditions.

Hence, the invention may provide a sampling arrangement for sampling from a reactor. The term "sampling arrangement" may herein refer to an element, especially a plurality of elements, configured to facilitate sampling from a container, especially a reactor, such as a (pressurized) vessel, especially an autoclave. In particular, the sampling arrangement may be functionally coupled to the reactor (for sampling). Further, the sampling arrangement may be functionally coupled to a gas inlet. Yet further, the sampling arrangement may be functionally coupled to a solvent inlet. Yet further, the sampling arrangement may be functionally coupled to an outlet, especially a dispenser.

The term "reactor" may herein especially refer to a reactor wherein a (bio)chemical transformation/reaction of interest takes place, such as an autoclave, a pressurized vessel, or a bioreactor.

In embodiments, the reactor may comprise a pressurized stream. A pressurized stream may herein refer to (a reactor that is operated in) continuous flow. For example, several sampling arrangements may be arranged along a reactor axis to sample as a function of the reactor axis.

In embodiments, the sampling arrangement may comprise a solvent compartment. The solvent compartment may especially be configured to host a solvent portion, especially a solvent portion of a predefined volume. The solvent portion may comprise a solvent. Essentially, any solvent suitable for the sample (and any intended post-processing) may be used, including, for example, relatively-challenging-in-use solvents such as acetone and THF. The person skilled in the art will be capable of selecting a suitable solvent for the specific application intended. The solvent compartment may especially be filled during the first operational mode, and may especially be emptied during the second operational mode.

In further embodiments, the sampling arrangement may comprise a sampling compartment. The sampling compartment may especially be configured to host a sample, especially a sample of a predefined volume. The sampling compartment may especially be filled during the first operational mode, and may especially be emptied during the second operational mode.

The term “compartment” may herein refer to a space for hosting a fluid. A compartment may, for example, comprise a microfluidic chamber and/or a loop.

Hence, in embodiments, the solvent compartment may comprise a microfluidic solvent chamber. In further embodiments, the solvent compartment may comprise a solvent loop.

Similarly, in embodiments, the sampling compartment may comprise a microfluidic sampling chamber. In further embodiments, the sampling compartment may comprise a sampling loop.

In embodiments, the sampling arrangement may comprise one or more multiple-position (multi-way) valves. The term “multi-position valve” may herein especially refer to a valve having a plurality of positions (or “connectors”), wherein the valve is configurable in at least a first configuration and a second configuration, wherein the valve provides fluid contact between the positions based on whether the valve is configured in the first configuration or in the second configuration. For example, a four-position two-way valve may in a first configuration (or: “first way”) provide a fluid contact between positions 1-2, and between positions 3-4, while providing fluid separation between positions 1-3, 1-4, 2-3, and 2-4, whereas in the second configuration (or: “second way”) the four-position two-way valve may provide a fluid contact between positions 1-4, and 2-3, while providing fluid separation between positions 1-2, 1-3, 4-2, and 4-3.

In embodiments, the sampling arrangement may be operable in a first operational mode and in a second operational mode.

In further embodiments, in the first operational mode the one or more multiple-position valves may be configured to provide fluid contact between a solvent inlet and the solvent compartment. In further embodiments, in the first operational mode the one or more multiple-position valves may be configured to provide fluid contact between the reactor and the sampling compartment. In further embodiments, in the first operational mode the one or more multiple-position valves may be configured to provide fluid separation between the solvent compartment and the sampling compartment.

In further embodiments, in the second operational mode the one or more multiple-position valves may be configured to provide fluid contact between (successively) a gas inlet, the solvent compartment, the sampling compartment, and an outlet. In particular, the gas inlet may be configured to provide an inlet gas to the outlet via the solvent compartment and the sampling compartment, wherein the solvent compartment is arranged upstream of the sampling compartment. Hence, in the second operational mode, the one or more multiple-position valves may be configured to provide a fluid contact between the gas inlet and the outlet via the solvent compartment and the sampling compartment, wherein the solvent compartment is arranged upstream of the sampling compartment (relative to the gas inlet), *i.e.*, the gas inlet is closer to the solvent compartment than to the sampling compartment.

During the second operational mode, the sampling compartment may be under constant positive pressure from the inlet gas, which may thereby prevent contamination with other gases, e.g., oxygen, from the outlet, which could otherwise potentially enter the reactor.

In further embodiments, in the second operational mode, the one or more multiple-position valves may be configured to provide fluid separation between the solvent inlet and the solvent compartment. In further embodiments, in the second operational mode, the one or more multiple-position valves may be configured to provide fluid separation between the reactor and the sampling compartment.

Hence, in specific embodiments, the sampling arrangement may comprise a solvent compartment, one or more multiple-position valves, and a sampling compartment, wherein in a first operational mode the one or more multiple-position valves are configured to provide: (i) fluid contact between a solvent inlet and the solvent compartment; (ii) fluid contact between the reactor and the sampling compartment; and (iii) fluid separation between the solvent compartment and the sampling compartment; and wherein in a second operational mode the one or more multiple-position valves are configured to provide fluid contact between (successively) a gas inlet, the solvent compartment, the sampling compartment, and an outlet.

In specific embodiments, the sampling arrangement may comprise a solvent compartment and a sampling compartment, wherein in a first operational mode, the sampling compartment is in fluid contact with the reactor such that the sampling compartment is filled with a sample (from the reactor), and wherein the solvent compartment is in fluid contact with a solvent inlet such that the solvent compartment is filled with a solvent portion (from the solvent inlet); and wherein in a second operational mode, a gas inlet may be in fluid contact with the solvent compartment, the sampling compartment and an outlet, wherein the gas inlet is configured to provide an inlet gas at a pressure above an atmospheric pressure; and wherein the solvent compartment and the sampling compartment are configured such that: (i) in the first operational mode the solvent compartment and the sampling compartment are in fluid separation; and (ii) in the second operational mode the solvent compartment is arranged upstream from the sampling compartment, and the sampling compartment is arranged upstream from the outlet.

In embodiments, the one or more multiple-position valves may comprise a 10-position valve, especially a 10-position two-way valve, wherein the 10-position valve is (at least) configurable in a first configuration (or "first way") and in a second configuration (or: "second way"). In further embodiments, the sampling arrangement may be in the first operational mode when the 10-position valve is in the first configuration, and the sampling arrangement may be in the second operational mode when the 10-position valve is in the second configuration.

It will be clear to the person skilled in the art that the beneficial arrangement described herein with respect to a 10-position valve may also be attained using a valve with more positions, especially by leaving one or more positions (essentially) unused. Hence, the term "10-position valve" may herein refer to a multi-position valve that has at least 10 positions, such as a 12-way valve. In further embodiments, the 10-position valve may have exactly 10 positions.

In principle, the same configurations attainable with a 10-position valve may be attained with two six-position valves operated in sync. The use of a plurality of valves may, however, inherently provide for more complex operations and the possibility that the valves are operated out of sync, which may provide undesirable fluid contacts. Therefore, the 10-position valve may be particularly beneficial as it may facilitate independently switching between the first operational mode and the second operational mode (of the sampling arrangement) without the need for any additional valves. Thereby, the 10-position valve may contribute both to preventing undesired fluid contacts, and to simplifying the (operation of) the sampling arrangement.

The sampling compartment and the solvent compartment may generally be configured to host predefined volumes of fluid. In particular, the solvent compartment may be configured to host a larger volume (of solvent portion) than the sampling compartment (of sample), which may be beneficial with regards to the washing of the sampling compartment by the solvent portion.

Hence, in embodiments, the sampling compartment may have a sampling volume V_{150}. In further embodiments, the sampling volume $V_{150} \geq 10$ μl, such as ≥ 30 μl, especially ≥ 50 μl, such as ≥ 100 μl. In further embodiments, the sampling volume $V_{150} \leq 10$ ml, such as ≤ 5 ml, especially ≤ 3 ml, such as ≤ 1 ml. In further embodiments, the sampling volume V_{150} may be selected from the range of 50 μl – 5 ml.

In further embodiments, the solvent compartment may have a solvent volume V_{130}, especially wherein $V_{130} \geq V_{150}$, such as $V_{130} \geq 2*V_{150}$, especially $V_{130} \geq 3*V_{150}$, such as $V_{130} \geq 5*V_{150}$, especially $V_{130} \geq 10*V_{150}$, such as $V_{130} \geq 20*V_{150}$.

In particular, a ratio between the solvent volume V_{130} and the sampling volume V_{150} may be selected such that the sampling compartment is sufficiently washed by the solvent portion. Hence, in further embodiments, a ratio between the solvent volume V_{130} and the sampling volume V_{130} V_{130}/V_{150} may be selected from the range of 2 - 20, especially from the range of 5 - 10.

In embodiments, the solvent compartment may be detachably attached to the one or more multiple-position valves. Thereby, the solvent compartment may be easily replaced by a solvent compartment of a different volume, allowing for increased flexibility in sampling.

In further embodiments, the sampling compartment may be detachably attached to the one or more multiple-position valves. Thereby, the sampling compartment may be easily replaced by a sampling compartment of a different volume, allowing for increased flexibility in sampling.

In embodiments the sampling arrangement may comprise or be functionally coupled to a dip-tube installation, wherein the dip-tube installation is configured for insertion into the reactor. The dip-tube installation may be beneficial for sampling from a pressurized reactor.

In embodiments wherein the sampling arrangement comprises or is functionally coupled to a pump, the sampling arrangement may comprise or be functionally coupled to a return capillary, wherein the return capillary is configured for insertion into the reactor. The return capillary may be particularly useful when the sampling system is daisy chained in a series of analytical devices. For example, in embodiments, a spectrometer may be functionally coupled to the sampling arrangement, especially to the sample flow path, such that both the sample can be measured, as well as such that spectroscopical changes on the corresponding mixture (as it was going through or is going through the loop only seconds earlier/later) can be observed. In further embodiments, the spectrometer may be selected from the group comprising a UV-VIS spectrometer, an IR spectrometer, a XAS spectrometer, and an NMR spectrometer.

In further embodiments, the sampling compartment may during operation be arranged external to the reactor, *i.e.*, the sampling arrangement may be configured such that during operation the sampling compartment is arranged external to the reactor. The external arrangement of the sampling compartment may be beneficial as the presence of a mass in the reactor may affect, especially perturb, conditions in the reactor, particularly with regards to homogenization, such as in the context of aeration, and surface effects.

In a second aspect, the invention may provide a system comprising the sampling arrangement according to the invention. In embodiments, the system may comprise a control system. In further embodiments, the control system may be configured to control the one or more multiple-position valves. In further embodiments, the control system may be configured to in a first mode of operation consecutively execute the first operational mode and the second operational mode.

Hence, the control system may facilitate (automated) sampling with the sampling arrangement. For example, in further embodiments, the control system may be configured to follow a predefined sampling (time) schedule. In further embodiments, the control system may be configured to execute the first operational mode (or the second operational mode) based on a signal, such as a sensor signal, especially a sensor signal related to a reactor status, more especially a sensor signal related to one or more previously taken samples.

For example, the control system may be configured to select a sampling interval based on the signal, especially based on a (first) sensor signal related to one or more previously taken samples and based on a second (sensor) signal related to a (mixture) volume in the reactor. Specifically, the control system may be configured to balance a need to sample at a specific timepoint versus the remaining (mixture) volume in the reactor. Sample too rarely, and the data may not adequately describe the process. Sample too often, and resources may be wasted and product may be lost. Hence, in embodiment, the control system may be configured to sample based on an (input) sensor signal, wherein the (input) sensor signal is related to one or more of a gas uptake (rate) (in the reactor), a calorimetry measurement (with respect to reaction energetics), and/or an spectroscopy measurement, especially an *in situ* spectroscopy measurement, more especially an operando spectroscopy measurement.

In embodiments, the control system may be configured to control the one or more multiple-position valves, *i.e.*, the control system may be configured to change the position of one or more of the one or more multiple-position valves, especially of all of the one or more multiple-position valves. Thereby, the control system may be configured to (have the system, especially the sampling arrangement) execute the first operational mode, and to (have the system, especially the sampling arrangement) execute the second operational mode, *i.e.*, the control system may be configured to (have the system, especially the sampling arrangement) switch between the first operational mode and the second operational mode.

In further embodiments, the control system may be configured to – in a first mode of operation - consecutively execute the first operational mode and the second operational mode, *i.e.*, the control system may be configured to execute the first operational mode a plurality of times interspersed with executing the second operational mode. In further embodiments, the control system may be configured to further execute a third operational mode, wherein the third operational mode may be temporally arranged prior to, in between or after the consecutive execution of the first operational mode and the second operational mode.

In further embodiments, the control system may be configured to in a first mode of operation consecutively and successively execute the first operational mode and the second operational mode.

In embodiments, the system may comprise or be functionally coupled to a gas supply. Especially, the gas supply may be functionally coupled to the gas inlet. Hence, during the second operational mode, the outlet may be in fluid contact with the gas supply via the solvent gas inlet, the solvent compartment and the sampling compartment, especially such that the gas supply provides an inlet gas to drive the solvent portion from the solvent compartment and the sample from the sampling compartment to the outlet.

The gas supply may, in further embodiments, be configured to provide an inert gas, especially an inert gas selected from the group comprising N_2 and Ar.

The gas supply may be configured to, during the second operational mode, provide an inlet gas to drive the solvent portion and the sample to the outlet. Therefore, the gas supply may be configured to provide an inlet gas at a pressure suitable to drive the solvent portion and the sample. Hence, in further embodiments, the gas supply may be configured to provide an inlet gas (to the gas inlet) at a pressure exceeding ambient pressure, especially a pressure exceeding atmospheric pressure, more especially a pressure of at least 1.1 atm, such as at least 2 bar, especially at least 3 bar, such as at least 5 bar, especially at least 10 bar. In particular, by providing the inlet gas at a higher pressure, the sample may be dispensed quicker, which may increase the overall sampling rate.

In further embodiments, the gas supply may be configured to provide an inlet gas (to the gas inlet) at a pressure of at most 1000 bar, such as at most 800 bar, especially at most 500 bar, such as at most 350 bar, especially at most 250 bar.

In embodiments, the system may comprise or be functionally coupled to a solvent supply. Especially, the solvent supply may be functionally coupled, especially fluidically coupled, to the solvent inlet. Hence, during the first operational mode, the solvent compartment may be in fluid contact with the solvent supply via the solvent inlet, especially such that a solvent portion is provided to the solvent compartment from the solvent supply (via the solvent inlet).

In further embodiments the system may comprise a solvent supply pressurizer. The solvent supply pressurizer may especially be configured to pressurize the solvent supply during the first operational mode. Pressurizing the solvent supply during the first operational mode may facilitate providing the solvent portion to the solvent compartment during the first operational mode. In particular, pressurizing the solvent supply may accelerate providing the solvent portion to the solvent compartment during the first operational mode, which may allow for faster sampling, which may facilitate a higher sampling frequency. In further embodiments, the solvent supply pressurizer may be configured to provide a pressure to a solvent in the solvent supply at least exceeding an ambient pressure, especially exceeding atmospheric pressure, more especially a pressure of at least 1.1 atm, such as at least 2 bar, especially at least 3 bar, such as at least 5 bar, especially at least 10 bar. In particular, by providing a higher pressure in the solvent supply, the solvent compartment may be filled with the solvent portion more quickly, which may increase the overall sampling rate. In further embodiments, the solvent supply pressurizer may be configured to provide a pressure to the solvent in the solvent supply of at most 350 bar, such as at most 250 bar, especially at most 100 bar, such as at most 80 bar, especially at most 50 bar, such as at most 20 bar. In embodiments, the solvent supply pressurizer may be configured to provide a pressure to the solvent in the solvent supply selected from the range of 5-50 bar, especially from the range of 10-20 bar.

In further embodiments, the solvent supply pressurizer may be configured to pressurize the solvent supply during the second operational mode. Pressurizing the solvent supply during the first operational mode may provide the benefit that the solvent supply may already be pressurized upon switching to the first operational mode, which may increase the initial rate of providing the solvent portion to the solvent compartment, and may thereby facilitate increasing the overall achievable sampling rate.

In further embodiments, the solvent supply pressurizer may be functionally coupled to the gas supply, wherein the gas supply is configured to provide an inlet gas to the solvent supply pressurizer to pressurize the solvent in the solvent supply.

The sample obtained from the reactor may be dispensed from the system, especially from the sampling arrangement. In particular, the system may comprise or be functionally coupled to a dispenser valve (or: “selector valve”). The dispenser valve may especially be functionally coupled to the outlet. In embodiments, the dispenser valve may be configured to dispense a fluid, especially comprising the solvent portion and the sample, to one or more outlet containers (or: “sampling containers”). In particular, the dispenser valve may be functionally coupled to one or more outlet containers, and depending on the position of the dispenser valve, the dispenser valve may be configured to dispense a fluid to an outlet container of the one or more outlet containers.

In particular, the dispenser valve may be configured in a dispensing position relative to an outlet container in order to dispense to the outlet container during the second operational mode. In embodiments, the dispenser valve may be configured to move into a desired (next) dispensing position during the first operational mode, thereby eliminating time loss for moving into position during the second operational mode.

In further embodiments, the control system may be configured to control the dispenser valve.

In further embodiments, the control system may be configured to generate a time stamp upon dispensing the sample (from the outlet, especially from the dispenser), thereby recording the actual time of sampling rather than a desired or planned time. Deviations between the actual sampling time and a desired sampling time may, for example, occur when a high sampling rate is desired and conditions in the reactor (unexpectedly) change and delay the filling of the sampling compartment. For example, the pressure in the reactor could decrease and/or the viscosity of the reactor contents could increase, thereby decreasing the sampling rate. Alternatively, based on a (sensor) signal a washing/rinsing operation may be needed/beneficial, which may delay the sampling. Further, a software and/or hardware issue could delay sampling. Hence, it may be beneficial to (consistently) record the actual time of sampling.

During the first operational mode, the sampling compartment may be filled with a sample from the reactor. If the reactor is operated at a pressure above the pressure in the sampling compartment at the start of the first operational mode, the sampling compartment may be filled due to the pressure difference. Hence, in embodiments, the sampling arrangement may be configured for sampling from a reactor, wherein during operation the reactor is operated at a pressure above atmospheric pressure, especially a pressure of at least 1.5 bar, such as at least 2 bar, especially at least 3 bar, such as at least 5 bar. Pressure-based sampling may be beneficial as the system may operate independent of a pump, which may otherwise be costly (especially because of moving pump parts). Hence, in further embodiments, the system, especially the sampling arrangement, may be a pump-free system.

However, in certain conditions a pump may also be beneficial, especially with regards to a reactor operated at or under atmospheric pressure, or in conditions wherein a higher sampling rate is desired.

Hence, in embodiments, the system may further comprise a pump. In such embodiments, in the first operational mode the one or more multiple-position valves may be configured to provide a fluid contact between the pump, the sampling compartment and the reactor.

In further embodiments, the pump may comprise a vacuum pump configured to provide a vacuum during the first operational mode to draw a sample from the reactor into the sampling compartment. The use of a vacuum pump to sample may inherently provide the benefit that no contamination may enter the reactor that is being sampled from. The vacuum pump may further be beneficial in that a “dead volume” with respect to sampling may be small.

In further embodiments, in the first operational mode the one or more multiple-position valves may provide a sampling pump flow path from the reactor via the sampling compartment back to the reactor, wherein the (circulation) pump is configured to control a sampling pump flow through (or: “along”) the sampling flow path. In such embodiment, the (circular) sampling pump flow path may provide the benefit that other systems, such as analytical equipment, may be conveniently functionally coupled to the sampling arrangement, especially at the sampling pump flow path, such as in a daisy chain.

In such a daisy chain, the fluid in the sampling pump flow path may spend some time outside of the (heated/cooled) reactor, which can lead to changes in temperature.

Hence, in embodiments, an insulation material may be arranged along (at least part of) the sampling pump flow path.

In further embodiments, a temperature control element may be arranged along (at least part of) the sampling pump flow path, wherein the temperature control element is configured to control the temperature of (a fluid in) the sampling pump flow, especially within a temperature range around the reactor temperature T_R, such as from the range of T_R-10° - T_R+10°.

In further embodiments, the control system may be configured to control the pump. In further embodiments, the control system may be configured to control a sampling flow from the reactor to the sampling compartment, especially by controlling the pump. In further embodiments, the control system may be configured to control a sampling pump flow from the reactor via the sampling compartment to the reactor, especially by controlling the pump.

In further embodiments, the control system may be configured to control a solvent loop flow from the solvent supply to the solvent loop.

In further embodiments, the control system may be configured to control an outlet flow from the gas supply via the solvent compartment and the sampling compartment to the outlet.

In embodiments, the control system may further be configured to control one or more of a gas pressure of inlet gas, a solvent supply pressure, a solvent compartment pressure, a sampling compartment pressure, and a reactor pressure.

Samples withdrawn from the reactor ideally remain representative of the reaction mixture at the time of acquisition (from the reactor). Hence, in embodiments, the sampling arrangement may be configured to quench (the reaction in) the sample with a quenching agent (also see below) or by imposing a temperature and/or pressure suitable to quench the (reaction in the) sample.

In embodiments, the system may comprise a temperature control system configured to control the temperature of the system, especially of one or more of (i) the one or more multi-position valves, (ii) the sampling compartment, (iii) the outlet, (iv) the sampling flow path, (v) the solvent flow path, (vi) the outlet flow path, (vii) the dispenser, and (viii) the outlet container. In embodiments, the temperature control system may be configured to quench the (reaction in the) sample. In further embodiments, the temperature control system may be configured to provide a temperature selected to accommodate sampling of viscous reaction mixtures and “solid samples”, wherein “solid samples” refers to samples that may solidify at room temperature, but are liquid under the reactor conditions. In the absence of a temperature control system, such a “solid sample” may solidify in the sampling arrangement, which may generally be undesirable.

In further embodiments, the control system may be configured to control the temperature control system.

In further embodiments, the temperature control system may be configured to control the temperature control element.

In specific embodiments, the system may comprise a gas supply, a solvent supply, a solvent compartment, a sampling compartment, and an outlet, wherein the system is operable in a first operational mode and in a second operational mode, wherein in the first operational mode, the sampling compartment is in fluid contact with the reactor such that the sampling compartment is filled with a sample (from the reactor), and wherein the solvent compartment is in fluid contact with the solvent supply such that the solvent compartment is filled with a solvent portion (from the solvent supply); wherein in the second operational mode, the gas supply is in fluid contact with the solvent compartment, the sampling compartment and the outlet, wherein the gas supply is configured to provide an inlet gas at a pressure above an atmospheric pressure; and wherein the solvent compartment and the sampling compartment are configured such that: (i) in the first operational mode the solvent compartment and the sampling compartment are in fluid separation; and (ii) in the second operational mode the solvent compartment is arranged upstream (with respect to a gas flow from the gas inlet) from the sampling compartment, and the sampling compartment is arranged upstream from the outlet.

In a further aspect, the invention may provide a method for sampling from a reactor using the sampling arrangement according to the invention or the system according to the invention. Especially, the method may comprise consecutively executing the first operational mode and the second operational mode, especially successively and consecutively executing the first operational mode and the second operational mode. In embodiments, the method may comprise providing an inlet gas from the gas inlet during at least part of the second operational mode.

In embodiments, the method may comprise switching between (executing) the first operational mode and (executing) the second operational mode using the one or more multiple-position valves. Hence, the method may comprise switching the one or more multiple-position valves between a first configuration and a second configuration, wherein in the first configuration the one or more multiple-position valves provide the first operational mode, and wherein in the second configuration the one or more multiple-position valves provide the second operational mode.

In embodiments, the method may comprise providing a lower pressure in the sampling compartment than in the reactor during at least part of the first operational mode. Hence, the method may comprise filling the sampling compartment from the reactor based on a pressure difference.

In further embodiments, the method may comprise providing during at least part of the first operational mode a solvent at the solvent inlet with a solvent pressure exceeding the pressure in the solvent compartment. In particular, in embodiments wherein the solvent inlet is functionally coupled to a solvent supply, the method may comprise providing a lower pressure in the solvent compartment than in the solvent supply during at least part of the first operational mode. Hence, the method may comprise filling the solvent compartment (from the solvent inlet, especially from the solvent supply) based on a pressure difference.

During the second operational mode, the inlet gas provided from the gas inlet may drive the solvent portion and the sample to the outlet, especially through the outlet. Therefore, in embodiments, the inlet gas may be provided at a pressure suitable to drive the solvent portion and the sample to the outlet. In particular, the method may comprise providing the inlet gas at a pressure exceeding ambient pressure, especially a pressure exceeding atmospheric pressure, more especially a pressure of at least 1.1 atm, such as at least 2 bar, especially at least 3 bar such as at least 5 bar. In particular, by providing the inlet gas at a higher pressure, the sample may be dispensed quicker, which may increase the overall sampling rate.

In further embodiments, the method may comprise providing the inlet gas at a pressure of at most 1000 bar, such as at most 800 bar, especially at most 500 bar, such as at most 350 bar, especially at most 250 bar.

The inlet gas may come in direct contact with the sample. Hence, it may be beneficial for the inlet gas to be inert with respect to the sample or, alternatively, to interact with the sample in a desired manner.

Hence, in embodiments, the inlet gas may be an inert gas, especially an inert gas selected from the group comprising CO_2, SF_6, He, Ne, Kr, Xe, N_2 and Ar, more especially an inert gas selected from the group comprising N_2 and Ar, especially Ar. Ar may be beneficial in view of its high density as it may effectively blanket the sample. In particular, the inert gas is inert with respect to the (compounds in the) reaction mixture, especially (potentially) in the sample.

In further embodiments, the inlet gas may be selected to quench the sample, *i.e.*, to “freeze” the current composition of the sample with respect to the reaction(s) performed in the reactor. Hence, in further embodiments, the inlet gas may comprise a quenching agent. The term “quenching agent” may herein especially refer to a compound suitable to quench the sample.

Similarly, in embodiments, the solvent (comprised by the solvent portion) may be selected to quench the sample. Hence, in further embodiments, the solvent, especially the solvent portion, may comprise a quenching agent.

In further embodiments, the reaction may be quenched due to a pressure difference. In particular, the reaction may require a specific pressure regime, and the gas inlet may be configured to provide the inlet gas at a pressure outside of the pressure regime.

In particular, the term “quench” may herein refer to (essentially) instantaneously stop the reaction of interest, such that the reaction mixture is (essentially) stable over time and can be analyzed accurately (and repeatedly if required). The person skilled in the art will be capable of selecting a gaseous quenching agent and/or liquid quenching agent and/or quenching conditions for the reaction of interest.

In specific embodiments, the method may comprise consecutively executing the first operational mode and the second operational mode, wherein the method may comprise in the first operational mode (i) filling the sampling compartment with a sample (from the reactor); (ii) filling the solvent compartment with a solvent portion (from the solvent inlet); and wherein the method may comprise providing an inlet gas from the gas inlet during at least part of the second operational mode, especially thereby providing the solvent portion and the sample to the outlet.

In a further aspect, the invention may provide a computer program product comprising instructions for execution on a computer wherein the instructions, when executed by the computer, cause the computer to carry out the method according to the invention. In embodiments, the computer may especially comprise the control system (comprised by the system of the invention).

In a further aspect, the invention may provide a use of the sampling arrangement according to any one of claims 1-3 to sample from a reactor, especially from a reactor under a controlled atmosphere.

The term “controlled atmosphere” may herein refer to conditions with (sufficiently) accurate control of one or more of temperature, stirring rate, pressure, internal atmosphere, etc.

The terms “upstream” and “downstream” herein relate to an arrangement of items or features relative to the propagation of gas from a gas supply, wherein relative to a first position within a gas flow from the gas supply, a second position in the gas flow closer to the gas supply is “upstream”, and a third position within the gas flow further away from the gas supply is “downstream”.

The embodiments described herein are not limited to a single aspect of the invention. For example, an embodiment describing the sampling arrangement with respect to the operational modes may, for example, further relate to the system and the method. Similarly, an embodiment of the method describing the solvent or the inlet gas may further relate to the (operation of) the sampling arrangement or the system. In particular, an embodiment of the method describing an operation of the sampling arrangement (or the system) may indicate that the sampling arrangement (or the system) may, in embodiments, be configured for and/or be suitable for the operation.

BRIEF DESCRIPTION OF THE DRAWINGS

Embodiments of the invention will now be described, by way of example only, with reference to the accompanying schematic drawings in which corresponding reference symbols indicate corresponding parts, and in which: Fig. 1A-B schematically depict an embodiment of the sampling arrangement (105). Fig. 2 schematically depicts an embodiment of the system (100). The schematic drawings are not necessarily on scale.

DETAILED DESCRIPTION OF THE EMBODIMENTS

Fig. 1A-B schematically depict an embodiment of a sampling arrangement 105 for sampling from a reactor 50. The sampling arrangement 105 comprises a solvent compartment 130, one or more multiple-position valves 140, and a sampling compartment 150. The sampling arrangement may be configured operable in a first operational mode 10 and a second operational mode 20. In the depicted embodiments, the one or more multiple-position valves 140 comprises a 10-position valve, especially a 10-position two-way valve. The one or more multiple-position valves 140, especially the 10-position valve, are operable in a first configuration and in a second configuration, wherein the sampling arrangement 105 is in the first operational mode 10 when the one or more multiple-position valves 140 are in the first configuration, and wherein the sampling arrangement 105 is in the second operational mode 20 when the one or more multiple-position valves 140 are in the second configuration. The solid lines in Fig. 1A indicate fluid contacts between (adjacent) positions of the 10-position valve in the first configuration, and the solid lines in Fig. 1B indicate the fluid contacts between (adjacent) positions of the 10-position valve in the second configuration (Fig. 1B).

Fig. 1A depicts an embodiment of the sampling arrangement 105 in the first operational mode 10. In the first operational mode 10 the one or more multiple-position valves 140 are configured to provide: a fluid contact between a solvent inlet 120 and the solvent compartment 130; a fluid contact between the reactor 50 and the sampling compartment 150; and fluid separation between the solvent compartment 130 and the sampling compartment 150. In particular, in further embodiments, in the first operational mode 10 the one or more multiple position valves 140 may be configured to provide a solvent flow path 13 from the solvent inlet 120 to the solvent compartment 130. In further embodiments, in the first operational mode 10 the one or more multiple position valves 140 may be configured to provide a sampling flow path 15 from the reactor 50 to the sampling compartment 150.

In embodiments, the sampling arrangement 105 may further comprise or be functionally coupled to a pump 170, especially wherein in the first operational mode 10 the one or more multiple-position valves 140 are configured to provide a fluid contact between the pump 170, the sampling compartment 150 and the reactor 50. In further embodiments, in the first operational mode the one or more multiple-position valves 140 may provide a sampling pump flow path 17 from the reactor 50 via the sampling compartment 150 back to the reactor 50, especially wherein the pump 170 is configured to control a sampling flow through the sampling pump flow path 17. The sampling pump flow path 17 may especially comprise the sampling flow path 15.

Fig. 1B depicts an embodiment of the sampling arrangement 105 in the second operational mode 20. In the second operational mode 20 the one or more multiple-position valves 140 are configured to provide: fluid contact between (successively) a gas inlet 110, the solvent compartment 130, the sampling compartment 150, and an outlet 160.

In further embodiments, in the second operational mode 20 the one or more multiple-position valves 140 are configured to provide fluid separation between the solvent inlet 120 and the solvent compartment 130. In further embodiments, in the second operational mode 20 the one or more multiple-position valves 140 are configured to provide fluid separation between the sampling compartment 150 and the reactor 50.

In the depicted embodiment, the sampling arrangement 105 comprises a 10-position valve, wherein the 10-position valves comprises 10 positions (P_1-P_{10}), wherein: a first position P_1 indicates a gas inlet position; a second position P_2 indicates a solvent compartment inlet; a third position P_3 indicates a solvent inlet position; a fourth position P_4 indicates a solvent stop; a fifth position P_5 indicates a solvent outlet position; a sixth position P_6 indicates a sampling compartment inlet; a seventh position P_7 indicates a reactor inlet position; an eighth position P_8 indicates a sampling stop; a ninth position P_9 indicates a sampling compartment outlet; and a tenth position P_{10} indicates an outlet position. Especially, in the first operational mode 10: P_{10} may be in fluid contact with P_1; P_2 may be in fluid contact with P_3; P_4 may be in fluid contact with P_5; P_6 may be in fluid contact with P_7; and P_8 may be in fluid contact with P_9, and in the second operational mode 20: P_1 may be in fluid contact with P_2; P_3 may be in fluid contact with P_4; P_5 may be in fluid contact with P_6; P_7 may be in fluid contact with P_8; and P_9 may be in fluid contact with P_{10}.

In further embodiments, the first position P_1 is functionally coupled to the gas inlet 110, the third position P_3 is functionally coupled to the solvent inlet 120, the seventh position P_7 is functionally coupled to the reactor 50, and the tenth position P_{10} is functionally coupled to the outlet. In further embodiments, the fourth position P_4 may be functionally coupled to a blinding nut. Similarly, in further embodiments, the eighth position P_8 may be functionally coupled to a blinding nut.

In further embodiments, the sampling compartment 150 may have a sampling volume V_{150} selected from the range of 50 µl – 5 ml and the solvent compartment 130 may have a solvent volume $V_{130} \geq 2V_{150}$. The sampling volume may herein specifically refer to the total volume in between the respective connected positions (P_6, P_9) of the multi-position valve, i.e.. it may refer to the volume of the sampling compartment 150 as well as the volume of any connected tubing. Essentially, however, the volume of the sampling compartment 150 primarily dictates the sampling volume. Further, it will be clear to the person skilled in the art that in many applications the exact available sampling volume may not directly dictate the volume of the sample. For example, a 50 µl loop used with sampling from a pressurized autoclave may not give exactly 50 µl of liquid. For example, prior to sampling the loop may be filled (with a gas) at a pressure of 1 atm, which may be compressed by an incoming liquid at an operating pressure (i.e., approx. to 1/50th of the volume at an operating pressure of 50 atm). It will further be clear to the person skilled in the art that a deviation in the exact sampling volume can be addressed in downstream analyses, particularly when an internal standard is used.

In the depicted embodiment, the sampling compartment 150 is (configured to be) arranged external to the reactor 50 during operation of the sampling arrangement 150. However, in further embodiments, the sampling compartment 150 may be (configured to be) arranged inside of the reactor 50 during operation of the sampling arrangement 150.

Fig. 2 schematically depicts an embodiment of the system 100 comprising the sampling arrangement 105. In the depicted embodiment, the system 100 further comprises a control system 300, wherein the control system 300 is configured to control the one or more multiple-position valves 140. In further embodiments, the control system may be configured to in a first mode of operation consecutively execute the first operational mode 10 and the second operational mode 20.

In the depicted embodiment, the system comprises or is functionally coupled to a gas supply 115, wherein the gas supply 115 is functionally coupled to the gas inlet 110.

In the depicted embodiment, the system 100 comprises or is functionally coupled to a solvent supply 125, wherein the solvent supply 125 is functionally coupled to the solvent inlet 120. Further, the system 100 comprises a solvent supply pressurizer 121 configured to pressurize the solvent supply 125 during the first operational mode 10. In the depicted embodiment, the solvent supply pressurizer 121 is functionally coupled to the gas supply 115, especially via a solvent supply valve 124. Especially, the gas supply 115 may be configured to provide a gas, especially the inlet gas, to pressurize the solvent in the solvent supply 125. In further embodiments, the solvent supply pressurizer 121 may (alternatively) be functionally coupled to a second gas supply.

The system 100, in the depicted embodiment, further comprises or is functionally coupled to a dispenser valve 164, wherein the dispenser valve 164 is functionally coupled to the outlet 160. The dispenser valve 164 may be configured to dispense fluid, especially the solvent portion and the sample, to an outlet container 60. In particular, the dispenser valve 164 may be configured to dispense successive samples (with corresponding solvent portions) to different outlet containers 60. In further embodiments, the control system 300 may be configured to control the dispenser valve 164.

In embodiments, the outlet container 60 may be a chromatography vial, especially a chromatography vial suitable for subsequent analysis, such as for GC or HPLC analysis.

In embodiments, the outlet container 60 may comprise a quenching agent configured to quench the sample upon being dispensed to the outlet container 60.

In further embodiments, the system 100 may further comprise a pump 170, especially wherein in the first operational mode 10 the one or more multiple-position valves 140 are configured to provide a fluid contact between the pump 170, the sampling compartment 150 and the reactor 50. In further embodiments, in the first operational mode the one or more multiple-position valves 140 provide a sampling pump flow path 17 from the reactor 50 via the sampling compartment 150 back to the reactor 50, especially wherein the pump 170 is configured to control a sampling flow through the sampling pump flow path 17.

In such embodiments, the method may in the first operational mode 10 comprise providing a sampling pump flow, especially along a sampling pump flow path 17, from the reactor 50 via the sampling compartment 150 to the reactor 50.

The system 100 may be configured to drive fluid based on pressure differences, *i.e.*, the system may be configured for one or more of: (i) filling the sampling compartment 150 with a sample from the reactor 50 based on a pressure difference, (ii) filling the solvent compartment 130 with a solvent portion from the solvent inlet 120, especially the solvent supply 125, based on a pressure difference, and (iii) driving the solvent portion and the sample to the outlet 160 by providing a (pressurized) inlet gas from the gas inlet 110. Hence, in further embodiments, the control system 300 may be configured to control one or more of a gas pressure of inlet gas, a solvent supply pressure, a solvent compartment pressure, a sampling compartment pressure, and a reactor pressure.

Fig. 1A-B and Fig. 2 further schematically depict embodiments of the method for sampling from a reactor 50. The method may comprise consecutively executing the first operational mode 10 and the second operational mode 20. The method may further comprise providing an inlet gas from the gas inlet 110, especially from the gas supply 115, during at least part of the second operational mode 20.

In further embodiments, the method may comprise providing one or more flow paths. In further embodiments, in the first operational mode 10 the method may comprise providing a solvent flow, especially along a solvent flow path 13, from the solvent inlet 120, especially from the solvent supply 125, to the solvent compartment 130. In further embodiments, in the first operational mode 10 the method may comprise providing a sampling flow, especially along a sampling flow path 15, from the reactor 50 to the sampling compartment 150.

In further embodiments, the method may comprise providing a lower pressure in the sampling compartment 150 than in the reactor 50 during at least part of the first operational mode 10, especially such that the sampling compartment 150 is filled with a sample from the reactor 50. In further embodiments, the method may comprise providing during at least part of the first operational mode 10 a solvent at the solvent inlet 120, especially from the solvent supply 125, with a solvent pressure exceeding the pressure in the solvent compartment 130, especially such that the solvent compartment 130 is filled with a solvent portion from the solvent inlet 120, especially from the solvent supply 125.

In further embodiments, in the second operational mode 20 the method may comprise providing an outlet flow, especially along an outlet flow path 26, from the gas inlet 110, especially from the gas supply 115, via the solvent compartment 130 and the sampling compartment 150 to the outlet 160. In further embodiments, the method may comprise (during the second operational mode 20) providing the inlet gas at a pressure suitable to drive the solvent portion and the sample to the outlet 160, especially providing the inlet gas at a pressure above atmospheric pressure.

In embodiments, the method may comprise switching between the first operational mode 10 and the second operational mode 20 using the one or more multiple-position valves, especially using the 10-position valve.

Fig. 1A-B and Fig. 2 further depict a use of the sampling arrangement 105 according to sample from a reactor 50, wherein the reactor 50 is especially (operated) under a controlled atmosphere.

The term “plurality” refers to two or more. Furthermore, the terms “a plurality of” and “a number of” may be used interchangeably.

The terms “substantially” or “essentially” herein, and similar terms, will be understood by the person skilled in the art. The terms “substantially” or “essentially” may also include embodiments with “entirely”, “completely”, “all”, etc. Hence, in embodiments the adjective substantially or essentially may also be removed. Where applicable, the term “substantially” or the term “essentially” may also relate to 90% or higher, such as 95% or higher, especially 99% or higher, even more especially 99.5% or higher, including 100%. Moreover, the terms ”about” and “approximately” may also relate to 90% or higher, such as 95% or higher, especially 99% or higher, even more especially 99.5% or higher, including 100%. For numerical values it is to be understood that the terms “substantially”, “essentially”, “about”, and “approximately” may also relate to the range of 90% - 110%, such as 95%-105%, especially 99%-101% of the values(s) it refers to.

The term “comprise” includes also embodiments wherein the term “comprises” means “consists of”.

The term “and/or” especially relates to one or more of the items mentioned before and after “and/or”. For instance, a phrase “item 1 and/or item 2” and similar phrases may relate to one or more of item 1 and item 2. The term "comprising" may in an embodiment refer to "consisting of" but may in another embodiment also refer to "containing at least the defined species and optionally one or more other species".

Furthermore, the terms first, second, third and the like in the description and in the claims, are used for distinguishing between similar elements and not necessarily for describing a sequential or chronological order. It is to be understood that the terms so used are interchangeable under appropriate circumstances and that the embodiments of the invention described herein are capable of operation in other sequences than described or illustrated herein.

The devices, apparatus, or systems may herein amongst others be described during operation. As will be clear to the person skilled in the art, the invention is not limited to methods of operation, or devices, apparatus, or systems in operation.

The term “further embodiment” and similar terms may refer to an embodiment comprising the features of the previously discussed embodiment, but may also refer to an alternative embodiment.

It should be noted that the above-mentioned embodiments illustrate rather than limit the invention, and that those skilled in the art will be able to design many alternative embodiments without departing from the scope of the appended claims.

In the claims, any reference signs placed between parentheses shall not be construed as limiting the claim.

Use of the verb "to comprise" and its conjugations does not exclude the presence of elements or steps other than those stated in a claim. Unless the context clearly requires otherwise, throughout the description and the claims, the words “comprise”, “comprising”, “include”, “including”, “contain”, “containing” and the like are to be construed in an inclusive sense as opposed to an exclusive or exhaustive sense; that is to say, in the sense of “including, but not limited to”.

The article "a" or "an" preceding an element does not exclude the presence of a plurality of such elements.

The invention may be implemented by means of hardware comprising several distinct elements, and by means of a suitably programmed computer. In a device claim, or an apparatus claim, or a system claim, enumerating several means, several of these means may be embodied by one and the same item of hardware. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage.

The invention also provides a control system that may control the device, apparatus, or system, or that may execute the herein described method or process. Yet further, the invention also provides a computer program product, when running on a computer which is functionally coupled to or comprised by the device, apparatus, or system, controls one or more controllable elements of such device, apparatus, or system.

The invention further applies to a device, apparatus, or system comprising one or more of the characterizing features described in the description and/or shown in the attached drawings. The invention further pertains to a method or process comprising one or more of the characterizing features described in the description and/or shown in the attached drawings. Moreover, if a method or an embodiment of the method is described being executed in a device, apparatus, or system, it will be understood that the device, apparatus, or system is suitable for or configured for (executing) the method or the embodiment of the method respectively.

The various aspects discussed in this patent can be combined in order to provide additional advantages. Further, the person skilled in the art will understand that embodiments can be combined, and that also more than two embodiments can be combined. Furthermore, some of the features can form the basis for one or more divisional applications.

Conclusies

1. Een bemonsteringsinrichting (105) voor bemonstering uit een reactor (50), waarbij de bemonsteringsinrichting (105) een gasinlaat (110), een oplosmiddelinlaat (120), een oplosmiddelcompartiment (130), één of meer multipositiekleppen (140), een bemonsteringscompartiment (150) en een uitlaat omvat, waarbij in een eerste operationele modus (10) de één of meer multipositiekleppen (140) geconfigureerd zijn om te verschaffen:

fluïdisch contact tussen de oplosmiddelinlaat (120) en het oplosmiddelcompartiment (130);

fluïdisch contact tussen de reactor (50) en het bemonsteringscompartiment (150); en

fluïdische scheiding tussen het oplosmiddelcompartiment (130) en het bemonsteringscompartiment (150);

en waarbij in een tweede operationele modus (20) de één of meer multipositiekleppen (140) geconfigureerd zijn om te verschaffen:

fluïdisch contact tussen de gasinlaat (110), het oplosmiddelcompartiment (130), het bemonsteringscompartiment (150) en de uitlaat (160).

2. De bemonsteringsinrichting (105) volgens conclusie 1, waarbij de één of meer multipositiekleppen (140) een 10-positieklep omvatten, waarbij de 10-positieklep in een eerste configuratie en in een tweede configuratie configureerbaar is, waarbij de bemonsteringsinrichting (105) in de eerste operationele modus (10) is wanneer de 10-positieklep in de eerste configuratie is, en waarbij de bemonsteringsinrichting (105) in de tweede operationele modus (20) is wanneer de 10-positieklep in de tweede configuratie is.

3. De bemonsteringsinrichting (105) volgens één van de voorgaande conclusies, waarbij het bemonsteringscompartiment (150) een bemonsteringsvolume V_{150} gekozen uit het bereik van 50 µl - 5 ml heeft, en waarbij het oplosmiddelcompartiment (130) een oplosmiddelvolume V_{130} heeft, waarbij $V_{130} \geq 2*V_{150}$.

4. De bemonsteringsinrichting (105) volgens één van de voorgaande conclusies, waarbij tijdens bedrijf van de bemonsteringsinrichting (105) het bemonsteringscompartiment (150) buiten de reactor (50) gerangschikt is.

5. Een systeem (100) omvattende de bemonsteringsinrichting (105) volgens één van de voorgaande conclusies, waarbij het systeem (100) een besturingssysteem (300) omvat, waarbij het besturingssysteem (300) geconfigureerd is om de één of meer multipositiekleppen (140) te controleren, en waarbij het besturingssysteem (300) geconfigureerd is om in een eerste operatiemodus achtereenvolgens de eerste operationele modus (10) en de tweede operationele modus (20) uit te voeren.

6. Het systeem (100) volgens conclusie 5, waarbij het systeem (100) een oplosmiddeltoevoer (125) omvat of daar functioneel aan gekoppeld is, waarbij de oplosmiddeltoevoer (125) fluïdisch aan de oplosmiddelinlaat (120) gekoppeld is, waarbij het systeem (100) een oplosmiddeltoevoerdrukverschaffer (121) omvat die geconfigureerd is om de oplosmiddeltoevoer (125) tijdens de eerste operationele modus (10) onder druk te zetten.

7. Het systeem (100) volgens één van de voorgaande conclusies 5-6, waarbij het systeem (100) een dispenserklep (164) omvat of daar functioneel aan gekoppeld is, waarbij de uitlaat (160) functioneel aan de dispenserklep (164) gekoppeld is, en waarbij de dispenserklep (164) geconfigureerd is om fluïdum aan één of meer uitlaatcontainers (60) af te geven.

8. Het systeem (100) volgens één van de voorgaande conclusies 5-7, waarbij het systeem (100) verder een pomp (170) omvat, waarbij in de eerste operationele modus (10) de één of meer multipositiekleppen (140) geconfigureerd zijn om een fluïdisch contact te verschaffen tussen de pomp (170), het bemonsteringscompartiment (150) en de reactor (50).

9. Het systeem (100) volgens conclusie 8, waarbij in de eerste operationele modus de één of meer multipositiekleppen (140) een bemonsteringspompstroompad (17) vanuit de reactor (50) via het bemonsteringscompartiment (150) terug naar de reactor (50) verschaffen, waarbij de pomp (170) geconfigureerd is om een bemonsteringspompstroom door het bemonsteringspompstroompad (17) te controleren.

10. Het systeem (100) volgens één van de voorgaande conclusies 5-9, waarbij het besturingssysteem (300) geconfigureerd is om één of meer van een gasdruk van inlaatgas, een oplosmiddeltoevoerdruk, een oplosmiddelcompartimentdruk, een bemonsteringscompartimentdruk en een reactordruk te controleren.

11. Een werkwijze voor het bemonsteren uit een reactor (50) met behulp van de bemonsteringsinrichting (105) volgens één van de voorgaande conclusies 1-4 of het systeem (100) volgens één van de voorgaande conclusies 5-10, de werkwijze omvattende het opeenvolgend uitvoeren van de eerste operationele modus (10) en de tweede operationele modus (20), waarbij de werkwijze verder het verschaffen van een inlaatgas uit de gasinlaat (110) gedurende ten minste een deel van de tweede operationele modus (20) omvat.

12. De werkwijze volgens conclusie 11, waarbij de werkwijze het schakelen tussen de eerste operationele modus (10) en de tweede operationele modus (20) met behulp van de één of meer multipositiekleppen (140) omvat.

13. De werkwijze volgens één van de voorgaande conclusies 11-12, waarbij de werkwijze omvat:

het verschaffen van een lagere druk in het bemonsteringscompartiment (150) dan in de reactor (50) gedurende ten minste een deel van de eerste operationele modus (10); en/of

het gedurende ten minste een deel van de eerste operationele modus (10) verschaffen van een oplosmiddel bij de oplosmiddelinlaat (120) met een oplosmiddeldruk die de druk in het oplosmiddelcompartiment (130) overschrijdt.

14. De werkwijze volgens één van de voorgaande conclusies 11-13, waarbij de werkwijze het verschaffen van het inlaatgas op een druk boven atmosferische druk omvat, en waarbij het inlaatgas een inert gas is.

15. Gebruik van de bemonsteringsinrichting volgens één van de conclusies 1-3 om uit een reactor te bemonsteren.

16. Gebruik volgens conclusie 15, waarbij de reactor zich onder een gecontroleerde atmosfeer bevindt.

1/2

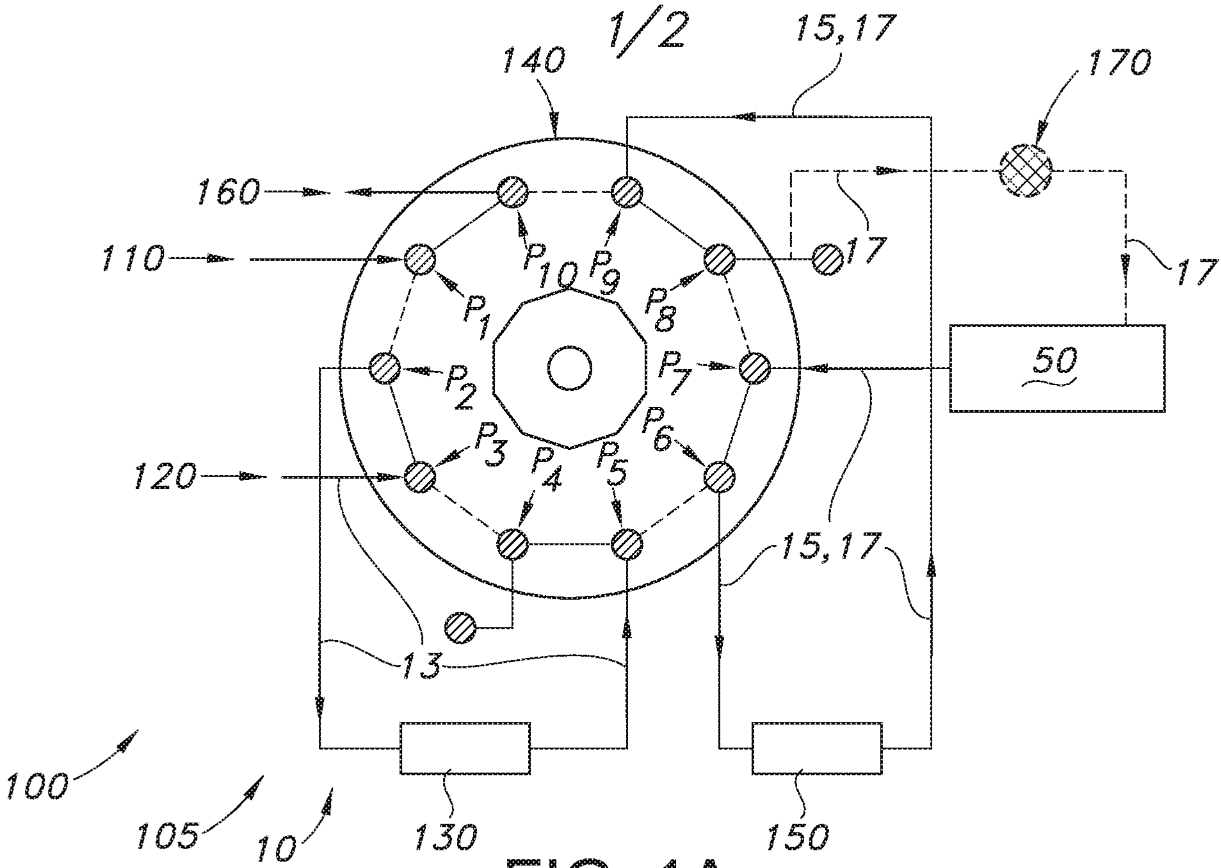

FIG. 1A

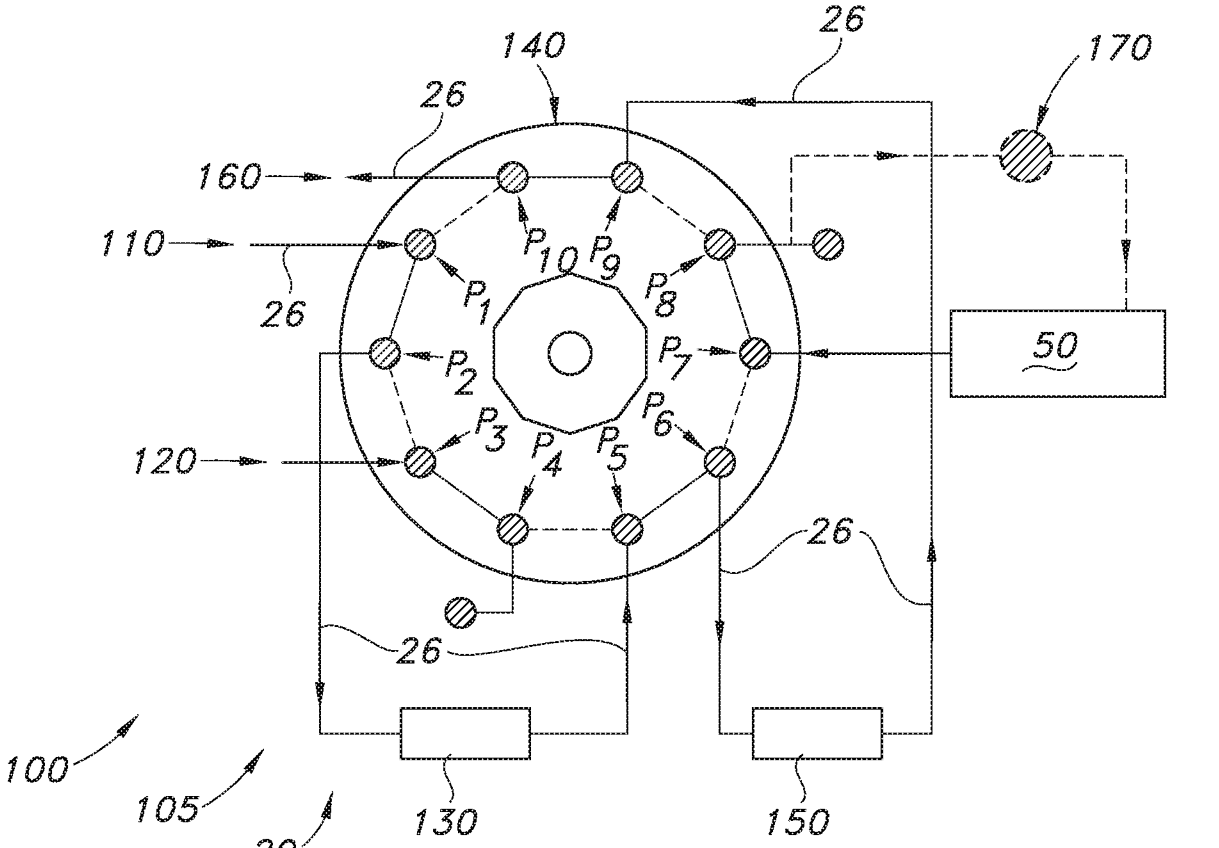

FIG. 1B

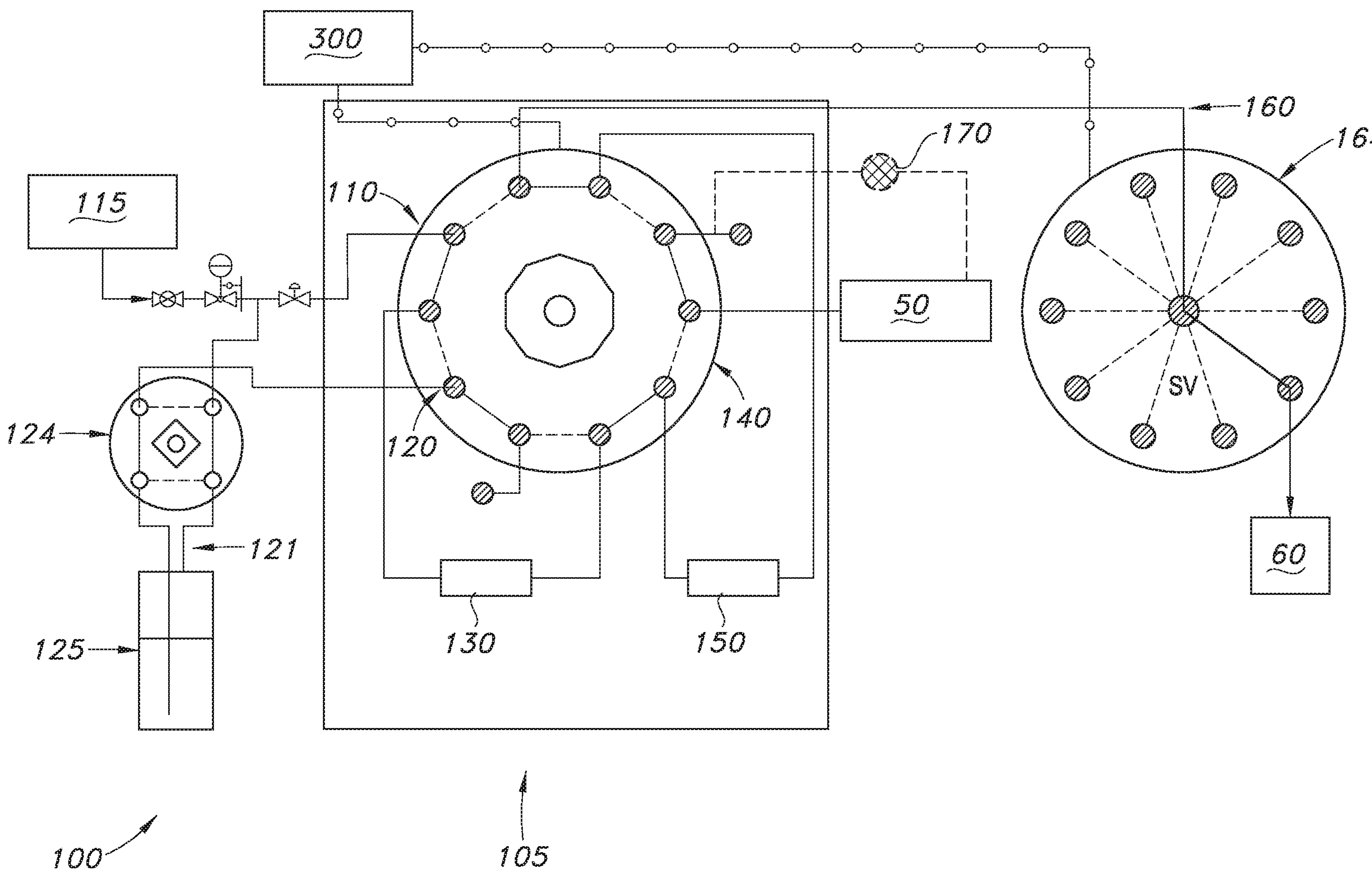
300
115
110
120
124
121
125
130
150
140
170
50
160
164
SV
60
100
105

FIG. 2

SAMENWERKINGSVERDRAG (PCT)

RAPPORT BETREFFENDE NIEUWHEIDSONDERZOEK VAN INTERNATIONAAL TYPE

IDENTIFICATIE VAN DE NATIONALE AANVRAGE	**KENMERK VAN DE AANVRAGER OF VAN DE GEMACHTIGDE** **P1600136NL00**
Nederlands aanvraag nr. **2024908**	Indieningsdatum **14-02-2020**
	Ingeroepen voorrangsdatum
Aanvrager (Naam) **Technische Universiteit Delft**	
Datum van het verzoek voor een onderzoek van internationaal type **21-03-2020**	Door de Instantie voor Internationaal Onderzoek aan het verzoek voor een onderzoek van internationaal type toegekend nr. **SN75765**

I. CLASSIFICATIE VAN HET ONDERWERP (bij toepassing van verschillende classificaties, alle classificatiesymbolen opgeven)

Volgens de internationale classificatie (IPC)

Zie onderzoeksrapport

II. ONDERZOCHTE GEBIEDEN VAN DE TECHNIEK

Onderzochte minimumdocumentatie

Classificatiesysteem	Classificatiesymbolen
IPC	**Zie onderzoeksrapport**

Onderzochte andere documentatie dan de minimum documentatie, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen

III.	☐	**GEEN ONDERZOEK MOGELIJK VOOR BEPAALDE CONCLUSIES**	(opmerkingen op aanvullingsblad)
IV.	☐	**GEBREK AAN EENHEID VAN UITVINDING**	(opmerkingen op aanvullingsblad)

Form PCT/ISA 201 A (11/2000)

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Nummer van het verzoek om een onderzoek naar de stand van de techniek
NL 2024908

A. CLASSIFICATIE VAN HET ONDERWERP
INV. G01N35/10
ADD. G01N1/20

Volgens de Internationale Classificatie van octrooien (IPC) of zowel volgens de nationale classificatie als volgens de IPC.

B. ONDERZOCHTE GEBIEDEN VAN DE TECHNIEK

Onderzochte miminum documentatie (classificatie gevolgd door classificatiesymbolen)
G01N B01J

Onderzochte andere documentatie dan de mimimum documentatie, voor dergelijke documenten, voor zover dergelijke documenten in de onderzochte gebieden zijn opgenomen

Tijdens het onderzoek geraadpleegde elektronische gegevensbestanden (naam van de gegevensbestanden en, waar uitvoerbaar, gebruikte trefwoorden)

EPO-Internal

C. VAN BELANG GEACHTE DOCUMENTEN

Categorie °	Geciteerde documenten, eventueel met aanduiding van speciaal van belang zijnde passages	Van belang voor conclusie nr.
A	EP 2 711 076 A2 (TOTAL SYNTHESIS LTD [CA]) 26 maart 2014 (2014-03-26) * alineas [0082] - [0091], [0113] - [0116]; figuren 2-5,12,13 * -----	1-16
A	EP 3 043 178 A1 (WATERS TECHNOLOGIES CORP [US]) 13 juli 2016 (2016-07-13) * alineas [0054], [0055]; figuren 2,3 * -----	1-16
A	US 2013/240449 A1 (COLLIER LEE [US]) 19 september 2013 (2013-09-19) * alinea [0052]; figuur 4 * -----	1-16

☐ Verdere documenten worden vermeld in het vervolg van vak C.

☒ Leden van dezelfde octrooifamilie zijn vermeld in een bijlage

° Speciale categorieën van aangehaalde documenten

"A" niet tot de categorie X of Y behorende literatuur die de stand van de techniek beschrijft
"D" in de octrooiaanvrage vermeld
"E" eerdere octrooi(aanvrage), gepubliceerd op of na de indieningsdatum, waarin dezelfde uitvinding wordt beschreven
"L" om andere redenen vermelde literatuur
"O" niet-schriftelijke stand van de techniek
"P" tussen de voorrangsdatum en de indieningsdatum gepubliceerde literatuur
"T" na de indieningsdatum of de voorrangsdatum gepubliceerde literatuur die niet bezwarend is voor de octrooiaanvrage, maar wordt vermeld ter verheldering van de theorie of het principe dat ten grondslag ligt aan de uitvinding
"X" de conclusie wordt als niet nieuw of niet inventief beschouwd ten opzichte van deze literatuur
"Y" de conclusie wordt als niet inventief beschouwd ten opzichte van de combinatie van deze literatuur met andere geciteerde literatuur van dezelfde categorie, waarbij de combinatie voor de vakman voor de hand liggend wordt geacht
"&" lid van dezelfde octrooifamilie of overeenkomstige octrooipublicatie

Datum waarop het onderzoek naar de stand van de techniek van internationaal type werd voltooid	Verzenddatum van het rapport van het onderzoek naar de stand van de techniek van internationaal type
5 oktober 2020	

Naam en adres van de instantie	De bevoegde ambtenaar
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Böhler, Robert

ONDERZOEKSRAPPORT BETREFFENDE HET RESULTAAT VAN HET ONDERZOEK NAAR DE STAND VAN DE TECHNIEK VAN HET INTERNATIONALE TYPE

Informatie over leden van dezelfde octrooifamilie

Nummer van het verzoek om een onderzoek naar de stand van de techniek
NL 2024908

In het rapport genoemd octrooigeschrift		Datum van publicatie	Overeenkomend(e) geschrift(en)			Datum van publicatie
EP 2711076	A2	26-03-2014	EP	2711076	A2	26-03-2014
			US	2014087036	A1	27-03-2014
EP 3043178	A1	13-07-2016	EP	3043178	A1	13-07-2016
			JP	2016126019	A	11-07-2016
			US	2016195564	A1	07-07-2016
			US	2018149625	A1	31-05-2018
US 2013240449	A1	19-09-2013	CN	104302362	A	21-01-2015
			EP	2825266	A1	21-01-2015
			JP	2015517092	A	18-06-2015
			US	2013240449	A1	19-09-2013
			WO	2013138070	A1	19-09-2013

WRITTEN OPINION

File No. SN75765	Filing date *(day/month/year)* 14.02.2020	Priority date *(day/month/year)*	Application No. NL2024908
International Patent Classification (IPC) INV. G01N35/10 ADD. G01N1/20			
Applicant Technische Universiteit Delft			

This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the application
- ☐ Box No. VIII Certain observations on the application

	Examiner
	Böhler, Robert

Application number

WRITTEN OPINION

NL2024908

Box No. I Basis of this opinion

1. This opinion has been established on the basis of the latest set of claims filed before the start of the search.
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ on paper

   ☐ in electronic form

   c. time of filing/furnishing:

   ☐ contained in the application as filed.

   ☐ filed together with the application in electronic form.

   ☐ furnished subsequently for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. V Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty	Yes:	Claims	1-16
	No:	Claims	
Inventive step	Yes:	Claims	1-16
	No:	Claims	
Industrial applicability	Yes:	Claims	1-16
	No:	Claims	

2. Citations and explanations

   see separate sheet

Reference is made to the following documents:

D1 EP 2 711 076 A2 (TOTAL SYNTHESIS LTD [CA]) 26 maart 2014 (2014-03-26)

D2 EP 3 043 178 A1 (WATERS TECHNOLOGIES CORP [US]) 13 juli 2016 (2016-07-13)

D3 US 2013/240449 A1 (COLLIER LEE [US]) 19 september 2013 (2013-09-19)

Point V

1 The present application does meet the criteria of patentability, because the subject-matter of **independent claims 1** does involve an inventive step.

1.1 D1 is regarded as being the prior art closest to the subject-matter of claim 1, and discloses:

Een bemonsteringsinrichting voor bemonstering uit een reactor, *(Fig. 2 - 5)*

waarbij de bemonsteringsinrichting een gasinlaat, *(e.g. par .82; Fig. 2: 308)*

een oplosmiddelinlaat, *(Fig. 3: 112, 115; par. 88 - 91)*

een oplosmiddelcompartiment, *(Fig. 3: 116; par. 88 - 91)*

één of meer multipositiekleppen, *(Fig. 3: 102; par. 88 - 91)*

een bemonsteringscompartiment *(Fig. 3: 302)*

en een uitlaat omvat, *(Fig. 3: 305; par. 84)*

waarbij in een eerste operationele modus de één of meer multipositiekleppen geconfigureerd zijn om te verschaffen:

fluïdisch contact tussen de oplosmiddelinlaat en het oplosmiddelcompartiment; *(Fig. 3: always given between 116 and 112)*

fluïdisch contact tussen de reactor en het bemonsteringscompartiment; *(Fig. 3: 104, 106)*

en fluïdische scheiding tussen het oplosmiddelcompartiment en het bemonsteringscompartiment; *(Fig. 3: 112, 106)*

en waarbij in een tweede operationele modus de één of meer multipositiekleppen geconfigureerd zijn om te verschaffen: *(Fig. 4)*

~~fluïdisch contact tussen de gasinlaat, het oplosmiddelcompartiment, het bemonsteringscompartiment en de uitlaat.~~

The subject-matter of claim 1 therefore is new differs from this known device in

in een tweede operationele modus de één of meer multipositiekleppen geconfigureerd zijn om te verschaffen:

fluïdisch contact tussen de gasinlaat, het oplosmiddelcompartiment, het bemonsteringscompartiment en de uitlaat.

The technical effect of this difference is direct connection between the mentioned features for a fluid transport therethrough.

The problem to be solved by the present invention may therefore be regarded as how to make a washing simpler and the hence improve such device (application p. 2: l. 17 - p. 3: l. 2).

D1 (par. 89) discloses only a washing process of one valve component and only in another embodiment (Fig. 12, 13: 1208; par. 113 - 116) the use of a pressurized gas source to move the liquids in the system.

It is not obvious to use a system as claimed since such sampling systems can be built in multiple manners (see e.g. D2: Fig. 2 & 3 or D3: Fig. 4) with respective advantages and disadvantages.

Such systems can therefore include also several ways of cleaning. D2 discloses hereby a separate cleaning reservoir (par. 54 - 55; Fig. 2) for a similar device as in D1 but rather complicated. A cleaning mechanism by pushing a solvent through a sample preparation system is disclosed e.g. in D3 (par. 52). D3 discloses also a sampling system (Fig. 4) which is however much more complicated then the claimed one or the one of D1. It would be therefore very unlikely for one in the art to combine these teachings to arrive at the invention as defined in claim 1.

Hence, the solution proposed in claim 1 of the present application can be considered to involve an inventive step.

1.2 A similar reasoning can be obtained for claims 5 (system), 11 (method), and 15 (use) which all relate to the device of claim 1.

1.3 Claims 2 - 4, 6 - 10, 12 - 14, and 16 are dependent on former mentioned claims and as such also meet the requirements of inventive step.