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(54) **MICROREACTOR**

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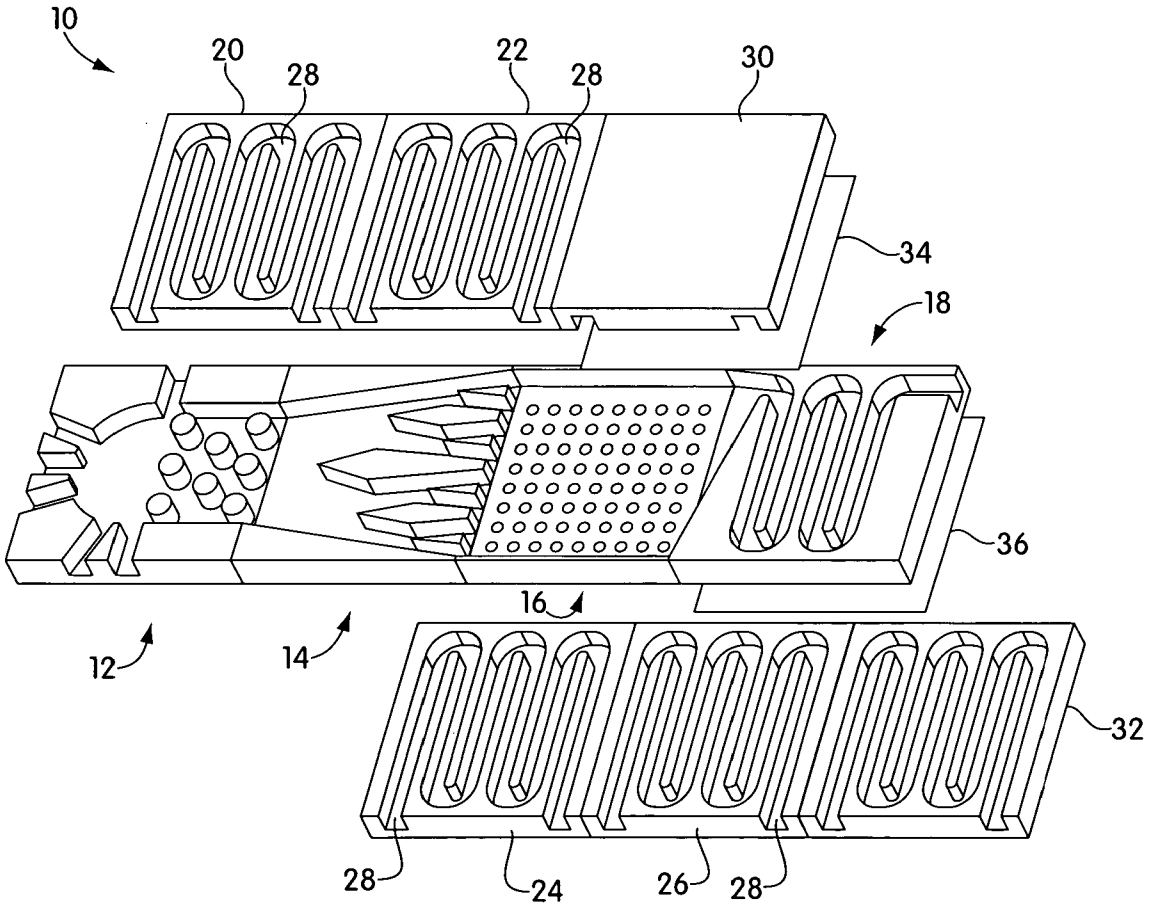
(57) **ABSTRACT**

Chemical and biological reactors, including microreactors, are provided. Exemplary reactors include a plurality of reactors operable in parallel, where each reactor has a small volume and, together, the reactors produce a large volume of product. Reaction systems can include mixing chambers, heating/dispersion units, reaction chambers, and separation units. Components of the reactors can be readily formed from a variety of materials. For example, they can be etched from silicon. Components are connectable to and separable from each other to form a variety of types of reactors, and the reactors can be attachable to and separable from each other to add significant flexibility in parallel and/or series reactor operation.



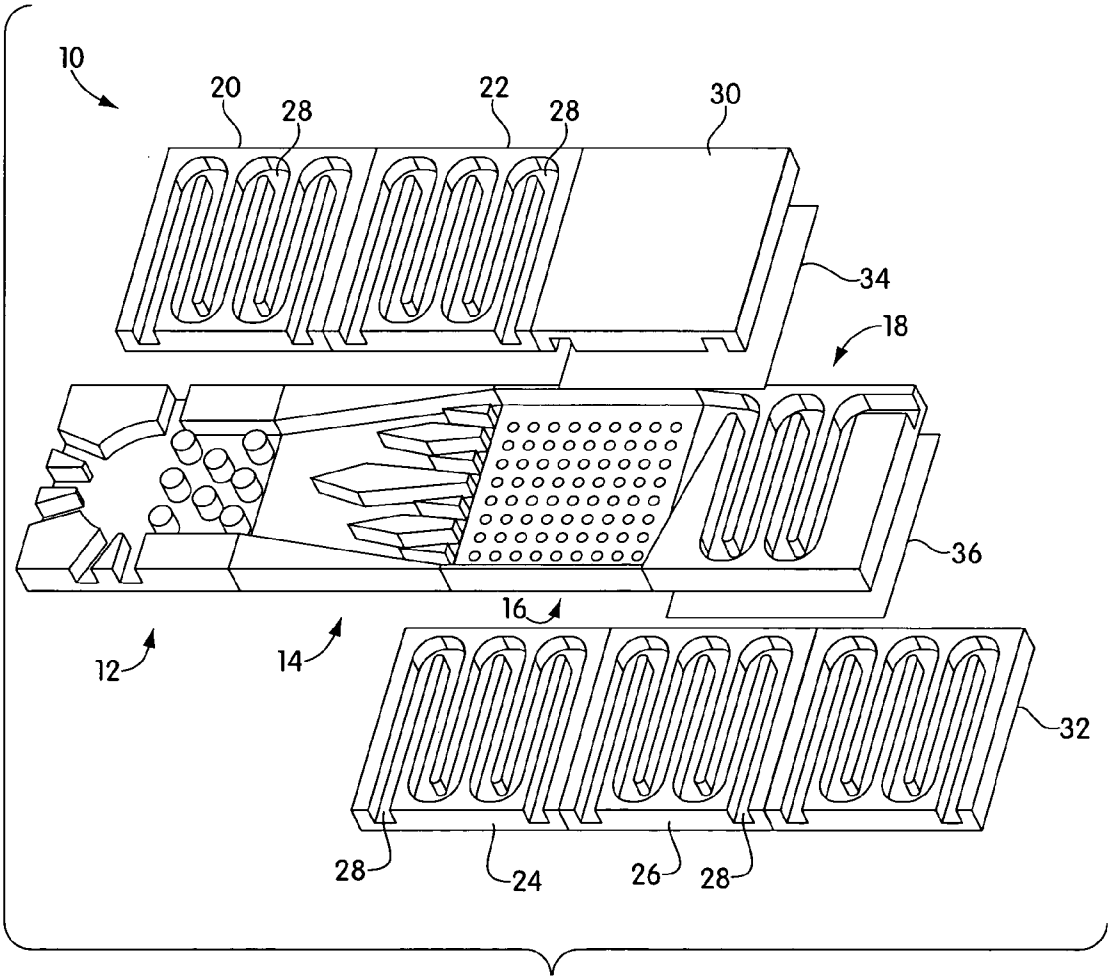


Fig. 1

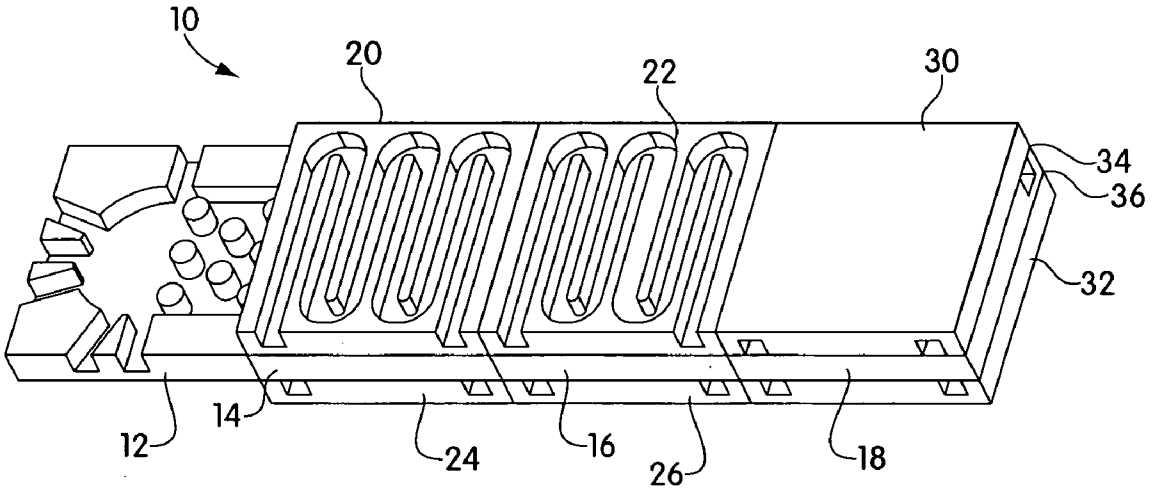


Fig. 2

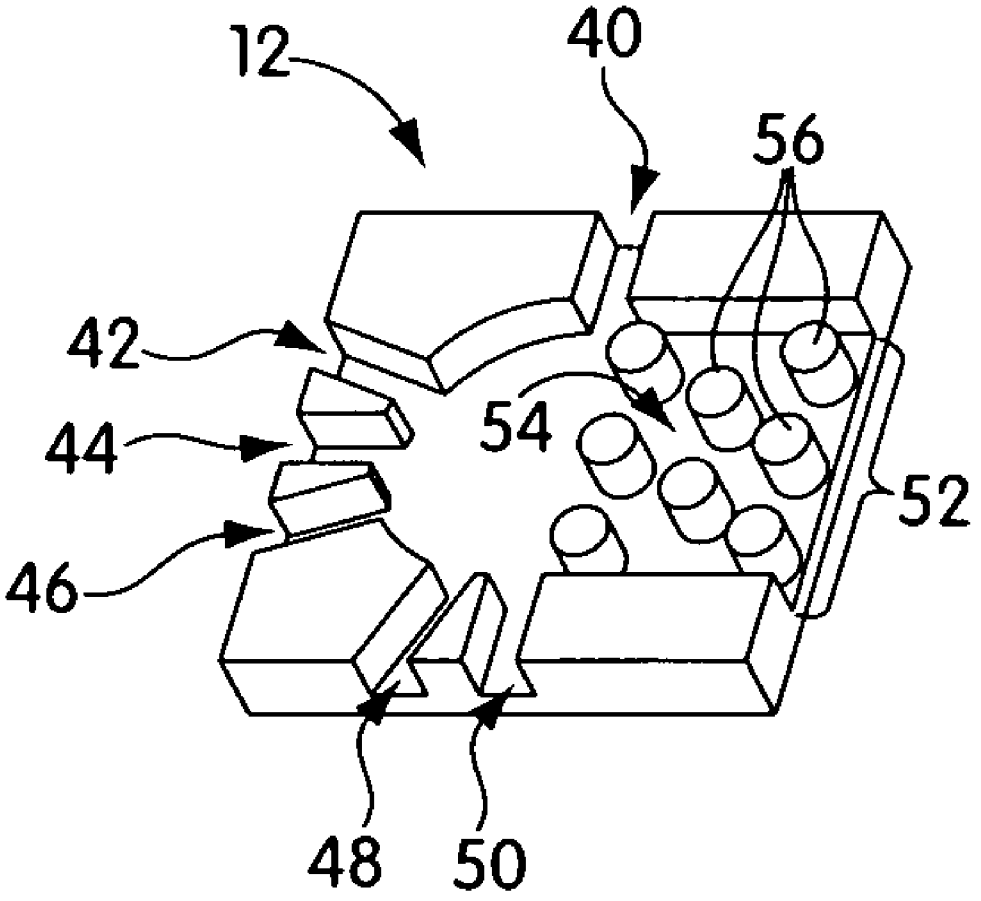


Fig. 3

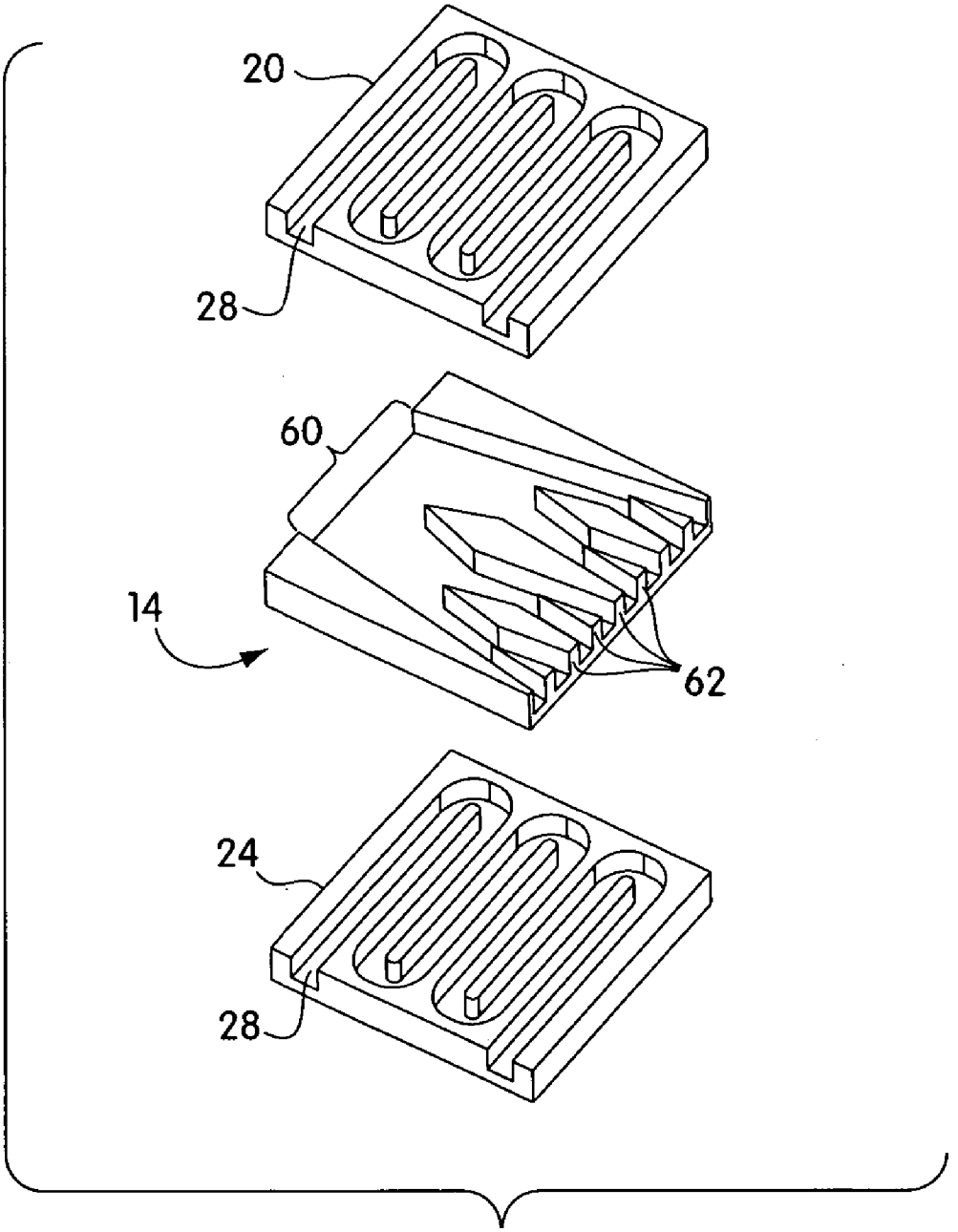


Fig. 4

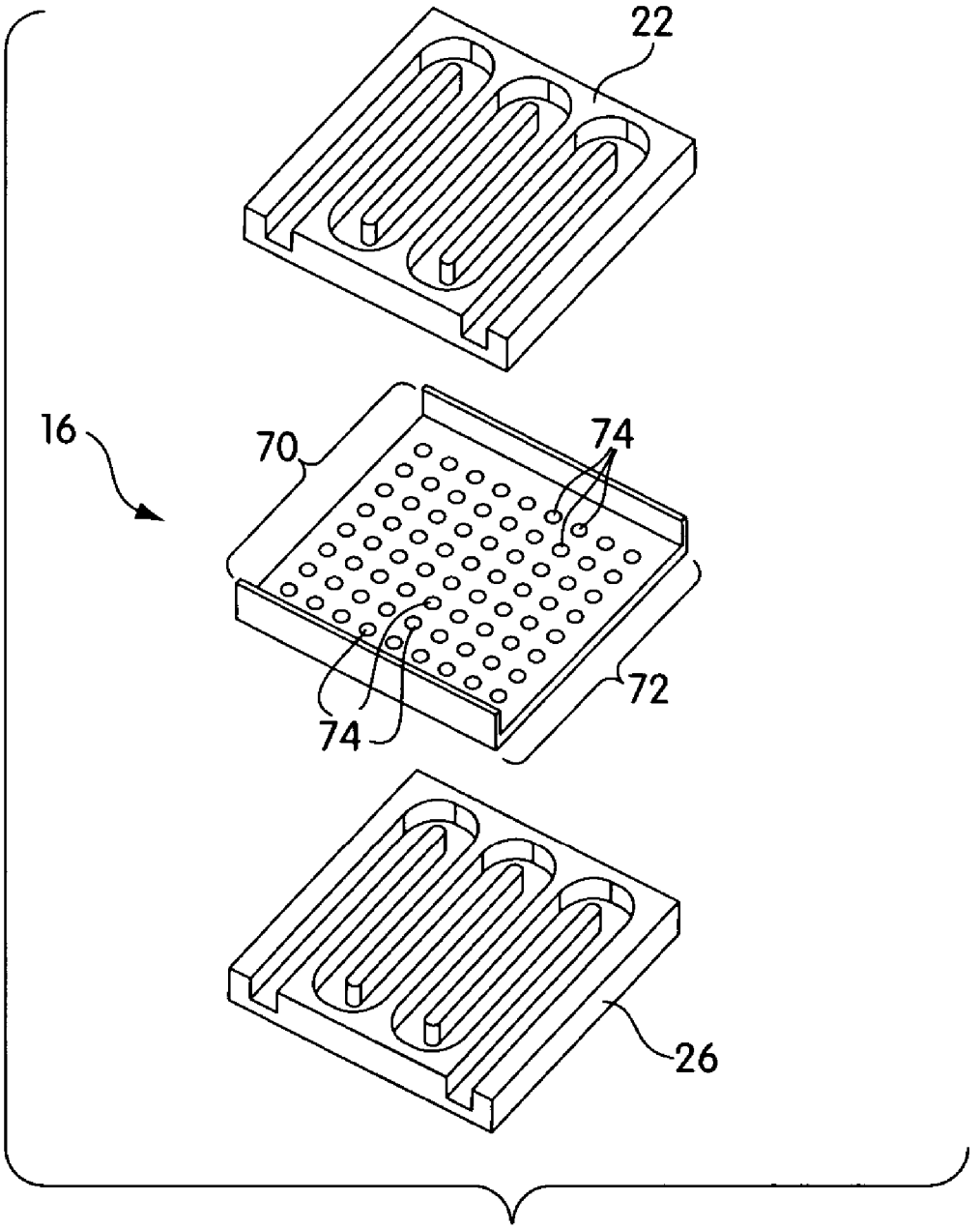


Fig. 5

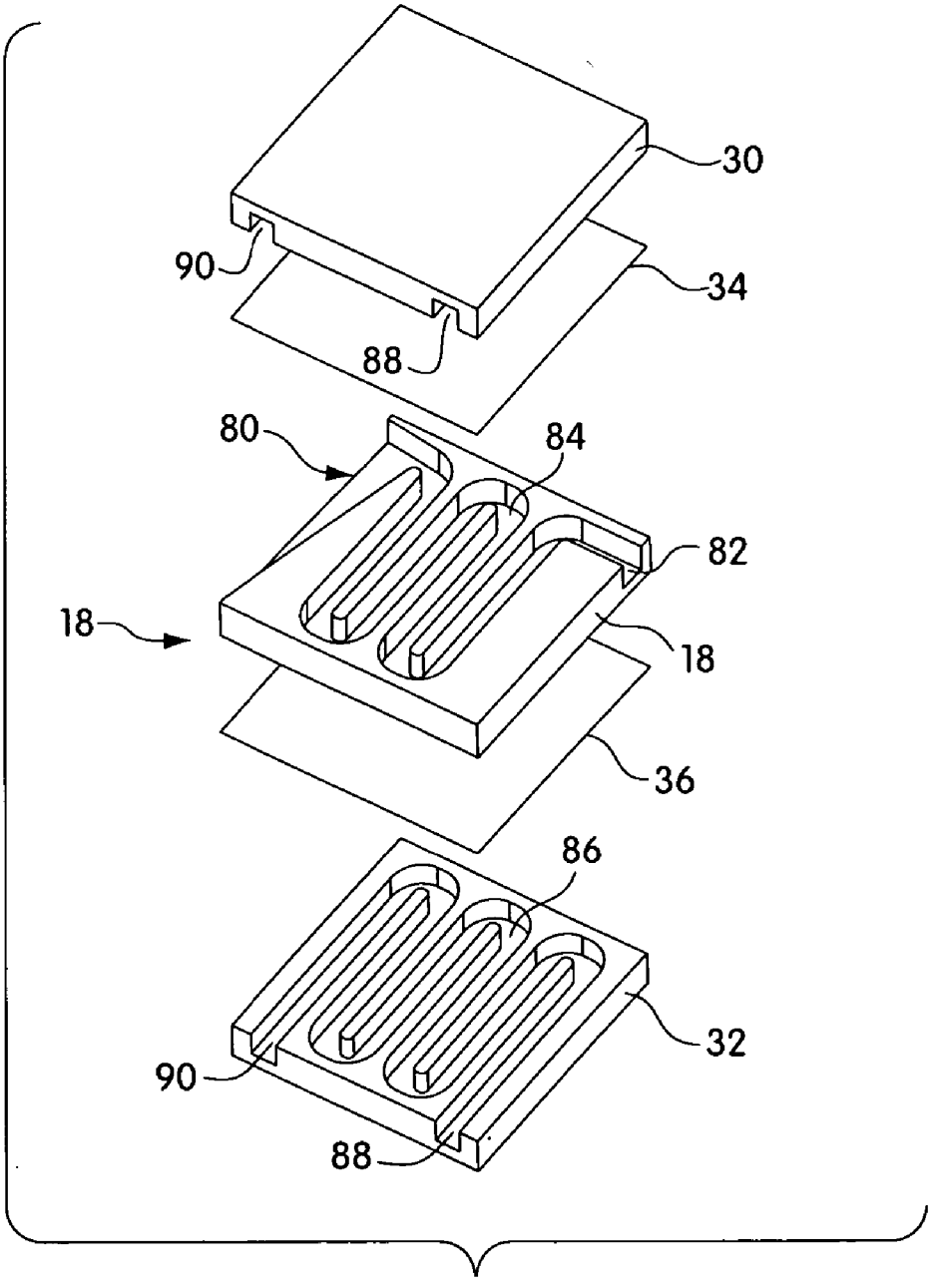


Fig. 6

MICROREACTOR

RELATED APPLICATION

[0001] This application claims the benefit of priority under 35 U.S.C. §120 to U.S. patent application Ser. No. 09/707,852, filed Nov. 7, 2000, which application claims the benefit of priority under 35 U.S.C. §119(e) of U.S. Provisional Patent Application Serial No. 60/188,275, filed Mar. 10, 2000. These applications are incorporated herein by reference.

FIELD OF THE INVENTION

[0002] The present invention relates generally to chemical or biochemical microreactors, and more particularly to a microreactor for the production of the product of a chemical or biochemical reaction, including a plurality of individuated microreactors constructed to operate in parallel.

BACKGROUND OF THE INVENTION

[0003] A wide variety of reaction systems are known for the production of the product of chemical or biochemical reactions. Chemical plants involving catalysis, biochemical fermenters, pharmaceutical production plants, and a host of other systems are well-known.

[0004] Systems for housing chemical and biochemical reactions not necessarily for the production of product also are known. For example, continuous-flow systems for the detection of various analytes in bodily fluids including blood, such as oxygen, glucose, and the like are well known.

[0005] In many of these and other systems, the capacity of the system (the volume of material that the system is designed to produce, process, or analyze) is adjusted in accordance with the volume of reactant, product, or analyte desirably processed or analyzed. For example, in large-scale chemical or pharmaceutical production, reactors are generally made as large as possible to generate as large a volume of product as possible. Conversely, in many areas of clinical diagnosis, where it is desirable to obtain as much information as possible from as small a physiological sample as possible (e.g., from a tiny drop of blood), it is a goal to minimize the size of reaction chambers of sensors. Several examples of small-scale reactor systems, including those used in clinical diagnoses and other applications, follow.

[0006] U.S. Pat. No. 5,387,329 (Foos, et al.; Feb. 7, 1995) describes an extended use planar clinical sensor for sensing oxygen levels in a blood sample.

[0007] U.S. Pat. No. 5,985,119 (Zanzucchi, et al.; Nov. 16, 1999) describes small reaction cells for performing synthetic processes in a liquid distribution system. A variety of chemical reactions including catabolic, anabolic reactions, oxidation, reduction, DNA synthesis, etc. are described.

[0008] U.S. Pat. No. 5,674,742 (Northrup, et al.; Oct. 7, 1997) describes an integrated microfabricated instrument for manipulation, reaction, and detection of microliter to picoliter samples. The system purported by is suitable for biochemical reactions, particularly DNA-based reactions such as the polymerase chain reaction.

[0009] U.S. Pat. No. 5,993,750 (Ghosh, et al.; Nov. 30, 1999) describes an integrated micro-ceramic chemical plant having a unitary ceramic body formed from multiple ceramic layers in the green state which are sintered together defining a mixing chamber, passages for delivering and reacting fluids, and means for delivering mixed chemicals to exit from the device.

[0010] Biochemical processing typically involve the use of a live microorganism (cells) to produce a substance of interest. Biochemical and biomedical processing account for about 50% of the total drug, protein and raw amino-acid production worldwide. Approximately 90% of the research and development (R&D) budget in pharmaceutical industries is currently spent in biotechnology areas.

[0011] Currently bioreactors (fermentors) have several significant operational limitations. The most important being maximum reactor size which is linked to aeration properties, to nutrient distribution, and to heat transfer properties. During the progression of fermentation, the growth rate for cells accelerates, and the measures required to supply the necessary nutrients and oxygen sets physical and mechanical constraints on the vessel within which the cells are contained. Powerful and costly drives are needed to compensate for inefficient mixing and low mass-transfer rates. Additionally, as metabolism of cells accelerates, the cells generate increased heat which needs to be dissipated from the broth.

[0012] The heat transfer characteristics of the broth and the vessel (including heat exchanger) impose serious constraints on the reaction scale possible (see Table 1). While the particular heat load and power requirements are specific to the reaction, the scale of reaction generally approaches limitations at ~10 m^3 as in the case of *E. coli* fermentation (Table 1). The amount of heat to be dissipated becomes excessive due to limits on heat transfer coefficients of the broth and vessel. Consequently, the system of vessel and broth will rise in temperature. Unfortunately, biological compounds often have a relatively low upper limit on temperature for which to survive (<45° C. for many). Additionally, power consumption to disperse nutrients and oxygen and coolant requirements to control temperature make the process economically unfeasible (see Table 1).

TABLE 1

Oxygen- and Heat- Transfer Requirements for *E. coli*: Effects of Scale

OTR (mmol/ L · h)	Volume[a] (m^3)	Pressure (psig)	Power (hp)	Heat Load (Btu/h)	Coolant[b] (° F.)
150	1	15	5.0	84 000	40
200	1	25	4.9	107 000	40
300	1	35	7.1	161 000	40
400	1	35	6.9	208 000	40
150	10	15	50.2	884 000	40
200	10	25	50.0	1 078 000	40
300	10	35	75.7	1 621 000	22
400	10	35	77.0	2 096 000	5

[a]Liquid volume
[b]Coolant flow is 35 gal/min for 1-m^3 vessel and 100 gal/min for 10-m^3 vessel
[c]Charles, M. and Wilson, J. Fermentor Design; In: Bioprocess Engineering; Lydersen, B. K., D'Elia, N. A., Nelson, K. L., Ed.; John Wiley & Sons, Inc., New York, 1994.

[0013] Aside from reactor scalability, the design of conventional fermentors has other drawbacks. Due to the batch and semi-batch nature of the process, product throughput is low. Also, the complexity and coupled nature of the reaction

parameters, as well as the requirement of narrow ranges for these parameters, makes control of the system difficult. Internal to the system, heterogeneity in nutrient and oxygen distribution due to mixing dynamics creates pockets in the broth characterized by insufficient nutrients or oxygen resulting in cell death. Finally, agitation used to produce as homogeneous a solution as possible (typically involving impellar string to simultaneously mix both cells and feeds of oxygen and nutrients) causes high strains which can fracture cell membranes and cause denaturation.

[0014] While a wide variety of useful reactors for a variety of chemical and biological reactions, on a variety of size scales exist, a need exists in the art for improved reactors. In particular, there is a current need to significantly improve the design of bioreactors especially as the pharmaceutical and biomedical industries shift increasingly towards bioprocessing.

SUMMARY OF THE INVENTION

[0015] The present invention provides systems, methods, and reactors associated with small-scale chemical or biochemical reactions.

[0016] In one aspect the invention provides a chemical or biochemical reactor. The reactor includes a reaction unit including a chamber having a volume of less than one milliliter. The chamber includes an inlet connectable to a source of a chemical or biological starting material and an outlet for release of a product of a chemical or biological reaction involving the starting material. A collection chamber is connectable to the outlet of the reaction chamber. The collection chamber has a volume of greater than one liter.

[0017] In another aspect the invention involves a chemical or biochemical reactor system. The system includes a mixing chamber including a plurality of inlets connectable to a plurality of sources of chemical or biochemical reagents, and an outlet. A reaction chamber is connectable to and removable from the mixing chamber, and has a volume of less than one milliliter. The reaction chamber includes an inlet connectable to and removable from the outlet of the mixing chamber, and an outlet for release of a product of a chemical or biological reaction involving the starting material.

[0018] In another aspect the invention provides methods. One method includes carrying out a chemical or biological reaction in a plurality of reaction chambers operable in parallel, where each reaction chamber has a volume of less than one milliliter. Product of the reaction is discharged from the plurality of reaction chambers simultaneously into a collection chamber having a volume of greater than one liter.

[0019] Other advantages, novel features, and objects of the invention will become apparent from the following detailed description of the invention when considered in conjunction with the accompanying drawings, which are schematic and which are not intended to be drawn to scale. In the figures, each identical or nearly identical component that is illustrated in various figures is represented by a single numeral. For purposes of clarity, not every component is labeled in every figure, nor is every component of each embodiment of the invention shown where illustration is not necessary to allow those of ordinary skill in the art to understand the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] **FIG. 1** illustrates a microbioreactor of the invention including mixing, heating/dispersion, reaction, and separation units, in expanded view;

[0021] **FIG. 2** illustrates the system of **FIG. 1** as assembled;

[0022] **FIG. 3** illustrates the mixing unit of the system of **FIG. 1**;

[0023] **FIG. 4** is an expanded view of the heating/dispersion unit of the system of **FIG. 1**;

[0024] **FIG. 5** is an expanded view of the reaction chamber of the system of **FIG. 1**; and

[0025] **FIG. 6** is an expanded view of the separation unit of the system of **FIG. 1**.

DETAILED DESCRIPTION OF THE INVENTION

[0026] The present invention provides a chemical or biochemical reactor that can be used for a variety of very small-scale techniques. In one embodiment, a microreactor of the invention comprises a matrix of a few millimeters to a few centimeters in size containing reaction channels with dimensions on the order of hundreds of microns. Reagents of interest are allowed to flow through these microchannels, mixed, and reacted together. The products can be recovered, separated, and treated within the system. While one microreactor may be able only to hold and react a few microliters of the substances of interest, the technology allows for easy scalability and tremendous parallelization. With enhanced oxygen and nutrient distribution, a microreactor of the invention demonstrates increased performance in terms of cell viability. The microreactor geometry resembles closely the natural environment of cells whereby diffusional oxygen and nutrient transfer take place through a high surface area, thin layer interface.

[0027] With regard to throughput, an array of many microreactors can be built in parallel to generate capacity on a level exceeding that allowed by current vessels and more uniform in product quality than can be obtained in a batch method. Additionally, an advantage is obtained by maintaining production capacity at the scale of reactions typically performed in the laboratory. In general, the coupled parameters for heat and mass transfer that are determined on the lab-scale for a process do not scale linearly with volume. With conventional reactors, as the magnitude of volume is increased 1,000-1,000,000 times for production, these parameters need to be re-evaluated, often involving a large capital-investment. The use of small production volumes, although scaled in parallel, reduces the cost of current scale-up schemes.

[0028] Furthermore, the process can be implemented on a simple platform, such as an etched article for example, a silicon wafer. With the effort of semiconductor manufacturing being towards the reduction in the dimensions of channels, an opportunity to utilize excess capacity within these production facilities (with unused equipment for the larger dimensions) is provided. Mass production of these units can be carried out at very low cost and an array of many reactors, for example thousands of microreactors typically can be built for a price lower than one traditional bioreactor.

[0029] Referring now to **FIG. 1, a** chemical or biochemical reactor in accordance with one embodiment of the invention is illustrated schematically. The reactor of **FIG. 1** is, specifically, a microbioreactor for cell cultivation. It is to be understood that this is shown by way of example only, and the invention is not to be limited to this embodiment. For example, systems of the invention can be adapted for pharmaceutical production, hazardous chemical production, or chemical remediation of warfare reagents, etc.

[0030] Microreactor **10** includes four general units. A mixing unit **12**, a heating/dispersion unit **14**, a reaction unit **16**, and a separation unit **18**. That is, in the embodiment illustrated, processes of mixing, heating, reaction, purification are implemented in series. Although not shown, pressure, temperature, pH, and oxygen sensors can be included, for example embedded within the network to monitor and provide control for the system. Due to the series format, the opportunity for several reaction units in series for multi-step chemical syntheses, for several levels of increased purification, or for micro-analysis units is provided as well.

[0031] **FIG. 1** shows microreactor **10** in expanded view. As illustrated, each of units **14** and **16** (heating/dispersion and reaction units, respectively) includes at least one adjacent temperature control element **20-26** including a channel **28** through which a temperature-control fluid can be made to flow. As illustrated, temperature control units **20** and **24** are positioned above and below unit **14** and units **22** and **26** are positioned above and below unit **16**. Separation unit **18** includes upper and lower extraction solvent fluid units **30** and **32**, respectively, separated from unit **18** by membranes **34** and **36**, respectively.

[0032] Referring now to **FIG. 2**, reactor **10** is illustrated as assembled. The individual units of microreactor **10** will now be described in greater detail.

[0033] Referring now to **FIG. 3**, mixing unit **12** is illustrated. Mixing unit **12** is designed to provide a homogeneous mixture of starting materials or reactants to be provided to the reaction units, optionally via the heating/dispersion unit. In the specific example of the microbioreactor, mixing unit **12** is designed to provide a homogeneous broth with sufficient nutrients and oxygen, and at the required pH, for cells. Rather than combine the mixing process with simultaneous nourishment of the cells, the process is performed in a preliminary stage and then fed to the reaction stage where cells are immobilized. In this manner, the cells do not experience any shear stress due to mixing and a homogeneous mixture of feed requirements is guaranteed.

[0034] As is the case for other components of the reactor, mixing unit **12** can be manufactured using any convenient process. In preferred embodiments the unit is etched into a substrate such as silicon via known processes such as lithography. Other materials from which mixing unit **12**, or other components of the systems of the. invention can be fabricated, include glass, fused silica, quartz, ceramics, or suitable plastics. Silicon is preferred. The mixing unit includes a plurality of inlets **40-50** which can receive any of a variety of reactants and/or fluid carriers. Although six inlets are illustrated, essentially any number of inlets from one to tens of hundreds of inlets can be provided. Typically, less than ten inlets are needed for a given reaction. Mixing unit **12** includes an outlet **52** and, between the plurality of inlets and the outlet, a mixing chamber **54** constructed and arranged to coalesce a plurality of reactant fluids provided through the inlets. It is a feature of the embodiment illustrated that the mixing chamber is free of active mixing elements. Instead, the mixing chamber is constructed to cause turbulence in the fluids provided through the inlets thereby mixing and delivering a mixture of the fluids through the outlet without active mixing. Specifically, the mixing unit includes a plurality of obstructions **56** in the flow path that causes mixture of fluid flowing through the flow path. These obstructions can be of essentially any geometrical arrangement. As illustrated, they define small pillars about which the fluid must turbulently flow as it passes from the inlets through the mixing chamber toward the outlet. As used herein "active mixing elements" is meant to define mixing elements such as blades, stirrers, or the like which are movable relative to the reaction chamber itself, that is, movable relative to the walls defining the reaction chamber.

[0035] The volume of the mixing chamber, that is, the volume of the interior of mixing unit **12** between the inlets and the outlet, can be very small in preferred embodiments. Specifically, the mixing chamber generally has a volume of less than one liter, preferably less than about 100 microliters, and in some embodiments less than about 10 microliters. The chamber can have a volume of less than about five microliters, or even less than about one microliter.

[0036] Specifically, in the microbioreactor illustrated, six separate feed streams empty into the mixing chamber under pressure. One feed stream provides gaseous oxygen (O_2) as a cell requirement. One stream, respectively, provides carbon dioxide (CO_2) and nitrogen (N_2) for altering pH. The remaining three channels provide the broth solution including solvent and nutrients. One of these latter streams can also be utilized to provide any additional requirements for the system such as antifoaming agents. Antifoaming agents are sometimes necessary to prevent production of foam and bubbles that can damage cells within the broth. The feed of the various streams into the chamber provides enough turbulence for mixing of the different streams. Flow within microfluidic devices is characterized by a low Reynolds number indicating the formation of lamina. While the turbulence created by the injection streams should provide sufficient mixing before the development of laminar flow, pilon-like obstructions **56** are placed in the flow path of the stream leaving the primary mixing chamber in order to enhance mixing of the lamina. By splitting a main stream into substreams followed by reunification, turbulence is introduced in the flow path, and a mechanism other than simple diffusion is used to facilitate further mixing. The length of this mixing field can be lengthened or shortened depending on the system requirements.

[0037] Referring now to **FIG. 4**, heating/dispersion unit **14** is shown. Unit **14** can be formed as described above with respect to other units of the invention. Unit **14** includes an inlet **60** in fluid communication with a plurality of outlets **62** in embodiments where dispersion as described below is desirable. In operation, a stream of homogeneous fluid exiting the mixing unit (feed broth in the specific microbioreactor embodiment shown) enters a dispersion matrix defined by a plurality of obstructions dividing the stream into separate flow paths directed toward the separate outlets **62**. The dispersion matrix is sandwiched between two temperature control elements **20** and **24** which, as illustrated,

include fluid flow channels **28** etched in a silicon article. Control unit **24** is positioned underneath unit **14**, thus etched channel **28** is sealed by the bottom of unit **14**. Control unit **20** is positioned atop unit **14** such that the bottom of unit **20** seals and defines the top of diffusion unit **14**. A cover (not shown) can be placed a top unit **20** to seal channel **28**.

[**0038**] Rather than for mixing, as in the previous case (**FIG. 3**), the splitting of the streams is to disperse the medium for its entrance into the reactive chamber in the next unit operation. In traditional reactor systems, fluid flow about a packing material containing catalysts produces the desired reaction. However, if the fluid is not evenly dispersed entering the chamber, the fluid will flow through a low resistance path through the reactor and full, active surface area will not be utilized. Dispersion in this case is to optimize reactor efficiency in the next stage.

[**0039**] With regard to the heating function of this unit, the platform functions as a miniaturized, traditional heat exchanger. Etched silicon platforms both above and below the central platform serve to carry a heated fluid. Cells typically require their environment to have a temperature of ~30° C. The fluids flowing in the etched coils both above and below the broth flow channel heating the broth through the thin silicon layer. The temperature of the fluid in the upper and lower heat exchangers can be modified to ensure proper temperature for the broth. Additionally, the platform can be extended for increased heating loads.

[**0040**] Although a combination heating/dispersion unit is shown, unit **14** can be either a dispersion unit or a heating unit. For example, dispersion can be provided as shown, without any temperature control. Alternatively, no dispersion need be provided (inlet **60** can communicate with a single outlet **62**, which can be larger than the outlets as illustrated) and heating units can be provided. Cooling units can be provided as well, where cooling is desired. Units **20** and **24** can carry any temperature-control fluid, whether to heat or cool.

[**0041**] Referring now to **FIG. 5**, reaction chamber **16** is shown, including temperature control units **22** and **26**, in expanded form. Units **22** and **26** can be the same as units **20** and **24** as shown in **FIG. 4**, with unit **22** defining the top of reaction chamber **16**. Reaction unit **16** includes an inlet **70** fluidly communicating with an outlet **72** and a reaction chamber defined therebetween. The reaction chamber, in microreactor embodiments of the invention, has a volume of less than one milliliter, or other lower volumes as described above in connection with mixing unit **12**. Inlet **70** is connectable to a source of a chemical or biological starting material, optionally supplied by mixing unit **12** and heating/dispersion unit **14**, and outlet **70** is designed to release the product of a chemical or biological reaction occurring within the chamber involving the starting material. Unit **16** can be formed from materials as described above.

[**0042**] The reactor unit is the core of the process. While the unit is designed to be interchangeable for biological or pharmaceutical reactions, the specific application as shown is for cell cultivation. As in the case of the previous unit, temperature control units such as heat exchanger platforms will sandwich the central reaction chamber. The heat exchangers will maintain the temperature of the reaction unit at the same temperature as discussed for the cell broth.

[**0043**] A feature of the unit is heterogeneous reaction on a supported matrix. Cell feed enters the reaction chamber under the proper pH, O_2 concentration, and temperature for cell cultivation. Cells, immobilized onto the silicon framework at locations **74** either by surface functionalization and subsequent reaction or entrapment within a host membrane, metabolize the nutrients provided by the feed stream and produce a product protein. The initial reaction platform can be a two-dimensional array of cells both on the top and bottom of the reaction chamber. This arrangement is to prevent a large pressure drop across the unit which would be detrimental to flow.

[**0044**] In this unit, oxygen and nutrients are diffused from the flowing stream to the immobilized cells. The cells, in turn metabolize the feed, and produce proteins which are swept away in the flowing stream. The flowing stream then enters the fourth chamber which removes the protein product from the solution.

[**0045**] Referring again to **FIG. 1**, it can be seen how dispersion unit **14** creates an evenly-divided flow of fluid (reactant fluid such as oxygen and nutrients in the case of cell cultivation) across each of locations **74** in reaction to chamber **16**.

[**0046**] Referring now to **FIG. 6**, separation unit **18** is shown in greater detail, in expanded view. Separation unit **18** defines a central unit including an inlet **80** communicating with an outlet **82**, and a fluid pathway **84** connecting the inlet with the outlet. Unit **18** can be fabricated as described above with respect to other components of the invention, and preferably is etched silicon. It may be desirable for fluid path **84** to completely span the thickness of unit **18** such that the pathway is exposed both above and below the unit. To maintain structural integrity, pathway **84** can be etched to some extent but not completely through unit **18** as illustrated, and a plurality of holes or channels can be formed through the bottom of the pathway exposing the bottom of the pathway to areas below the unit. Inlet **80** can be connectable to the outlet of reaction chamber **16**, and outlet **82** to a container for recovery of carrier fluid.

[**0047**] In the embodiment illustrated, membranes **34** and **36** cover exposed portions of fluid pathway **84** facing upward or downward as illustrated. Membranes **30** and/or **36** can be any membranes suitable for separation, i.e. extraction of product through the membrane with passage of effluent, or carrier fluid, through outlet **82**. Those of ordinary skill in the art will recognize a wide variety of suitable membranes including size-selective membranes, ionic membranes, and the like. Upper and lower extraction solvent fluid units **30** and **32**, which can comprise materials as described above including etched silicon, each include a fluid pathway **86** connecting an inlet **88** with an outlet **90**. Fluid pathway **86** preferably is positioned in register with fluid pathway **84** of unit **18** when the separation unit is assembled. In this way, two flowing streams of solvent through channels **86** of units **30** and **32** flow counter to the direction of flow of fluid in channel **84** of unit **18**, the fluids separated only by membranes **34** and **36**. This establishes a counter-current tangential flow filtration membrane system. By concentration gradients, products are selectively extracted from channel **84** into solvent streams flowing within channels **86** of unit **30** or **32**. Product is recovered through the outlet **90** of units **30** or **32** and recovered in a container (not shown) having a volume that can be greater than **1** liter. Outlets **90** thereby define carrier fluid outlets,

and a fluid pathway connects inlet **80** of unit **18** with the carrier fluid outlets **90** of units **30** and **32**, breached only by membranes **34** and **36**. Carrier fluid outlet **82** can be made connectable to a recovery container for recycling of reaction carrier fluids. In the example of a microbioreactor, residual oxygen and nutrients are recovered from outlet **82** and recycled back into the feed for the process.

[**0048**] The flowing streams of extraction solvent in channels **86** can be set at any desired temperature using temperature control units (not illustrated). In the case of a microbioreactor, these fluids can be set at approximately 4° C. The low temperature is needed to maintain the efficacy of the protein products and prevent denaturation. Additionally, several purification and clarification steps are often performed in industrial application. The necessity of further purification is remedied by the use of additional units in series.

[**0049**] Embedded within the production process can be control systems and detectors for the manipulation of temperature, pH, nutrients, and oxygen concentration. Where a microbioreactor is used, the viability of cells is dependent upon strict limits for the parameters mentioned above. Narrow set-point ranges, dependent on the cell system selected, can be maintained using thermocouples, pH detectors, O_2 solubility detectors, and glucose detectors between each unit. These measurements will determine the heat exchanger requirements, O_2, CO_2, N_2, and nutrient inputs.

[**0050**] Diaphragm and peristaltic pumps can be used to provide the necessary driving force for fluid flow in the units. Such pumps are also used to maintain flow in the heat exchanger units.

[**0051**] It is a feature of the invention that many of the microreactors as illustrated can be arranged in parallel. Specifically, at least ten reactors can be constructed to operate in parallel, or in other cases at least about 100, 500, 1,000, or even 10,000 reactors can be constructed to operate in parallel. These reactors can be assembled and disassembled as desired.

[**0052**] It is another feature of the invention that individual units **12**, **14**, **16**, and **18** can be constructed and arranged to be connectable to and separable from each other. That is, any arrangement of individual components can be created for a desired reaction. For example, with reference to **FIG. 1**, heating/dispersion unit **14** may not be necessary. That is, outlet **52** of mixing unit **12** can be connectable to either inlet **60** of heating/dispersion unit **14**, or inlet **70** of reaction unit **16** where a heating/dispersion unit is not used. Moreover, assembly and disassembly of reactors to create a system including many, many reactors operating in parallel, as described above, or in series is possible because of the connectability and separability of the components from each other to form systems containing specific desired components, and any number of those or other systems operating together. Equipment for connection and separation of individual components of a reactor can be selected among those known in the art, as can systems for connection of a variety of reactors in parallel or in series. Systems should be selected such that the individual components can be connectable to and separable from each other readily by laboratory or production-facility technicians without irreversible destruction of components such as welding, sawing, or the like. Examples of known systems for making readily reversible connections between components of reactors or between reactors to form parallel reactors or series reactors include male/female interconnections, clips, cartridge housings where components comprise inserts within the housings, screws, or the like.

[**0053**] Those skilled in the art would readily appreciate that all parameters listed herein are meant to be exemplary and that actual parameters will depend upon the specific application for which the methods and apparatus of the present invention are used. It is, therefore, to be understood that the foregoing embodiments are presented by way of example only and that, within the scope of the appended claims and equivalents thereto, the invention may be practiced otherwise than as specifically described. In the claims the words "including", "carrying", "having", and the like mean, as "comprising", including but not limited to.

What is claimed is:

1. A chemical or biochemical reactor comprising:

a reaction unit including a chamber having a volume of less than 1 ml, an inlet to the chamber connectable to a source of a chemical or biological starting material, and an outlet of the chamber for release of a product of a chemical or biological reaction involving the starting material; and

a collection chamber connectable to the outlet of the reaction chamber, the collection chamber having a volume of greater than 1 liter.

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