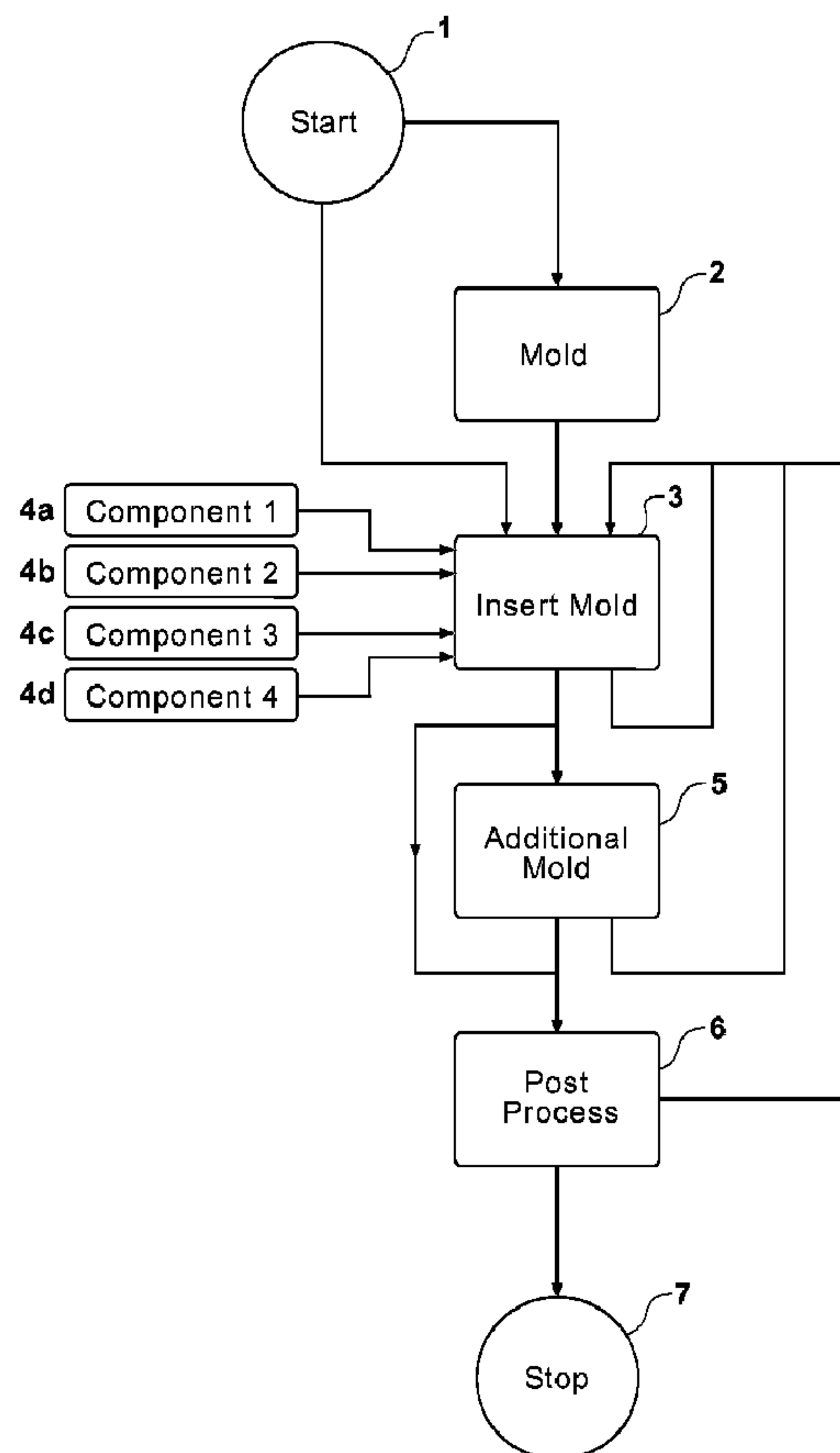




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(54) **Titre : ENSEMBLE BUSE D'UN SYSTEME DE CYTOMETRE DE FLUX ET PROCEDES DE FABRICATION**
(54) **Title: NOZZLE ASSEMBLY FOR A FLOW CYTOMETER SYSTEM AND METHODS OF MANUFACTURE**



(57) **Abrégé/Abstract:**

A method of manufacturing a nozzle assembly may include the step of over molding a nozzle housing, or a portion of a nozzle housing, onto at least one nozzle component, such as an injection tube. Nozzle assemblies and flow cytometers incorporating

(57) Abrégé(suite)/Abstract(continued):

nozzle assemblies may include any combination of straight smooth injection tubes, improved features for securing a nozzle assembly, improved features for debubbling a nozzle assembly, and aggressive orienting geometries. A method of sorting cells may include the step of magnetically coupling a nozzle assembly with a flow cytometer.

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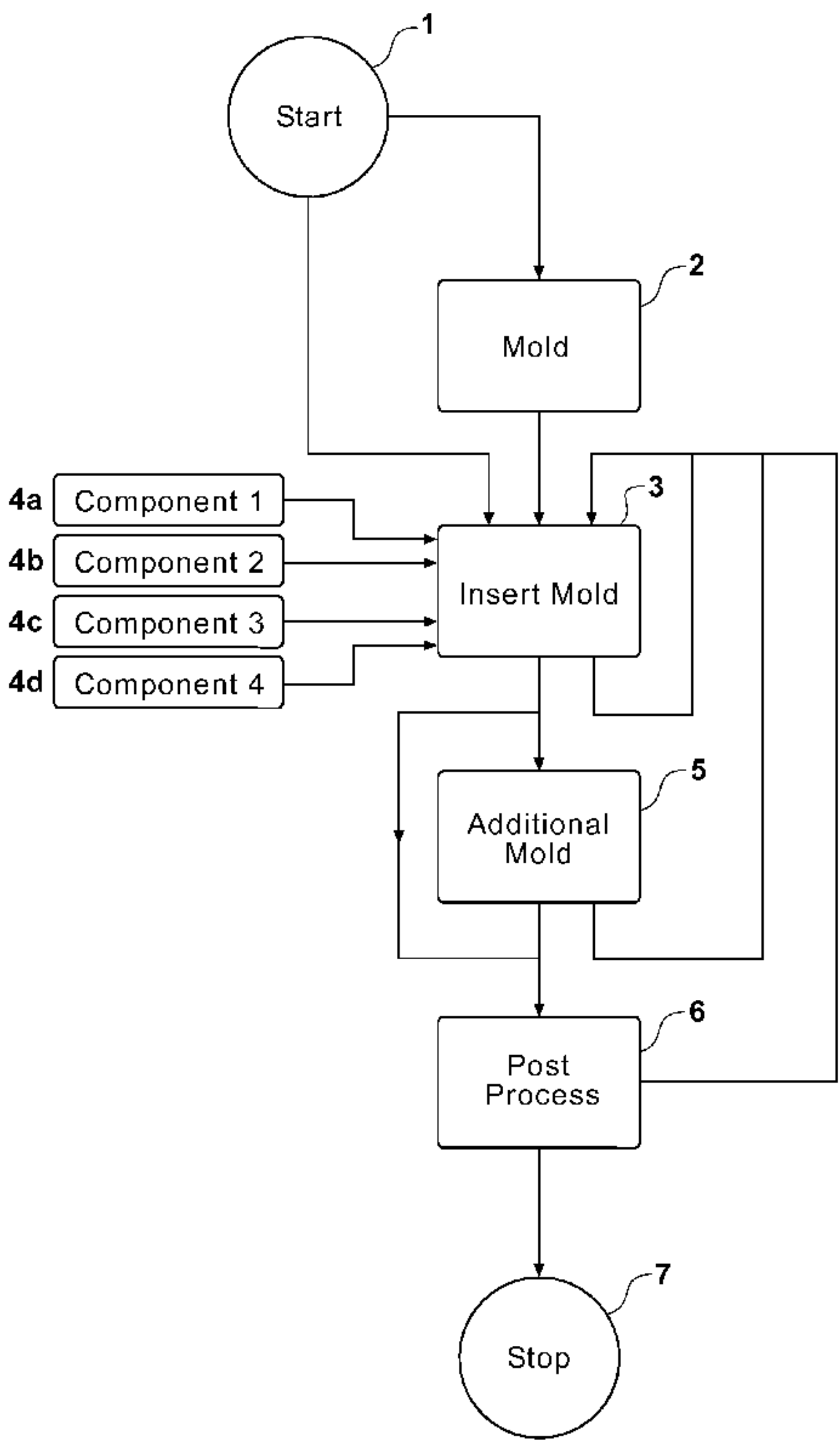
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(54) Title: NOZZLE ASSEMBLY FOR A FLOW CYTOMETER SYSTEM AND METHODS OF MANUFACTURE

(57) Abstract: A method of manufacturing a nozzle assembly may include the step of over molding a nozzle housing, or a portion of a nozzle housing, onto at least one nozzle component, such as an injection tube. Nozzle assemblies and flow cytometers incorporating nozzle assemblies may include any combination of straight smooth injection tubes, improved features for securing a nozzle assembly, improved features for debubbling a nozzle assembly, and aggressive orienting geometries. A method of sorting cells may include the step of magnetically coupling a nozzle assembly with a flow cytometer.



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NOZZLE ASSEMBLY FOR A FLOW CYTOMETER SYSTEM AND METHODS OF MANUFACTURE

This International Patent Cooperation Treaty Patent Application claims the benefit of United States Provisional Patent Application No. 61/703,102, filed September 19, 2012.

FIELD OF THE INVENTION

The present invention generally relates to the field of flow cytometry and more particularly to a nozzle assemblies for a flow cytometer systems and methods of manufacturing the same.

BACKGROUND

Flow cytometers have been known for analyzing and sorting particles, and are particularly suited to measure physical and chemical properties of biological materials, such as cells. In operation, a flow cytometer produces a fluid stream which includes a sample fluid containing particles of interest. These particles may be individually inspected in the fluid stream with a variety of sensing systems or detection devices and classified.

Sorters may additionally provide a mechanism for isolating subpopulations of particles based on their measured or determined properties. Jet-in-air flow cytometers achieve this separation through the creation and isolation of charged droplets containing particles of interest. The particle-containing droplets may be formed from the fluid stream and charged based upon a sort decision and, as they pass through an electrical field produced by deflection plates, their path is redirected into one of several predetermined trajectories for collection. The formation of these droplets may be achieved at a flow cytometer nozzle.

In addition to the function of droplet formation, a flow cytometer nozzle may aide in biasing particles toward a uniform orientation. This function enables the analysis and sorting of cells which have aspherical properties. In particular, the speeds at which sperm can be sorted into gender enriched populations have been increased, in part, due to the development of an orienting nozzle which presents a larger portion of the sperm in a relatively uniform orientation.

SUMMARY OF THE INVENTION

Certain embodiments of the claimed invention are summarized below. These embodiments are not intended to limit the scope of the claimed invention, but rather serve as brief descriptions of possible forms of the invention. The invention may encompass a variety of forms which differ from these summaries.

One embodiment relates to a method of manufacturing a nozzle assembly. Such a method may begin with the step of obtaining one or more nozzle components and continue with molding one or more nozzle housing pieces, such that at least one nozzle housing piece is over molded onto at least one of the nozzle components. Finally the nozzle housing pieces and nozzle components may be assembled into a nozzle assembly.

One embodiment provides for a nozzle assembly constructed from a nozzle housing which encloses a nozzle cavity. A sample inlet may be formed in the nozzle housing and connected to an injection tube having a sample outlet. The injection tube can be mounted to extend along the nozzle cavity and may include a flow path providing fluid communication between the sample inlet and a sample outlet. A nozzle exit orifice may be located downstream of the sample outlet and one or more sheath inlets may be in fluid communication with the nozzle cavity.

Another embodiment provides a flow cytometer system that can include a sample source supplying sample fluid containing particles of interest, as well as, a sheath source supplying sheath fluid to a nozzle assembly for forming a fluid stream. The nozzle assembly may produce a fluid stream along a flow path with sample and sheath fluid. The nozzle assembly may include a nozzle housing which encloses a nozzle cavity. A sample inlet may be formed in the nozzle housing. An injection tube having a sample outlet can be mounted with the nozzle housing and may extend along the nozzle cavity. The injection tube can have a flow path which provides fluid communication between the sample inlet and the sample outlet. The nozzle housing may further include one or more sheath inlets in fluid communication with the nozzle cavity and a nozzle exit orifice downstream of the sample outlet. The flow cytometer may further include an excitation source for interrogating particles within the fluid stream at an inspection zone and one or more detectors for producing signals representative of emitted or reflected electromagnetic radiation at the inspection zone. An analyzer may be included for analyzing

signals produced by the one or more detectors and for making a sort decision. A charge element may charge the fluid stream according to the sort decision for deflection by deflection plates.

Still another embodiment relates to a method of sorting cells which can begin with the step of magnetically coupling a nozzle assembly having a fluid flow path to a flow cytometer. Next a fluid stream may be formed at the nozzle assembly from a sheath fluid and a sample fluid. The fluid stream may be interrogated at an inspection zone which is then perturbed into droplets. Signals representative of emitted or reflected electromagnetic radiation at the inspection zone may then be produced and analyzed for making sort decisions. Finally, droplets may be separated according to the sort decision.

Yet another embodiment provides a nozzle assembly constructed from a nozzle housing which encloses a nozzle cavity. An injection tube having a sample outlet may be disposed within the nozzle cavity and the nozzle cavity may have an elliptical cross section with a major axis at least three times the length of the minor axis at the outlet of the injection tube. One or more sheath inlets may be in fluid communication with the nozzle cavity and a nozzle exit orifice may be located downstream of the sample outlet.

Yet still another embodiment provides a method of manufacturing a flow cytometer nozzle assembly, the method comprising the steps of: a) obtaining one or more flow cytometer nozzle components including at least one injection tube having a sample fluid flow path; b) injection molding a first flow cytometer nozzle housing piece; c) over molding a second flow cytometer nozzle housing piece having a sample inlet onto the at least one injection tube in a manner that provides fluid communication between the sample inlet and the sample fluid flow path of the at least one injection tube; and d) assembling the first flow cytometer nozzle housing piece, the second flow cytometer nozzle housing piece and the one or more flow cytometer nozzle components into the flow cytometer nozzle assembly.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 illustrates a flow chart of a process for producing a nozzle assembly for a flow cytometer.

FIG. 2 illustrates a sectional view of a flow cytometer system in accordance with certain embodiments of the present invention.

FIG. 3 illustrates an exploded view of a nozzle assembly in accordance with certain embodiments of the present invention.

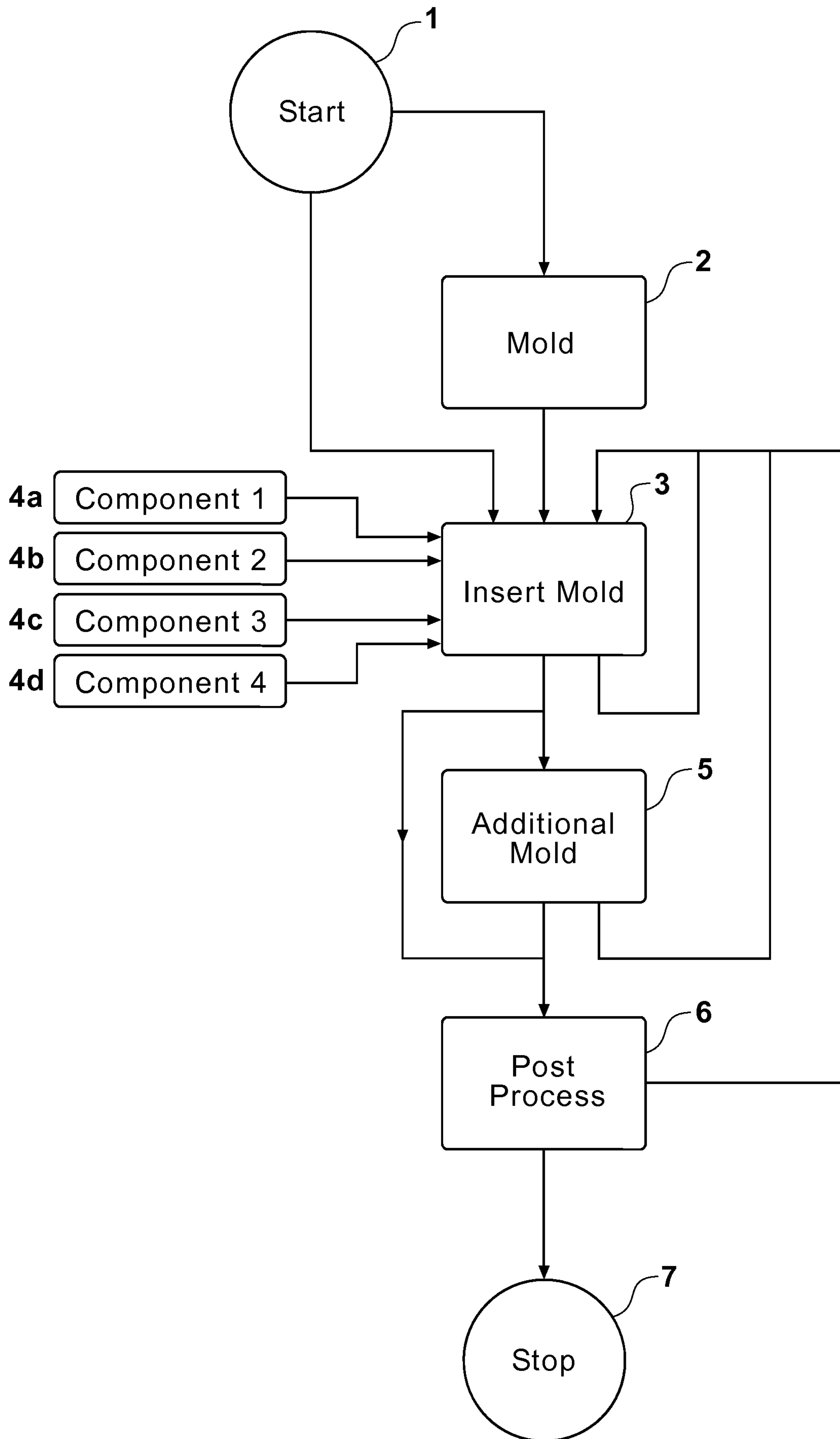
FIG. 4 illustrates a sectional view of a nozzle assembly and other flow cytometer components in accordance with certain embodiments of the present invention.

FIG. 5 illustrates a closer sectional view of a portion of a flow cytometer nozzle assembly in accordance with certain embodiments of the present invention.

FIG. 6 illustrates a sectional view of a nozzle assembly in accordance with certain embodiments of the present invention.

While the present invention may be embodied with various modifications and alternative forms, specific embodiments are illustrated in the figures and described herein by way of

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**FIG. 1**

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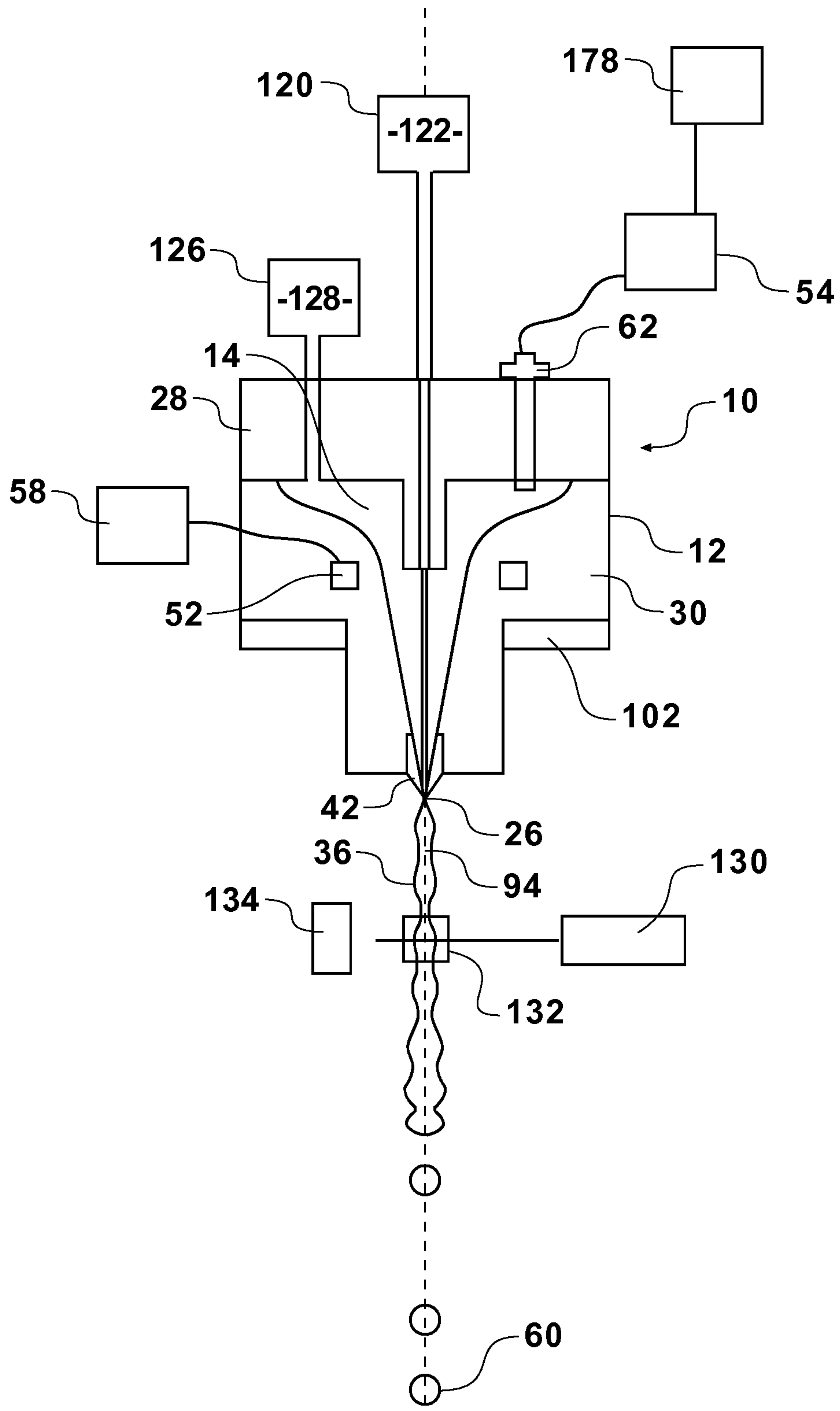


FIG. 2

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