

CLAIMS

1. A system for analysis of a biological sample, comprising:
 - a mobile device configured to receive at least one integrated chip; an integrated chip that performs a biological analysis of said sample; ~~said integrated chip being configured to analyze a biological sample loaded thereon, and~~ and said mobile device and said integrated chip together being configured to perform at least one of manipulation and control of a molecule or a fluidic system on said integrated chip; such that at least one of:
 - i) ~~a portable control assembly of the mobile device,~~
 - ii) ~~said integrated chip, and~~
 - iii) ~~a processor,~~are effective to precision control at least one and a computer processor configured to receive encoded feedback signals corresponding to at least one nanoscale parameter that governs to be controlled under closed-loop control, to thereby effect precision control of at least one of a plurality of steps of the analysis parameter related to the biological analysis of the biological sample on the integrated chip using closed loop feedback control of the nanoscale parameter, said biological analysis including extracting, optionally amplifying, and detecting at least one component of said sample.

2. The system of Claim 1, wherein said mobile device ~~and said integrated chip are together configured such that at least one of:~~ (i) ~~said portable control assembly of the mobile device,~~ (ii) said integrated chip, and (iii) said processor; are effective to precision control at least one of: fluid flow, fluid pressure, temperature, tension on a nucleic acid, and concentration of at least one reagent, on said integrated chip.

3. The system of Claim 1, wherein said integrated chip comprises:
 - an extraction module;
 - a nucleic acid amplification module, in fluid communication with an extraction module;
 - a biological sample detection module in fluid communication with said nucleic acid amplification module or said extraction module; and
 - said portable control assembly is configured to process said integrated chip to analyze a biological sample loaded thereon by employing:
 - an extraction control module;

a nucleic acid amplification control module operably connected to the extraction control module; and

a biological sample detection control module.

4. The system of Claim 3, wherein said extraction control module further comprises fluid pressure generating means for generating sufficient fluid pressure to shear cells in the biological sample loaded onto the integrated chip.
5. The system of Claim 3, wherein said extraction control module further comprises a means for retaining or capturing magnetic particles on said integrated chip.
6. The system of Claim 3, wherein the nucleic acid amplification control module is configured to effect precision control of the nucleic acid amplification module of the integrated chip.
7. The system of Claim 6, wherein the nucleic acid amplification control module is configured to apply tension to nucleic acid strands within said integrated chip.
8. The system of Claim 7, wherein said tension is applied using one or more of applying mechanical tension, hydrodynamic tension or electromagnetic tension.
9. The system of Claim 1, wherein at least one of said mobile device and said integrated chip are configured, individually or in combination, to quantify at least one of a viral load and a bacterial load in the biological sample.
10. A system for analysis of biological samples, comprising:
 - a computer processor;
 - a hardware system that receives at least one integrated chip,
 - ~~said~~ an integrated chip comprising:
 - a port for loading a biological sample and, optionally, one or more reagents, onto the integrated chip;
 - a nucleic acid extraction module;
 - a nucleic acid amplification module, in fluid communication with the nucleic acid extraction module; and
 - a nucleic acid separation module, in fluid communication with the nucleic acid amplification module,

wherein one or more of said hardware system and said integrated chip are configured to provide individually or in combination, at least one of:

- a nucleic acid extraction control module;
- a nucleic acid amplification control module; and
- a nucleic acid detection control module;

said computer processor being configured to receive encoded feedback signals corresponding to at least one nanoscale parameter to be controlled under closed-loop control, to thereby effect precision control of at least one parameter related to the biological analysis of the biological sample on said integrated chip using closed loop feedback control of the nanoscale parameter, said biological analysis including extracting, optionally amplifying, and detecting at least one component of said sample

~~at least one of the nucleic acid extraction module, nucleic acid amplification module, nucleic acid separation module, nucleic acid extraction control module, nucleic acid amplification control module, and nucleic acid detection control module, being configured to provide precision control of at least one parameter that governs at least one of a plurality of steps of the analysis of the biological sample using closed loop control;~~
and

a means for generating fluid pressure for moving at least one of the biological sample and a nucleic acid through the integrated chip.

11. The system of Claim 10, wherein one or more of said hardware system and said integrated chip are configured to provide, individually or in combination, at least one of: a means for retaining or capturing magnetic beads; a means for fluorescence detection; a data storage or processing device; a device configured to transfer data wirelessly; a means for displaying data; a processing unit for storing and executing instructions.
12. The system of Claim 10, wherein said system is configured to control a nanoscale parameter that governs a reaction used to analyze the biological sample to within plus or minus 10%, plus or minus 1%, plus or minus 0.1%, plus or minus 0.01%, plus or minus 0.001% or plus or minus 0.0001%.
13. A method for analysis of biological samples, comprising:
subjecting a biological sample to at least one of:

- i) precision control of at least one parameter that governs at least one of a plurality of steps of the analysis of the biological sample using closed loop control;
- ii) precision control of at least one environmental or operational parameter of the analysis of ~~biological~~ biological sample using closed loop control;
- iii) precision control of extraction to provide an extracted nucleic acid component of the biological sample using closed loop control;
- iv) precision control of amplification to provide an amplicon from the extracted nucleic acid component using closed loop control; and
- v) precision control of detection of the extracted nucleic acid component using closed loop control;

such that in each of i)—v) said precision control is performed using a computer processor configured to receive encoded feedback signals corresponding to at least one nanoscale parameter to be precision controlled under closed-loop control of said nanoscale parameter.

14. The method of Claim 13 ~~3~~ comprising performing precision control of at least one of: fluid flow, fluid pressure, temperature, tension on a nucleic acid, and concentration of at least one reagent, on said integrated chip.
15. The method of claim 14 ~~4~~, further comprising:
 - a) detecting a nucleic acid from the biological sample;
 - b) determining at least one biomarker associated with a person who is the source of the at least one biological sample; and
 - c) based on the at least one biomarker, determining at least one of:
 - i) a dosage of at least one drug to effect therapeutic treatment of a disease condition associated with the at least one biomarker;
 - ii) a combination of a plurality of drugs to effect therapeutic treatment of the disease condition associated with the at least one biomarker; and
 - iii) a determination of whether the person who is the source of the at least one biological sample is a responder to a drug therapy for the disease condition associated with the at least one biomarker.
16. The method of Claim 15 ~~5~~ comprising determining at least one of:

- i) a dosage of at least one drug to effect therapeutic treatment of a disease condition associated with the at least one biomarker; and
- ii) a combination of a plurality of drugs to effect therapeutic treatment of the disease condition associated with the at least one biomarker;

wherein the at least one biomarker is specific to a specific strain of a pathogen or disease, or to a specific health or wellness condition.

17. The method of Claim 16 ~~6~~, further comprising determining uniquely at least one of the dosage of the at least one drug and the combination of the plurality of drugs based on the specific strain.
18. The method of Claim 13 ~~3~~, further comprising providing information relevant to the condition of a subject, the condition being selected from the group consisting of: sports nutrition of the subject; diet of the subject; a nutritional allergy, deficiency, sensitivity or intolerance of the subject; an inflammatory marker, at least one RNA marker for at least one type of phenotypic expression in the subject; determining at least one probiotic or prebiotic that is deficient or altered in a microbiome of the subject; a nucleic acid indicative of a type or subtype of diabetes in the subject; a biomarker implicated in an atherosclerotic process in the subject.
19. The method of Claim 13 ~~3~~, further comprising diagnosing, classifying, or monitoring a chronic disease via a nucleic acid marker.
20. The method of Claim 13 ~~3~~, comprising performing at least one of:
 - point-of-care detection of an infectious disease or a cancer;
 - drug monitoring;
 - precision or personalized medicine;
 - prevention of mother to child transmission;
 - using a device as a prognostic indicator of disease; and
 - using a device as a theragnostic device.
21. The method of Claim 20, comprising performing at least one of: point-of-care detection of an HIV strain, point-of-care HIV viral load determination and point-of-care HIV genotyping.

22. The method of Claim 20, wherein the infectious disease comprises a hemorrhagic fever or hepatitis.
- ~~23. A method for analysis of biological samples, comprising:~~
- ~~a) providing at least one integrated chip, said integrated chip comprising:~~
 - ~~a protein extraction module; and~~
 - ~~a protein detection module, in fluid communication with the protein extraction module;~~
 - ~~b) loading the at least one biological sample onto the at least one integrated chip;~~
 - ~~c) operably connecting a portable control assembly with at least one integrated chip, said portable control assembly comprising:~~
 - ~~a protein extraction control module; and~~
 - ~~a protein detection control module operably connected with the protein extraction module; and~~
- ~~activating the portable control assembly to effect extraction and detection of protein from the biological sample loaded onto said integrated chip using closed loop control.~~
- 24~~23~~. A system for analysis of a biological sample, comprising:
- a mobile device configured to receive at least one integrated chip, ~~said~~ an integrated chip that performs a biological analysis of said sample; said mobile device and said integrated chip being configured to analyze a biological sample loaded thereon, and a computer processor configured to receive feedback signals corresponding to at least one nanoscale parameter to be controlled under closed-loop control, to thereby effect precision control of at least one of: ~~a) at least one parameter that governs at least one of a plurality of steps of the analysis of the biological sample; or b) at least one action of extraction, amplification or detection parameter related to the biological analysis of the biological sample on said integrated chip using closed loop feedback control of the nanoscale parameter, said biological analysis including extracting, optionally amplifying, and detecting at least one component of said sample.~~
- 25~~24~~. The system of Claim 24~~23~~, wherein said nanoscale parameter is selected from the group consisting of: fluid flow, fluid pressure, temperature, tension on a nucleic acid, and concentration of at least one reagent.

- ~~26~~25. The system of Claim ~~24~~23, wherein said integrated chip comprises:
- an extraction module;
 - a amplification module, in fluid communication with said extraction module; and
 - a biological sample detection module in fluid communication with said amplification module or said extraction module.
- ~~27~~26. The system of Claim ~~26~~25, wherein said computer processor receives feedback signals from at least one of said extraction module, said amplification module, and said biological sample detection module.
- ~~28~~27. The system of Claim 26, wherein said extraction module further comprises fluid pressure generating means for generating sufficient fluid pressure to shear cells in the biological sample loaded onto the integrated chip.
- ~~29~~28. The system of Claim 26, wherein said extraction module further comprises a means for retaining or capturing magnetic particles on said integrated chip.
- ~~30~~29. The system of Claim 26, wherein said computer processor receives feedback control signals from said amplification module to effect precision control of at least one parameter of amplification module.
- ~~31~~30. The system of Claim ~~30~~29, wherein the amplification module includes elements configured to apply tension to nucleic acid strands within said integrated chip.
- ~~32~~31. The system of Claim ~~31~~30, wherein said amplification module is configured to apply said tension mechanically, hydrodynamically, or electromagnetically.
- ~~33~~32. The system of Claim ~~24~~23, wherein said computer processor is further configured to determine a viral load or a bacterial load in said biological sample.
- ~~34~~33. A system for analysis of biological samples, comprising:
- an integrated chip, said integrated chip comprising:
 - a port for loading a biological sample and, optionally, one or more reagents, onto the integrated chip;
 - an extraction module in fluid communication with said port;
 - an amplification module in fluid communication with the nucleic acid extraction module; and

a separation module, in fluid communication with the amplification module;
 a fluid pressure generator in fluid communication with said integrated chip; and
 a computer processor configured to receive feedback signals from at least one of said
 extraction module, said amplification module, or said separation module, said feedback
 signals corresponding to at least one nanoscale parameter to be controlled under
 closed-loop control, to effect precision control of at least one of: a) at least one
~~parameter that governs at least one of a plurality of steps of the analysis of the~~
~~biological sample; or b) at least one action of extraction, amplification or~~
detection parameter related to the biological analysis of the biological sample on said
integrated chip using closed loop feedback control of the nanoscale parameter, said
biological analysis including extracting, optionally amplifying, and detecting at least
one component of said sample.

- ~~3534.~~ The system of Claim ~~3433~~, wherein said system further includes a biological sample
 detection module, and said computer processor receives feedback signals from at least
 one of said extraction module, said amplification module, said separation module, and
 said biological sample detection module.
- ~~3635.~~ The system of Claim ~~3433~~, wherein said extraction module further comprises fluid
 pressure generating means for generating sufficient fluid pressure to shear cells in the
 biological sample loaded onto the integrated chip.
- ~~3736.~~ The system of Claim ~~3635~~, wherein said extraction module further comprises a means for
 retaining or capturing magnetic particles on said integrated chip.
- ~~3837.~~ The system of Claim ~~3736~~, wherein said computer processor receives feedback control
 signals from said amplification module to effect precision control of at least one
 parameter of said amplification module.
- ~~3938.~~ The system of Claim ~~3433~~, wherein the amplification module includes elements
 configured to apply tension to nucleic acid strands within said integrated chip.
- ~~4039.~~ The system of Claim ~~3938~~, wherein said amplification module is configured to apply said
 tension mechanically, hydrodynamically, or electromagnetically.

~~4140~~. The system of Claim ~~3433~~, wherein said computer processor is further configured to determine a viral load or a bacterial load in said biological sample.

~~4241~~. A method for analyzing a biological sample using a mobile device configured to receive at least one integrated chip that is configured to analyze said biological sample, comprising:

receiving feedback signals from said integrated chip at a computer processor, said feedback signals corresponding to at least one nanoscale parameter to be controlled under closed-loop control, and said computer processor effect precision control of at least one ~~of a) at least one parameter that governs at least one of a plurality of steps of the analysis of the biological sample, or b) at least one action of extraction, amplification or detection, in response to said feedback signals~~ parameter related to the biological analysis of the biological sample on said integrated chip using closed loop feedback control of the nanoscale parameter, said biological analysis including extracting, optionally amplifying, and detecting at least one component of said sample.

~~4342~~. The method of Claim ~~4241~~, wherein said parameter is selected from the group consisting of: fluid flow, fluid pressure, temperature, tension on a nucleic acid, and concentration of at least one reagent.

~~4443~~. The method of Claim ~~4241~~, further comprising:

passing said sample into an extraction module located on said integrated chip to create a nucleic acid sample mixture;

passing said nucleic acid sample mixture into a amplification module on said integrated chip, said amplification module in fluid communication with said extraction module, to create an amplified nucleic acid mixture; and

passing said amplified nucleic acid mixture into a biological sample detection module in fluid communication with said amplification module or said extraction module.

- ~~45~~44. The method of Claim ~~44~~43, further comprising receiving feedback signals from at least one of said extraction module, said amplification module, and said biological sample detection module, at said computer processor.
- ~~46~~45. The method of Claim ~~44~~43, further comprising generating sufficient fluid pressure to shear cells in the biological sample loaded onto the integrated chip.
- ~~47~~46. The method of Claim ~~44~~43, further comprising retaining or capturing magnetic particles on said integrated chip.
- ~~48~~47. The method of Claim ~~44~~43, further comprising receiving feedback control signals from said amplification module at said computer processor to effect precision control of at least one nanoscale parameter of said amplification module.
- ~~49~~48. The method of Claim ~~48~~47, further comprising applying tension to nucleic acid strands using elements in said amplification module.
- ~~50~~49. The method of Claim ~~49~~48, wherein said amplification module is configured to apply said tension mechanically, hydrodynamically, or electromagnetically.
- ~~51~~50. The method of Claim ~~42~~41, further comprising determining a viral load or a bacterial load in said biological sample using said computer processor.
- ~~52~~51. A method for analysis of biological samples, comprising:
- loading said biological sample into a port for loading a biological sample and, optionally, one or more reagents, onto ~~the~~ an integrated chip;
 - extracting nucleic acids using said biological sample using an extraction module, said extraction module being in fluid communication with said port to create a mixture of nucleic acids;
 - amplifying at least one nucleic acid using said mixture of nucleic acids using an amplification module, said amplification module being in fluid communication with the nucleic acid extraction module to create amplified nucleic acids;
 - separating said nucleic acids using a separation module, said separation module being in fluid communication with the amplification module;

generating fluid pressure using a fluid pressure generator in fluid communication with said integrated chip; and

receiving feedback signals from said integrated chip at a computer processor, said feedback signals corresponding to at least one nanoscale parameter to be controlled under closed-loop control, and said computer processor effect precision control of at least one ~~of a) at least one parameter that governs at least one of a plurality of steps of the analysis of the biological sample, or b) at least one action of extraction, amplification or detection, in response to said feedback signals~~ parameter related to the biological analysis of the biological sample on said integrated chip using closed loop feedback control of the nanoscale parameter, said biological analysis including extracting, optionally amplifying, and detecting at least one component of said sample.

- ~~5352.~~ The method of Claim ~~5251~~, wherein said method further includes a biological sample detection module, and said computer processor receives feedback signals from at least one of said extraction module, said amplification module, said separation module, and said biological sample detection module.
- ~~5453.~~ The method of Claim ~~5251~~, wherein said extraction module further comprises fluid pressure generating means for generating sufficient fluid pressure to shear cells in the biological sample loaded onto the integrated chip, and said method further includes generating fluid pressure sufficient to shear said cells in said biological sample.
- ~~5554.~~ The method of Claim ~~5453~~, wherein said extraction module further comprises a means for retaining or capturing magnetic particles on said integrated chip, and said method includes retaining or capturing said magnetic particles.
- ~~5655.~~ The method of Claim ~~5554~~, wherein said computer processor receives feedback control signals from said amplification module, and said method further includes effecting precision control of at least one parameter of said amplification module using said feedback control signals.
- ~~5756.~~ The method of Claim ~~5251~~, wherein the amplification module includes elements configured to apply tension to nucleic acid strands within said integrated chip, and said method includes applying tension so said nucleic acid strands using said elements.

- ~~58~~57. The method of Claim ~~57~~56, wherein said tension is applied mechanically, hydrodynamically, or electromagnetically.
- ~~59~~58. The method of Claim ~~52~~51, further comprising using said computer processor to determine a viral load or a bacterial load in said biological sample.