CLAIMS

What is claimed is:

1. A method for manufacturing a polynucleotide using a microfluidic driver apparatus operating on a cartridge, the method comprising:

forming, in a cartridge, a therapeutic polynucleotide, and

determining, by the microfluidic driver apparatus, a concentration of the therapeutic polynucleotide by:

driving a first blank solution into an ultraviolet (UV) measurement chamber of the cartridge and taking a first absorption measurement through the cartridge,

driving a sample solution of the therapeutic polynucleotide into the UV measurement chamber of the cartridge and taking a second absorption measurement through the cartridge, and

estimating a concentration of the therapeutic polynucleotide from the first and second absorption measurements.

2. The method of claim 1, further comprising adjusting, in a processor of the microfluidic driver apparatus, the operation of the microfluidic driver apparatus based on the estimated concentration of the therapeutic polynucleotide.

3. The method of claim 1 or 2, further comprising comparing, by a processor of the microfluidic driver apparatus, the estimated concentration of the therapeutic polynucleotide to a concentration range, and based on this comparison, directing the therapeutic polynucleotide for one of: pooling with one or more additional batches of therapeutic polynucleotide formed in the cartridge, waste, or further analysis.

4. A method for manufacturing a polynucleotide using a microfluidic driver apparatus operating on a cartridge, the method comprising:

forming, in a cartridge, a therapeutic polynucleotide, wherein the therapeutic polynucleotide comprises a therapeutic mRNA;

determining, by the microfluidic driver apparatus, a concentration of the therapeutic mRNA by:

driving a first blank solution into an ultraviolet (UV) measurement chamber of the cartridge and taking a first absorption measurement through the cartridge,

driving a sample solution of the therapeutic polynucleotide into the UV measurement chamber of the cartridge and taking a second absorption measurement through the cartridge,

driving a second blank solution into the UV measurement chamber of the cartridge and taking a third absorption measurement through the cartridge, and

estimating a concentration of the therapeutic polynucleotide from the first, second and third absorption measurements; and

adjusting, in a processor of the microfluidic driver apparatus, the operation of the microfluidic driver apparatus based on the estimated concentration of the therapeutic polynucleotide.

5. A system for making and/or processing a polynucleotide, the system comprising: a cartridge mount;

a plurality of pressure lines;

a plurality of fluidic lines, each coupled with or configured to couple with a fluid source, wherein each fluidic line and at least a subset of the pressure lines are configured to be secured to inlet or outlet ports on a cartridge held in the cartridge mount;

an ultraviolet (UV) light source;

a UV light detector; and

a controller configured to control application of pressure through the pressure lines to drive fluid through the cartridge, wherein the controller is further configured to direct the formation of a therapeutic polynucleotide in the cartridge, and to estimate a concentration of the therapeutic polynucleotide by driving a first blank solution through a UV measurement chamber of the cartridge and taking a first absorption measurement using the UV light source and UV light receiver, driving a sample solution including the

therapeutic polynucleotide through the UV measurement chamber of the cartridge and taking a second absorption measurement using the UV light source and UV light receiver, further wherein the controller is configured to estimate the concertation of the therapeutic polynucleotide from the first and second absorption measurement.

6. The system of claim 5, wherein the controller is further configured to modify operation of the system based on the estimated concentration of the therapeutic polynucleotide.

7. The system of claim 5 or 6, wherein the controller is further configured to compare the estimated concentration of the therapeutic polynucleotide to a concentration range and, based on this comparison, to direct the therapeutic polynucleotide for one of: pooling with one or more additional batches of therapeutic polynucleotide formed in the cartridge, waste, or further analysis.

8. A system for making and/or processing a polynucleotide, the system comprising:

a cartridge; and

a microfluidic driver apparatus comprising:

a cartridge mount;

a plurality of pressure lines;

a plurality of fluidic lines, each coupled with or configured to couple with a fluid source, wherein each fluidic line and at least a subset of the pressure lines are configured to be secured to inlet or outlet ports on a cartridge held in the cartridge mount;

an ultraviolet (UV) light source;

a UV light detector; and

a controller configured to control application of pressure through the pressure lines to drive fluid through the cartridge, wherein the controller is further configured to direct the formation of a therapeutic polynucleotide, further wherein the controller is configured to estimate a concentration of the therapeutic

polynucleotide by driving a first blank solution through a UV measurement chamber of the cartridge and taking a first absorption measurement using the UV light source and UV light receiver, driving a sample solution including the therapeutic polynucleotide through the UV measurement chamber of the cartridge and taking a second absorption measurement using the UV light source and UV light receiver, and driving a second blank solution though the UV measurement chamber of the cartridge and taking a third absorption measurement using the UV light source and UV light receiver; modifying operation of the microfluidic driver apparatus based on the concertation of the therapeutic polynucleotide determined from the first, second and third absorption measurement.

9. A method for manufacturing a polynucleotide using a microfluidic driver apparatus operating on a cartridge, the method comprising:

forming, in a cartridge, a therapeutic polynucleotide; and

determining, by the microfluidic driver apparatus, a concentration of the therapeutic polynucleotide by:

driving a first blank solution into a concentration measurement chamber of the cartridge and taking a first measurement through the cartridge,

driving a sample solution of the therapeutic polynucleotide into the concentration measurement chamber of the cartridge and taking a second measurement through the cartridge, and

estimating a concentration of the therapeutic polynucleotide from the first and second measurements; and

comparing, by a processor of the microfluidic driver apparatus, the estimated concentration of the therapeutic polynucleotide to a concentration range, and based on this comparison, directing the therapeutic polynucleotide for one of: pooling with one or more additional batches of therapeutic polynucleotide formed in the cartridge, waste, or further analysis.

10. The method of claim 9, the concentration measurement chamber comprising an

ultraviolet (UV) measurement chamber, the first measurement comprising a. first absorption measurement, the second measurement comprising a second absorption measurement.

11. The method of claim 10, wherein estimating the concentration of the therapeutic polynucleotide further comprises changing one or more of a sensitivity of a UV detector and an intensity of a UV emitter of the microfluidic driver apparatus in response to the second absorption measurement through the cartridge.

12. The method of claim 10 or 11, further comprising pretreating the UV measurement chamber with UV light prior to taking the first absorption measurement through the cartridge.

13. A system for making and/or processing a polynucleotide, the system comprising:

a cartridge mount;

a plurality of pressure lines;

a plurality of fluidic lines, each coupled with or configured to couple with a fluid source, wherein each fluidic line and at least a subset of the pressure lines are configured to be secured to inlet or outlet ports on a cartridge held in the cartridge mount; and

a controller configured to control application of pressure through the pressure lines to drive fluid through the cartridge, wherein the controller is further configured to direct the formation of a therapeutic polynucleotide in the cartridge, and to estimate a concentration of the therapeutic polynucleotide by driving a first blank solution through a measurement chamber of the cartridge and taking a first measurement of the first blank sample in the measurement chamber, driving a sample solution including the therapeutic polynucleotide through the measurement chamber of the cartridge and taking a second measurement of the sample solution in the measurement chamber, further wherein the controller is configured to estimate the concertation of the therapeutic polynucleotide from the first and second measurement.

14. The system of claim 13, further comprising:

an ultraviolet (UV) light source; and

a UV light detector;

wherein the controller is configured to take the first measurement in the form of a first absorption measurement using the UV light source and the UV light receiver;

wherein the controller is configured to take the second measurement in the form of a second absorption measurement using the UV light source and the UV light receiver;

wherein the controller is configured to estimate the concertation of the therapeutic polynucleotide from the first and second absorption measurement.

15. The system of claim 14, wherein the controller is further configured to change one or more of a sensitivity of the UV detector and an intensity of the UV light source in response to the second absorption measurement through the cartridge.

16. The system of claim 14 or 15, wherein the controller is further configured to pretreat the UV measurement chamber with UV light prior to taking the first absorption measurement through the cartridge.

17. A method comprising:

emitting ultraviolet (UV) light through a UV measurement chamber of a cartridge, the UV measurement chamber being configured to receive fluid;

receiving the UV light at a UV light detector, the received UV light having passed through the UV measurement chamber of the cartridge;

measuring a maximum voltage of the UV light detector,

measuring a standard deviation of a signal from UV the light detector;

determining an upper limit of quantitation (LoQ) based on the measured maximum voltage and based on the measured standard deviation;

determining a lower LoQ based on the measured maximum voltage and based on the measured standard deviation;

determining whether the upper LoQ and the lower LoQ are acceptable; and

either:

allowing the cartridge to be used to generate a therapeutic polynucleotide if the upper LoQ and the lower LoQ are acceptable, or

providing an alert if one or both of the upper LoQ or the lower LoQ is not acceptable.

18. The method of claim 17, further comprising forming or processing a therapeutic polynucleotide on the cartridge.

19. A method comprising:

emitting ultraviolet (UV) light through a UV measurement chamber of a cartridge, the UV measurement chamber containing fluid;

receiving the UV light at a UV light detector, the received UV light having passed through the UV measurement chamber of the cartridge;

obtaining a first plurality of concentration measurements, each concentration measurement of the first plurality of concentration measurements indicating a respective concentration of fluid in the UV measurement chamber;

calculating a mean of the first plurality of concentration measurements;

comparing each concentration measurement of the first plurality of concentration measurements to the mean of the first plurality of concentration measurements;

identifying an outlier from among the first plurality of concentration measurements relative to the mean of the first plurality of concentration measurements;

establishing a second plurality of concentration measurements, the second plurality of concentration measurements comprising the first plurality of concentration measurements with the identified outlier removed;

calculating a mean of the second plurality of concentration measurements; and

reporting the mean of the second plurality of concentration measurements.

20. The method of claim 19, the first plurality of concentration measurements comprising four concentration measurements.

21. The method of claim 19 or 20, the second plurality of concentration measurements comprising three concentration measurements.