Claims

1. A method for preparing an aqueous solution of a defined pH comprising an acid, a base and optionally one or more additives, the method comprising the steps of:
a) calculating the theoretical concentrations of acid and base for the solution to have the defined pH using the Henderson-Hasselbach equation in combination with the Debye Huckel theory for at least 5 different additive concentrations;
b) preparing a sample of the solution for each additive concentration and measuring the actual pH for each additive concentration;
c) calculating a value for delta pH, ΔpH, being the difference between the theoretical pH and the actual pH, for each additive concentration;
d) generating a mathematical model describing the relationship of ΔpH with additive concentration for the at least 5 different additive concentrations;
e) selecting the defined pH and additive concentrations;
f) using the mathematical model generated in step d) to calculate ΔpH for the defined pH and additive concentration;
g) calculating a ΔpH-corrected pH by summing the defined pH and delta pH;
h) using the ΔpH-corrected pH to calculate the concentrations of acid and base using the Henderson-Hasselbach equation in combination with the Debye Huckel theory;
i) preparing the solution using the concentrations calculated in step h).

2. A method for preparing an aqueous solution of a defined pH comprising an acid, a base and optionally one or more additives, the method comprising the steps of:
a) calculating the theoretical concentrations of acid, base and additives for the solution to have the defined pH using the Henderson-Hasselbach equation in combination with the Debye Huckel theory for at least 5 different additive concentrations;
b) calculating a value for ΔpH, being the difference between the theoretical pH and a value, preferably a predetermined value, for the actual pH, for each additive concentration;
c) generating a mathematical model describing the relationship of ΔpH with additive concentration for the at least 5 different additive concentrations;
d) selecting the defined pH and additive concentration;
e) using the mathematical model generated in step c) to calculate ΔpH for the defined pH and additive concentration;
f) calculating a ΔpH-corrected pH by summing the defined pH and ΔpH;
g) using the ΔpH-corrected pH to calculate the concentrations of acid and base using the Henderson-Hasselbach equation in combination with the Debye Huckel theory;
h) preparing the solution using the concentrations calculated in step g).

3. A method for preparing an aqueous solution of a defined pH, comprising an acid, a base and an additive, the method comprising the steps of:
a) calculating the theoretical pH for the solution using the Henderson-Hasselbach equation in combination with the Debye Huckel theory;
b) calculating a ΔpH-corrected pH for the aqueous solution by comparing the theoretical pH with a pH value calculated from an equation determined from a mathematical model of the difference between the theoretical pH and a value, preferably a predetermined value, for the actual pH of the aqueous solution for at least 5 different additive concentrations;
c) using the ΔpH-corrected pH to calculate the concentrations of acid and base using the Henderson-Hasselbach equation in combination with the Debye Huckel theory;
d) preparing the solution using the concentrations calculated in step c).

4. A method according to any of claims 1 to 3, wherein the aqueous solution is a buffer, preferably a buffer employed in the processing of biomolecules.

5. A method according to claim 4, wherein the buffer is selected from the group consisting of tris buffers; sodium phosphate buffers; potassium phosphate buffers; sodium acetate buffers; MES buffers; and HEPES buffers.

6. A method according to any preceding claim, wherein the additive is a salt selected from the group consisting of NaCl, KCl, Na_2SO_4, $(NH_4)_2SO_4$ and $(NH_4)_3PO_4$ and mixtures thereof.

7. A method according to claim 6, wherein the salt is at a concentration of up to 2M.

8. A method according to any preceding claim, wherein the minimum additive concentration in the range of additive concentrations is selected to be below, and the maximum additive concentration in the range of additive concentrations is selected to be above, the additive concentration of the aqueous solution to be prepared.

9. A method according to any preceding claim, wherein the number of data points in the range of additive concentrations is from 5 to 10.

10. A method according to any preceding claim, wherein the defined pH is selected to be within 1 unit of the thermodynamic pKa value for the solution.

11. Apparatus for preparing an aqueous solution of a defined pH comprising a metering device capable of feeding into a mixing device an acid and a base, one or more additives, and optionally a diluent wherein the metering device operates under the control of control apparatus for carrying out steps a) and c) to h) of claim 1; steps a) to g) of claim 2; or steps a) to c) of claim 3.

12. Apparatus according to claim 11, and further comprising a means for carrying out a bioprocessing operation.

13. Apparatus according to claim 12, wherein the bioprocessing operation comprises chromatography, viral inactivation, filtration, refolding, ultrafiltration, diafiltration, microfiltration, in-line conditioning or refolding.

14. Apparatus according to any one of claims 11 to 13, wherein the metering device comprises a pump located downstream of a multiple inlet flow-controller and upstream of a mixing device.