



(12) **United States Patent**
Hellerbrand et al.

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(54) **PROCESS FOR STABILIZING PROTEINS**

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patent is extended or adjusted under 35
U.S.C. 154(b) by 0 days.

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(30) **Foreign Application Priority Data**

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Feb. 19, 1998 (EP) 98102846

(51) **Int. Cl.**⁷ **C12Q 1/34**; C12N 9/96;
C12N 5/02; G01N 33/53; A61K 39/395

(52) **U.S. Cl.** **424/130.1**; 435/188; 435/963;
435/390; 530/387.1; 530/350; 530/380;
424/177.1

(58) **Field of Search** 530/350, 380,
530/387.1, 390.5; 435/390.5, 188, 963,
18; 424/177.1, 130.1

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(57) **ABSTRACT**

An aqueous protein solution buffered with a potassium
phosphate buffer, in which the ratio of potassium ions to
sodium ions in the solution is at least 10:1, is resistant to the
formation of protein aggregates and particles under condi-
tions of freezing, thawing, lyophilization, and reconstitution.

45 Claims, 4 Drawing Sheets

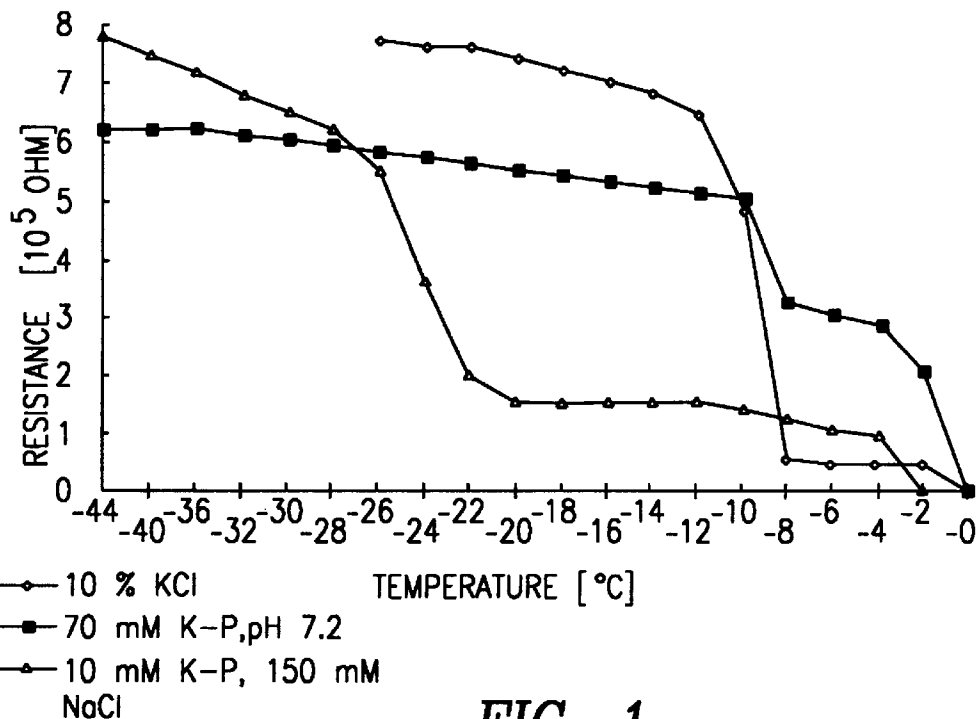


FIG. 1

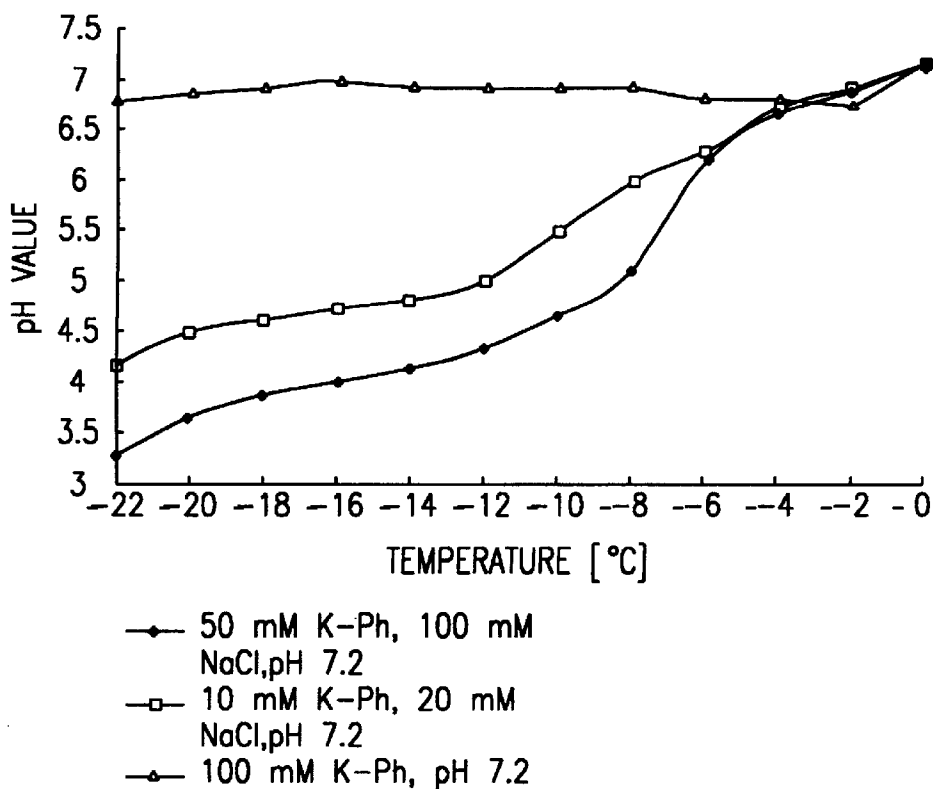


FIG. 2

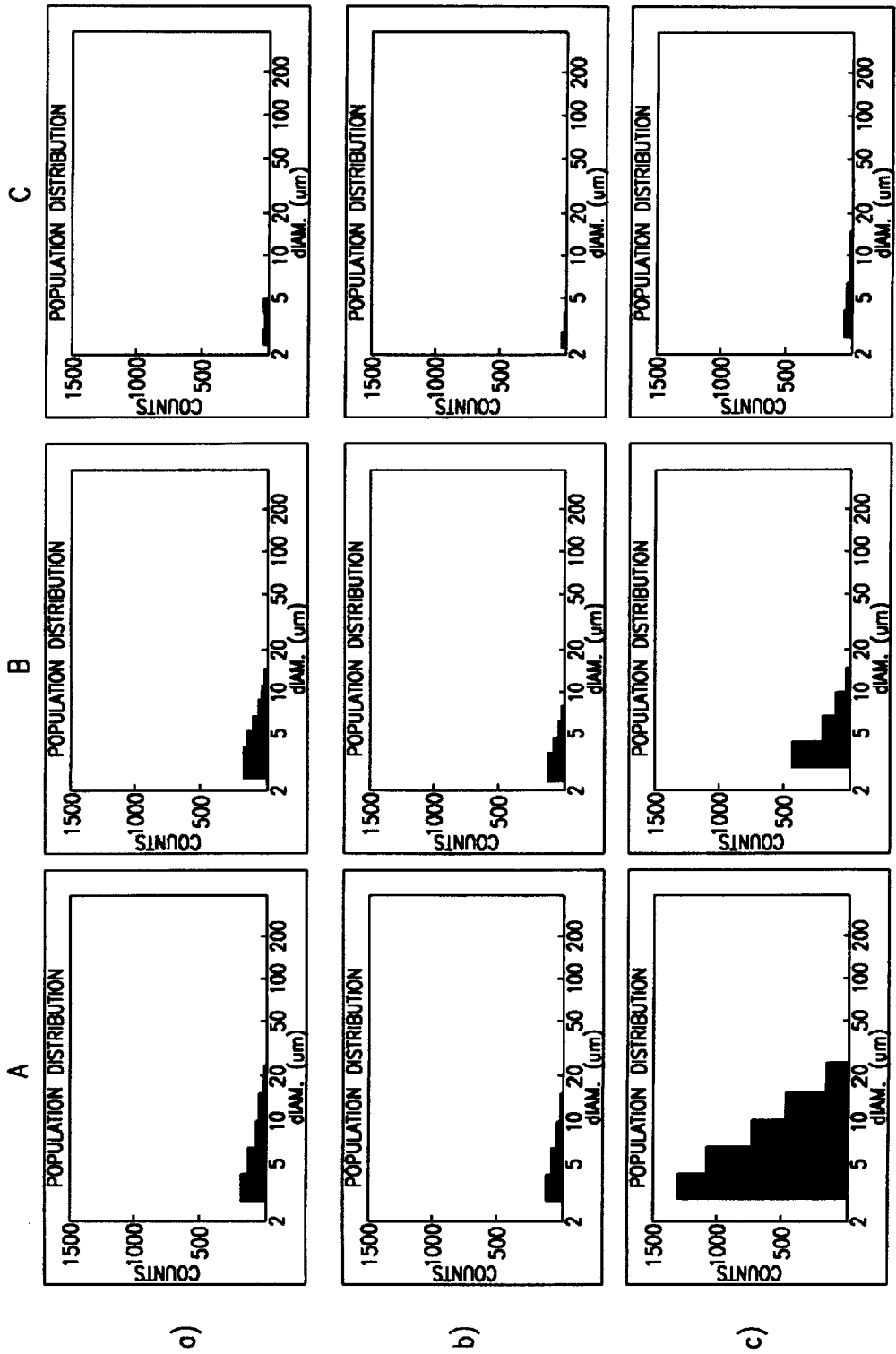


FIG. 3

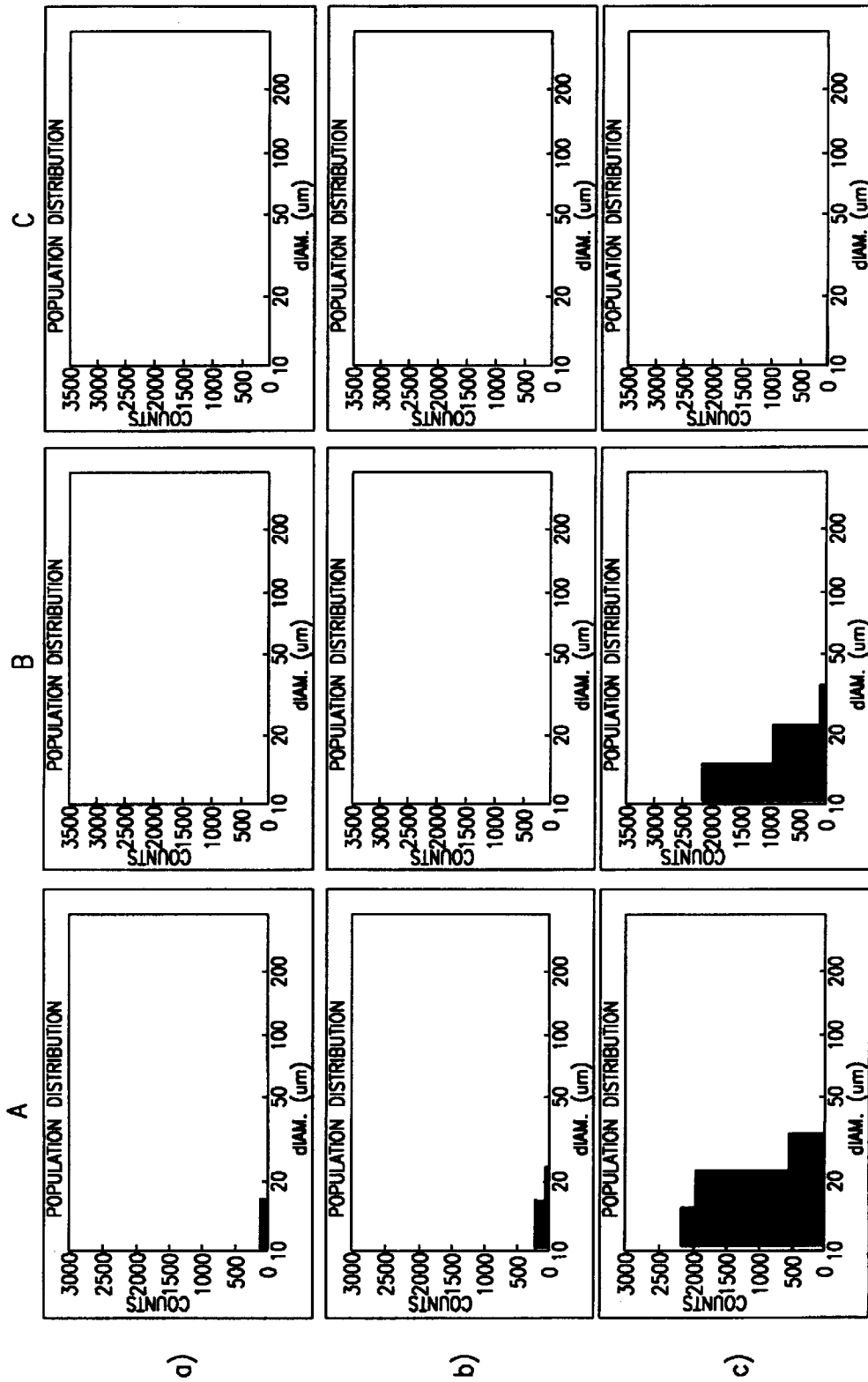


FIG. 4

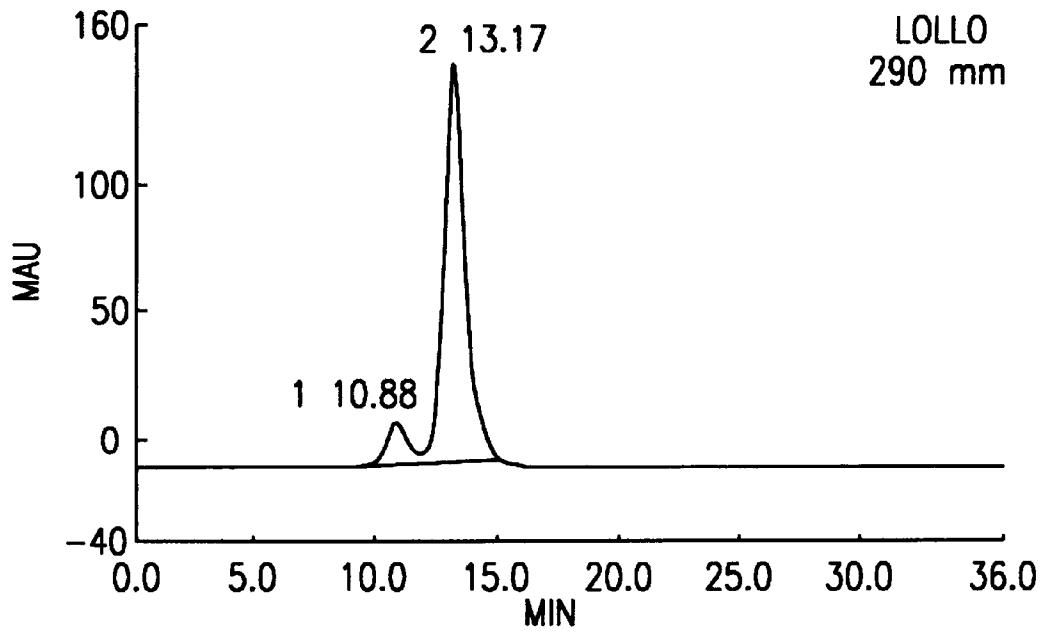


FIG. 5A

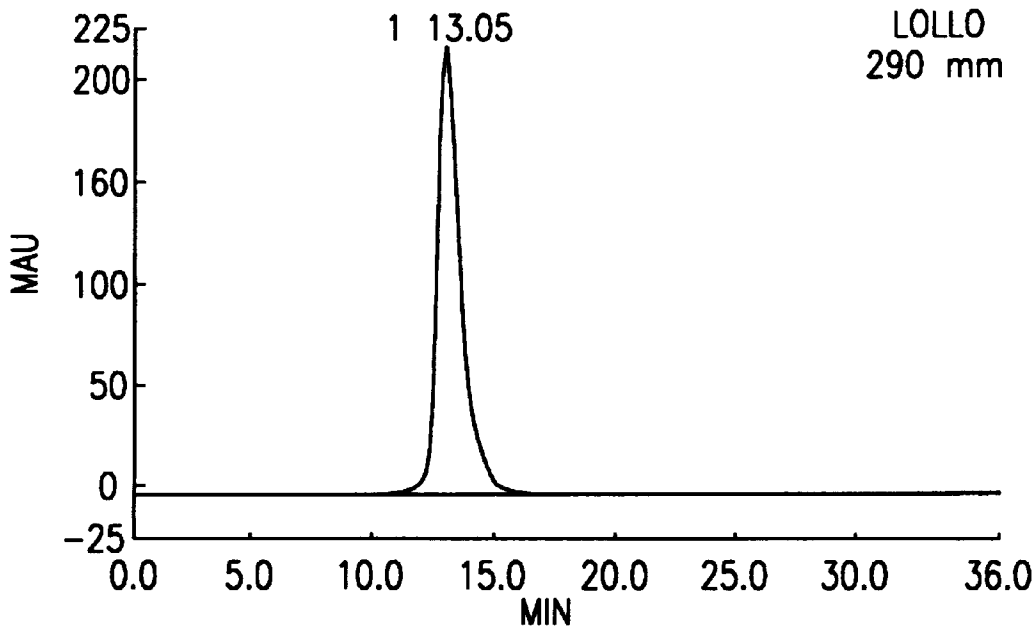


FIG. 5B

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