

Potentiometric detection of polyions based on functionalized magnetic nanoparticles

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Abstract

A novel potentiometric detection strategy based on functionalized magnetic nanoparticles has been developed for rapid and sensitive sensing of polyions. Highly dispersed magnetic nanoparticles coated with ion exchanger and plasticizer could promote an *in situ* cooperative ion-pairing interaction between the ion exchanger and the polyion analyte in sample solution by dramatically reducing the mass-transfer distance. With applying a magnetic field, the nanoparticles can be attached to the surface of ion exchanger free polymeric membrane. The observed potential signals are related to the polyion concentrations. The proposed polymeric membrane electrode exhibits a linear relationship between the greatest potential response slope (dE/dr) and the logarithm of protamine concentration in the range of 0.05–5 $\mu\text{g/mL}$ with a lower detection limit of 0.033 $\mu\text{g/mL}$.

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Potentiometric polyion selective membrane electrodes have received considerable attention over the last few years [1–3]. It has been found that appropriately formulated polymer membranes doped with appropriate lipophilic ion exchangers exhibit large and reproducible potentiometric responses toward various polyions [4]. Response of these so-called polyion sensors is ascribed to the favorable extraction of analyte polyion into the organic membrane phase by cooperative ion-pairing with the lipophilic ion exchanger species such as tridodecylmethylammonium cations (TDMAC) (for heparin) [2] or dinonylnaphthalene sulfonate anions (DNNS) (for protamine) [5]. A significant advance in polyion sensor technology involves the use of a novel rotating electrode configuration to greatly improve the sensitivity of polyion sensors by effectively decreasing the diffusion layer thickness of aqueous phase and thus enhancing mass-transfer of the analyte polyion to the membrane/sample interface [6]. However, such a rotating electrode design suffers from problems of complex instrumentation and large noises in potential signals.

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Functionalized nanoparticles can be widely dispersed in sample solution and dramatically promote the chemical reaction between the functional groups on the nanoparticles and the analyte in the sample, which is due to the much lower diffusion layer thickness as compared to their bulk counterparts. Among the nanoparticles being actively explored, magnetic nanoparticles, based on their interesting magnetic properties, are emerging as a potentially useful tool for a broad range of applications [7–9]. In this paper, we report a novel potentiometric detection strategy that makes use of magnetic nanoparticles to offer a very promising method for rapid and sensitive sensing of polyions.

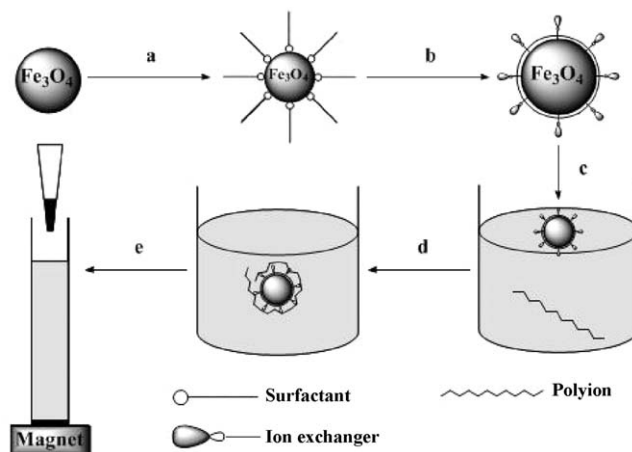
1. Experimental

Surfactant-coated magnetic fluids were prepared based on procedure reported previously [10]. 2.5 μL DNNS (50% (w/w) in hexane) and 90 μL 2-nitrophenyloctylether (*o*-NPOE) were successively dissolved in 1 mL tetrahydrofuran (THF). 1 mL of surfactant-coated magnetic fluids was added to the THF solution. By means of ultrasonic treatment for 30 min, a stable magnetic fluids solution was obtained. Through the evaporation of THF from the mixed solution for 24 h, the final magnetic fluids were obtained. The products were collected and stored at room temperature for use. The membrane contained poly(vinylchloride) (PVC) and *o*-NPOE 1:1 by mass and 2 wt% of the lipophilic salt tetradodecylammonium tetrakis(4-chlorophenyl) borate (ETH 500) with a thickness of 200 μm . Unless otherwise noted, the primary buffer solution used for all experiments was 50 mmol/L pH 7.4 Tris–HCl containing 0.12 mol/L NaCl. All electrodes were conditioned in the buffer solution identical to the inner filling solution overnight. Membrane potentials were measured in the galvanic cell: Ag/AgCl/external solution/membrane/inner solution/AgCl/Ag.

The rapid ion-pairing interaction of 1 min between the functional groups on the nanoparticles and the analyte in the sample occurred in a 200 μL sample solution with addition of 1 μL of the final magnetic fluids. The mixed solution was drawn into a 1 mL pipette and then injected into the inner solution of the membrane electrode. With applying a magnetic field, the induced membrane potential was measured. The calibration curve was plotted using the greatest slope (dE/dt) versus the concentration of protamine.

2. Results and discussion

Our strategy is described in Scheme 1. Magnetic nanoparticles have been synthesized by a classical co-precipitation method using sodium oleate as the surfactant. The plasticizer and ion exchanger are adsorbed on the magnetic nanoparticles. By adding the resulting magnetic fluids into the sample solution, the ion exchanger-functionalized magnetic nanoparticles could be dispersed in the solution swiftly and symmetrically. The ion exchanger–polyion binding equilibrium could be achieved much rapidly via an *in situ* cooperative ion-pairing interaction [11], which is attributed to the enhanced mass-transfer of the polyion analyte to the surface of the magnetic nanoparticles with



Scheme 1. Schematic representation of the proposed detection protocol: (a) surface modification of bare magnetic nanoparticles, (b) formation of ion exchanger-functionalized magnetic nanoparticles, (c) injection of the resulting fluids, (d) dispersion and the ion-pairing interaction, (e) potentiometric detection by injecting the mixed solution in the magnetic field.

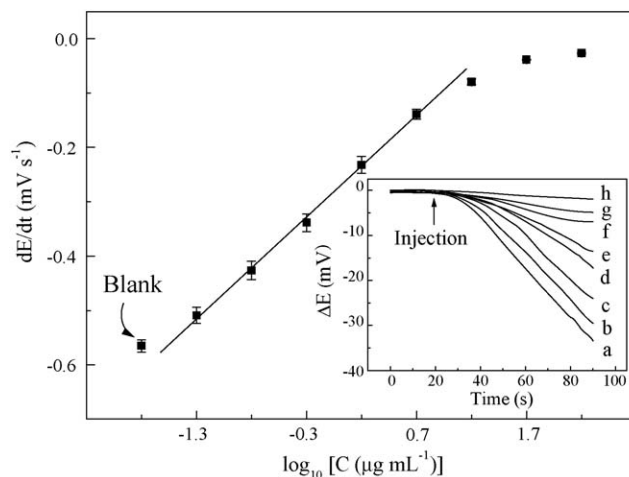


Fig. 1. Maximum rates of the potential changes as a function of the logarithm of protamine with the proposed method (error bars: SD, $N = 3$). Inset: typical dynamic potential responses of the polyion-sensitive electrodes in sample solutions upon addition of increasing concentrations of protamine: (a) 0 $\mu\text{g/mL}$, (b) 0.05 $\mu\text{g/mL}$, (c) 0.158 $\mu\text{g/mL}$, (d) 0.5 $\mu\text{g/mL}$, (e) 1.58 $\mu\text{g/mL}$, (f) 5 $\mu\text{g/mL}$, (g) 15.8 $\mu\text{g/mL}$, (h) 50 $\mu\text{g/mL}$.

adsorbed ion exchangers [12]. Upon the application of the magnetic field, the magnetic nanoparticles are aggregated to the inner side of the polymeric membrane and the ion exchanger and plasticizer adsorbed on the nanoparticles can be dissolved on the surface of the membrane, which yields a significant potentiometric response. In the absence of protamine in the sample solution, the observed large potential signal is due to the lipophilic anion sites in the membrane, while in the presence of protamine, the decreased potential change is due to the decreased anion sites induced by protamine.

Fig. 1 displays the observed calibration curve of protamine in the buffer solution. Detailed analysis of the experimental results reveals that there is a linear relationship between the greatest slope (dE/dt) and the logarithm of protamine concentration in the range of 0.05–5 ($R = 0.999$) $\mu\text{g/mL}$ with a lower detection limit of 0.033 $\mu\text{g/mL}$ (3σ). The detection limit is one order of magnitude lower than that of the conventional polyion sensor and comparable to the rotating polyion sensor [5,13]. The newly devised detection method can be used for determining heparin via endpoint detection of a protamine titration. Fig. 2 represents the titration curves. The observed endpoints of the titration were defined as the amount of protamine required to achieve half of the total dE/dt [6]. The observed endpoints were plotted

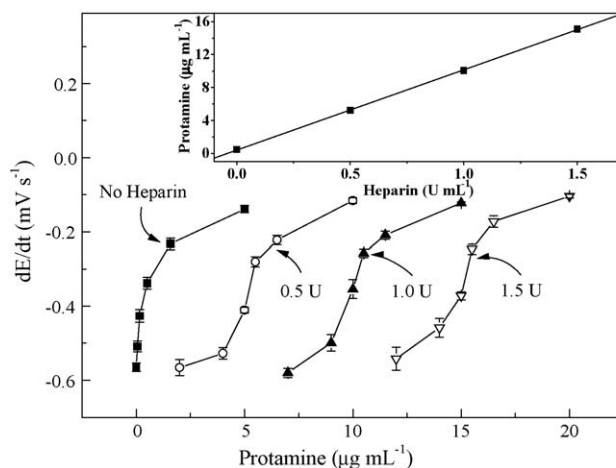


Fig. 2. Titration curves of heparin sample solutions with protamine using the proposed protocol. Inset: calibration curve; the amounts of protamine required to reach endpoint were calculated based on the values at $dE/dt_{1/2, \max}$.

as a function of the heparin concentration, and an expected linear relationship was found (see Inset). This is an indication that the system indeed responds to the polycationic species.

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