Supplemental Information

For PEI polyplexes, which are stabilized by electrostatic interactions, DLVO theory was utilized to estimate the stability ratio by summing the van der Waals attraction and electrostatic repulsion forces.

Calculation of the van der Waals potential

The attractive van der Waals potential Φ_A was calculated using the following equation [1]:

$$\Phi_A = -\frac{A_{eff}}{12}\left[\frac{1}{x(x+2)} + \frac{1}{(x+1)^2} + 2\ln\left(\frac{x(x+2)}{(x+1)^2}\right)\right] \tag{S1}$$

where $A_{\mathrm{eff}} = 1.05 \times 10^{-20}$ J is the effective Hamaker constant for poly(methyl methacrylate) (approximates the acrylate polymers used in this study) in water [2], a is the particle radius, H is the gap between particles, and $x = H/2a$. The potential profiles for 40L and PEI calculated using Eq (S1) are plotted below in Figure S1.

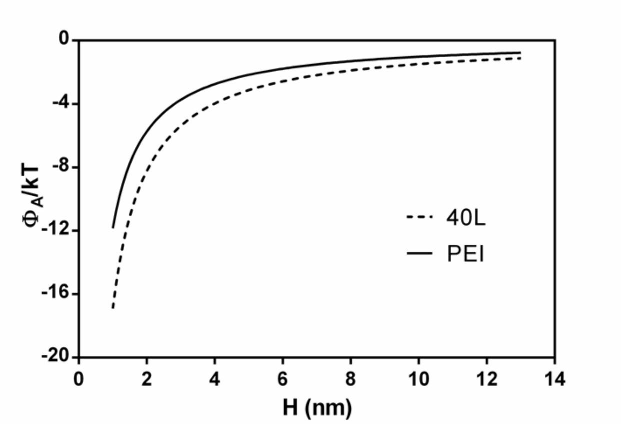

Figure S1. Van der Waals potential profiles calculated from Eq S1.

Calculation of the repulsive electrostatic potential for PEI polyplexes

Positively charged PEI polyplexes are stabilized by electrostatic repulsion. For small (*H* << *a*) separations, the electrostatic potential Φ_R between spheres can be calculated using the linearized Derjagiun approximation assuming that the dimensionless surface potential Ψ_s = ezζ/kBT remains constant [2]:

$$\Phi_R = -2\pi\varepsilon\varepsilon_0 \left(\frac{k_B T}{ze}\right)^2 a\Psi_s^2 \ln\left(1 - e^{-kH}\right) \tag{S2}$$

where ε = 78 is the permittivity factor for water, $\varepsilon_0 = 8.854 \times 10^{-12}$ C^2 N^{-1} m^{-2} is the permittivity of vacuum, $k_B = 1.38 \times 10^{-23}$ J K^{-1} is Boltzmann's constant, *e* = $1.602 \times 10_{-19}$ C is the electron charge, *z* is the valence of the electrolyte (assumed to be DPBS), and κ is the inverse double layer thickness. The overall potential was calculated as $\Phi_T = \Phi_A + \Phi_R$ and is plotted versus the gap H in Figure S2. Due to the relative weakness of the electrostatic repulsion, an energy barrier is not observed.

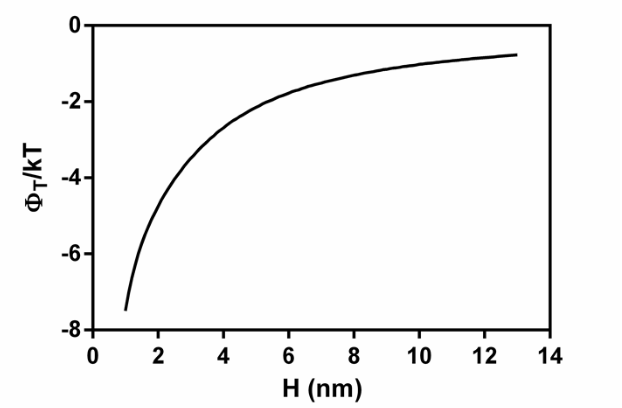

Figure S2. DLVO plot ($\Phi_T = \Phi_A + \Phi_R$) for PEI.

The stability ratio W has been reported to be a function of the height of the energy barrier $\Phi_{\max}$ [3]:

$$W = W_{\infty} + 0.25\left[\exp\left(\frac{\Phi_{\max}}{k_B T}\right) - 1\right] \tag{S3}$$

where W_{∞} represents the stability ratio resulting from dispersion effects alone. Considering that $\Phi_{\max} \approx 0$ and that W_{∞} is of $O(1)$, the stability ratio $W \approx 1$ for PEI polyplexes, and thus the aggregation kinetics are anticipated to follow the diffusion-controlled model [2].

Calculation of the interfacial layer thickness for poly(EG-b-(DMAEMA-co-BMA)) polyplexes

Due to the presence of the PEG corona, the copolymer polyplexes are sterically stabilized. To assess the colloidal stability of the polyplexes, the thickness of the PEG layer was calculated and compared to the length scale of the van der Waals attractive potential (Figure S1).

The thickness of the interfacial layer was calculated using mean field theory to describe the interactions between interacting layers from two particles. The polymer is modeled as a freely jointed chain of N segments of persistence length l. The hydrophilic PEG chains, with an average bond length l_0 = 0.147 nm, persistence length l = 0.38 nm [4], repeat unit molecular weight m_0 = 44 g/mol, and specific volume v' = 0.885 cm^3/g, are assumed to extend into the aqueous solution at the interface. The number of chains N is given by:

$$N = \frac{M_{PEG}}{c_{\infty} m_0} \tag{S4}$$

where $c_{\infty} = l/l_0$ and M_{PEG} is the molecular weight of the PEG chain. The excluded volume parameter v accounts for pairwise interactions [2]:

$$v = w^{1/2}\left(1 - 2\chi\right) \tag{S4}$$

where χ is the Flory parameter (~0.5 for PEG4000 at 45 C and 39 wt% PEG in water [5]) and w accounts for triplet interactions:

$$w^{1/2} = c_\infty \frac{v' m_0}{N_A} \tag{S5}$$

At equilibrium, the chemical potential of the solvent in the interfacial PEG layer is equal to that in the bulk. The equilibrium condition can be expressed in terms of the dimensionless layer thickness $\alpha_0 = L/N^{1/2}l$ [2]:

$$\alpha_0^3 - \left(1 + \tfrac{1}{9}\phi_p^2\right)\alpha_0^{-1} = \tfrac{1}{6}z \tag{S6}$$

where the dimensionless surface density $\phi_p = Nn_p w^{1/2}/l$, the dimensionless parameter $z = N^{3/2} n_p v/l$, and $n_p = a\rho_{chain} N_A / 3M_{chain}$ is the surface density of chains (chains/nm^2). For the 40L polyplex, the layer thickness L = 5.8 nm. Thus, the layers come into contact when the gap H = 11.6 nm, at which point the value of $\Phi_A/k_BT = -1.3$. As the particles further approach each other, interactions between the terminally grafted chains will result in steric repulsion. Thus, the relatively short-range van der Waals forces are anticipated to be screened by the relatively long-range steric repulsion, resulting in a high stability ratio.

References

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