

Supporting information for:

pH-Controlled Nano-Aggregation in Amphiphilic Polymer Co-Networks

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1 Molecular Theory of pH Responsive Hydrogels

The APCN is composed of cross-linked polymer chains and a solution of water (w), protons (H^+), hydroxyl ions (OH^-), and salt completely dissociated into anions ($-$) and cations ($+$). The polymer network contains both hydrophilic or polar (P) and hydrophobic (H) monomers. Some of the monomers are functionalized with acidic groups that can be either protonated (AH) or deprotonated (A^-). The ACPN is in equilibrium with a solution that provides a bath for all of the free species whose chemical potentials are determined by the bath pH and salt concentration, c . Our approach to study the thermodynamic behavior of such system consists in defining a self-consistent mean field theory that incorporates molecular details of the polymer network. This molecular theory was first introduced to investigate the response of a hydrophilic polyacid gel to changes in both pH and salt concentration of the bath solution.^{S1} In the following, we will briefly describe the most

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important features of the theory, particularly focusing on the modifications introduced to study an amphiphilic polymer co-network. A complementary description of the theory can be found in Ref. S1. The first step in this theoretical framework consists in writing the total Helmholtz free energy of the APCN, which is given by

$$F = -TS_{\text{conf}} - TS_{\text{mix}} + U_{\text{vdw}} + U_{\text{st}} + F_{\text{chm}} + U_{\text{elec}}, \quad (1)$$

where T is the system temperature, S_{conf} is the conformational entropy of the flexible network, S_{mix} is the translational entropy of the different free species in the solution, U_{vdw} is total attractive Van der Waals interaction, U_{st} is the repulsive steric (excluded volume) interaction, F_{chm} is the chemical free energy that accounts for the acid-base equilibrium, and U_{elec} is the total electrostatic energy. Next, we will present explicit relations for each of these contributions to the free energy: the conformational entropy of the APCN can be expressed as

$$S_{\text{conf}} = -k_B \sum_{\alpha} P(\alpha) \ln(P(\alpha)), \quad (2)$$

where $P(\alpha)$ is the probability of finding the network in conformation α , which denotes a particular spatial distribution of all the monomers; k_B is the Boltzmann constant. The translational entropy of the free species within the hydrogel is described by

$$S_{\text{mix}} = -k_B \sum_{\gamma \in \{w, +, -, H^+, OH^-\}} \int_V d\mathbf{r} \rho_{\gamma}(\mathbf{r}) [\ln(\rho_{\gamma}(\mathbf{r}) v_w) - 1], \quad (3)$$

where v_w is the volume of a water molecule, and $\rho_w(\mathbf{r})$, $\rho_+(\mathbf{r})$, $\rho_-(\mathbf{r})$, $\rho_{H^+}(\mathbf{r})$ and $\rho_{OH^-}(\mathbf{r})$ are the local number density of the different mobile species in the solution; the integral is over all the volume of the system, V , and $\mathbf{r}$ is the position vector. The total attractive Van der Waals energy between network monomers can be written as

$$U_{\text{vdw}} = \sum_{\alpha} P(\alpha) U_{\text{vdw}}(\alpha), \quad (4)$$

where $U_{\text{vdw}}(\alpha)$, which is the total Van der Waals energy of the network in conformation α , is given by

$$U_{\text{vdw}}(\alpha) = \frac{1}{2} \left(\sum_{i_H, j_H} u_{\text{HH}}(r_{i_H j_H}^\alpha) + \sum_{i_P, j_P} u_{\text{PP}}(r_{i_P j_P}^\alpha) + \sum_{i_H, j_P} u_{\text{HP}}(r_{i_H j_P}^\alpha) \right); \quad (5)$$

i_H and j_H run over the hydrophobic polymer segments, while i_P and j_P do so over the hydrophilic monomers. u_{HH} , u_{PP} , u_{HP} are respectively the attractive pairwise interaction between hydrophobic, hydrophilic and hydrophobic-hydrophilic monomers. $u_{AB}(r_{i_A j_B}^\alpha)$ ($\{A, B\} = \{H, P\}$), for example, gives the interaction between monomers i_A and j_B that, in configuration α , are separated by a distance $r_{i_A j_B}^\alpha$. The repulsive steric interactions are accounted for through the use of local incompressibility constraints. Namely, at each point in space, $\mathbf{r}$, the volume must be completely filled by some of the molecular species; that is:

$$\langle \phi_H(\mathbf{r}) \rangle + \langle \phi_P(\mathbf{r}) \rangle + \sum_{\gamma \in \{w, +, -, H^+, OH^-\}} \rho_\gamma(\mathbf{r}) v_\gamma = 1, \quad (6)$$

where $\langle \phi_H(\mathbf{r}) \rangle$ and $\langle \phi_P(\mathbf{r}) \rangle$ are the local volume fraction of hydrophobic and hydrophilic polymer, respectively, and v_+ , v_- , v_{H^+} and v_{OH^-} are the volume of the corresponding mobile molecules. The $\langle \rangle$ represent an ensemble average over the set of network configurations, $\{\alpha\}$. Namely,

$$\langle \phi_H(\mathbf{r}) \rangle = \sum_{\alpha} P(\alpha) \phi_H(\alpha, \mathbf{r}) \quad (7)$$

$$\langle \phi_P(\mathbf{r}) \rangle = \sum_{\alpha} P(\alpha) \phi_P(\alpha, \mathbf{r}), \quad (8)$$

where $\phi_H(\alpha, \mathbf{r})$ is the volume fraction of hydrophobic polymer at $\mathbf{r}$ when the network is in conformation α , and $\phi_P(\alpha, \mathbf{r})$ is defined analogously for the hydrophilic polymer. The total volume fraction of hydrophobic and hydrophilic polymer are $\phi_H = \frac{1}{V} \int_V d\mathbf{r} \langle \phi_H(\mathbf{r}) \rangle$ and $\phi_P = \frac{1}{V} \int_V d\mathbf{r} \langle \phi_P(\mathbf{r}) \rangle$, respectively, and the total volume fraction of polymer is $\phi_G = \phi_H + \phi_P$. The chemical free energy,

which takes into account the acid-base equilibrium ($AH \rightleftharpoons A^- + H^+$), can be written as follows:

$$\begin{aligned}\beta F_{\text{chm}} = & \int_V d\mathbf{r} \langle \rho_{IP}(\mathbf{r}) \rangle f_d(\mathbf{r}) (\ln f_d(\mathbf{r}) + \beta \mu_{A^-}^0) \\ & + \int_V d\mathbf{r} \langle \rho_{IP}(\mathbf{r}) \rangle (1 - f_d(\mathbf{r})) [\ln(1 - f_d(\mathbf{r})) + \beta \mu_{AH}^0] \\ & + \int_V d\mathbf{r} (\rho_{OH^-}(\mathbf{r}) \beta \mu_{OH^-}^0 + \rho_{H^+}(\mathbf{r}) \beta \mu_{H^+}^0),\end{aligned}\quad (9)$$

where $\beta = \frac{1}{k_B T}$, and $f_d(\mathbf{r})$ is the local degree of dissociation that gives the fraction of the ionizable monomers that are deprotonated in the element of volume between $\mathbf{r}$ and $\mathbf{r} + d\mathbf{r}$. The local (ensemble average) density of ionizable polymer is

$$\langle \rho_{IP}(\mathbf{r}) \rangle = \sum_{\alpha} P(\alpha) \rho_{IP}(\alpha, \mathbf{r}), \quad (10)$$

where $\rho_{IP}(\alpha, \mathbf{r})$ is the position-dependent number density of ionizable polymer of the network in conformation α . Thus, the density of charged polymer at $\mathbf{r}$ is $f_d(\mathbf{r}) \langle \rho_{IP}(\mathbf{r}) \rangle$, while that of ionizable uncharged polymer is $(1 - f_d(\mathbf{r})) \langle \rho_{IP}(\mathbf{r}) \rangle$. The quantities $\mu_{A^-}^0$ and μ_{AH}^0 are the standard chemical potentials of charged and uncharged ionizable monomers, respectively. In addition, $\mu_{H^+}^0$ and $\mu_{OH^-}^0$ are the standard chemical potentials of the protons and hydroxyl ions, respectively, which are included to explicitly account for the self-ionization of water ($H_2O \rightleftharpoons OH^- + H^+$). The last contribution to the free energy is the electrostatic energy, which is

$$\beta U_{\text{elec}} = \int_V d\mathbf{r} \left[\langle \rho_q(\mathbf{r}) \rangle \beta \Psi(\mathbf{r}) - \frac{1}{2} \beta \varepsilon(\mathbf{r}) (\nabla \Psi(\mathbf{r}))^2 \right], \quad (11)$$

where $\Psi(\mathbf{r})$ is the electrostatic potential, and $\varepsilon(\mathbf{r})$ denotes the dielectric permittivity of the medium at $\mathbf{r}$; the local density of electric charge is given by the following expression:

$$\langle \rho_q(\mathbf{r}) \rangle = \langle \rho_q^{IP}(\mathbf{r}) \rangle + \sum_{\gamma \in \{+, -, H^+, OH^-\}} \rho_{\gamma}(\mathbf{r}) q_{\gamma}, \quad (12)$$

where q_+ , q_- , q_{H^+} and q_{OH^-} denote the electric charge of the various charged free species, and $\langle \rho_q^{IP}(\mathbf{r}) \rangle$ is the (ensemble average) local density of charge on the polymer network, which is expressed as

$$\langle \rho_q^{IP}(\mathbf{r}) \rangle = f_d(\mathbf{r}) \langle \rho_{IP}(\mathbf{r}) \rangle q_{IP} \quad (13)$$

with q_{IP} representing the electric charge of the deprotonated ionizable monomer. The system must be globally electroneutral, so the charge density must satisfy the following constraint:

$$\int_V d\mathbf{r} \langle \rho_q(\mathbf{r}) \rangle = 0. \quad (14)$$

With all the expressions described before, the total Helmholtz free energy of the APCN can be written as:

$$\begin{aligned} \beta F = & \sum_{\alpha} P(\alpha) \ln(P(\alpha)) + \sum_{\alpha} P(\alpha) \beta U_{\text{vdw}}(\alpha) \\ & + \sum_{\gamma \in \{w, +, -, H^+, OH^-\}} \int_V d\mathbf{r} \rho_{\gamma}(\mathbf{r}) [\ln(\rho_{\gamma}(\mathbf{r}) v_w) - 1] \\ & + \int_V d\mathbf{r} \langle \rho_{IP}(\mathbf{r}) \rangle f_d(\mathbf{r}) (\ln f_d(\mathbf{r}) + \beta \mu_{A^-}^0) \\ & + \int_V d\mathbf{r} \langle \rho_{IP}(\mathbf{r}) \rangle (1 - f_d(\mathbf{r})) [\ln(1 - f_d(\mathbf{r})) + \beta \mu_{AH}^0] \\ & + \int_V d\mathbf{r} (\rho_{OH^-}(\mathbf{r}) \beta \mu_{OH^-}^0 + \rho_{H^+}(\mathbf{r}) \beta \mu_{H^+}^0) \\ & + \int_V d\mathbf{r} \left[\langle \rho_q(\mathbf{r}) \rangle \beta \Psi(\mathbf{r}) - \frac{1}{2} \beta \epsilon (\nabla \Psi(\mathbf{r}))^2 \right]. \end{aligned} \quad (15)$$

The APCN is in equilibrium with a homogeneous solution that provides a bath for all of the free species. Therefore, the proper thermodynamic potential to describe the system is the Lagrange transform of the free energy where the independent variables are the chemical potentials of the mobile species, which consist of the water molecules, the protons, the hydroxyl ions, and the salt anions and cations. The existence of two constraints, global charge neutrality and local incompressibility, reduces the total number of independent thermodynamic variables by two; the dissociation of water introduces an additional relation between the chemical potentials of some

of the free species. Thus, we can introduce exchange chemical potentials in such a way that the chemical potentials of water, protons and hydroxyl ions do not represent relevant thermodynamic variables (see Section 1.1). Then, the semi-grand canonical potential, $W = F - \mu_+ N_+ - \mu_- N_-$, with μ_+ and μ_- being the exchange chemical potentials conjugated to the number of salt cations (N_+) and anions (N_-), respectively, is indeed the thermodynamic potential whose minimum yields the equilibrium state. In our formalism, W is expressed as

$$W = F - \mu_+ \int_V d\mathbf{r} \rho_+(\mathbf{r}) - \mu_- \int_V d\mathbf{r} \rho_-(\mathbf{r}). \quad (16)$$

The unknowns in Eq. (16) consist of the probability density function, $P(\alpha)$, the local densities of the free species, $\rho_\gamma(\mathbf{r})$ ($\gamma \in \{w, -, +, H^+, OH^-\}$), the local degree of dissociation, $f_d(\mathbf{r})$, and the electrostatic potential, $\Psi(\mathbf{r})$. To obtain these quantities, the minimum of W with respect to each of these functions is found, subject to the two aforementioned constraints. Therefore, Lagrange multipliers are introduced to satisfy the constraints, and the functional that we need to minimize becomes explicitly:

$$\begin{aligned} \Phi = & \beta W + \lambda \int_V d\mathbf{r} \langle \rho_q(\mathbf{r}) \rangle \\ & + \int_V d\mathbf{r} \beta \pi(\mathbf{r}) \left(\langle \phi_H(\mathbf{r}) \rangle + \langle \phi_P(\mathbf{r}) \rangle + \sum_{\gamma \in \{w, +, -, H^+, OH^-\}} \rho_\gamma(\mathbf{r}) v_\gamma - 1 \right). \end{aligned} \quad (17)$$

$\pi(\mathbf{r})$ is the Lagrange multiplier conjugated to the local incompressibility constraint (Eq. (6)) at position $\mathbf{r}$, and λ is that conjugated to the global electroneutrality constraint (Eq. (14)). It can be shown that λ merely introduces an additive constant to the electrostatic potential, and charge neutrality can be satisfied by the proper choice of boundary conditions. Minimization of Φ yields

the following results for the densities of the free species:

$$\rho_w(\mathbf{r}) = \frac{1}{v_w} \exp(-\beta \pi(\mathbf{r}) v_w), \quad (18)$$

$$\rho_\gamma(\mathbf{r}) = \frac{\rho_\gamma^b}{(v_w \rho_w^b)^{v_\gamma/v_w}} \exp(-\beta \pi(\mathbf{r}) v_\gamma - \beta \Psi(\mathbf{r}) q_\gamma), \quad (19)$$

$$\text{with } \gamma \in \{H^+, OH^-, +, -\},$$

where ρ_γ^b is the number density of free species γ in the bath solution, which is a constant (*i.e.*, independent of position) that depends only on the bath pH and c (see Section 1.2). Moreover, assuming that the dielectric constant of the medium is constant ($\epsilon(\mathbf{r}) \equiv \epsilon$), the probability density function of network conformations is given by:

$$P(\alpha) = \frac{1}{Q} \exp \left(-\beta U_{\text{vdw}}(\alpha) - \int_V d\mathbf{r} [\phi_H(\alpha, \mathbf{r}) + \phi_P(\alpha, \mathbf{r})] \beta \pi(\mathbf{r}) \right) \\ \times \exp \left(- \int_V d\mathbf{r} \rho_{IP}(\alpha, \mathbf{r}) [\beta \Psi(\mathbf{r}) q_{IP} + \ln f_d(\mathbf{r})] \right), \quad (20)$$

where the factor Q ensures the satisfaction of $\sum_\alpha P(\alpha) = 1$. For the local degree of dissociation, we obtain:

$$\frac{f_d(\mathbf{r})}{1 - f_d(\mathbf{r})} = \frac{K_a^0}{v_w \rho_{H^+}^b} \left(v_w \rho_w^b \right)^{v_{H^+}/v_w} \exp(-\beta \Psi(\mathbf{r}) q_{IP}). \quad (21)$$

K_a^0 is the dimensionless thermodynamic equilibrium constant of the acid-base reaction, which is related to the standard chemical potentials of the protons, unprotonated and protonated species *via*

$$K_a^0 = \exp(\beta \mu_{AH}^0 - \beta \mu_{H^+}^0 - \beta \mu_{A^-}^0). \quad (22)$$

Note that the commonly encountered experimental equilibrium constant K_a , given in molar units, is defined as

$$K_a = \frac{[A^-][H^+]}{[AH]}, \quad (23)$$

so that K_a and K_a^0 are proportional ($K_a^0 = K_a N_A v_w$, with N_A being Avogadro's number). The stan-

standard chemical potentials of the protons and the hydroxyl ions are given by:

$$\exp\left(-\beta\mu_\gamma^0\right) = \frac{v_w\rho_\gamma^b}{\left(v_w\rho_w^b\right)^{v_\gamma/v_w}}, \text{ with } \gamma \in \{H^+, OH^-\}, \quad (24)$$

while the chemical potential of the salt ions are expressed as

$$\exp\left(\beta\mu_\gamma\right) = \frac{v_w\rho_\gamma^b}{\left(v_w\rho_w^b\right)^{v_\gamma/v_w}}, \text{ with } \gamma \in \{+, -\}. \quad (25)$$

In addition, the variation of Φ with respect to the electrostatic potential readily yields the Poisson equation

$$\epsilon\nabla^2\Psi(\mathbf{r}) = -\langle\rho_q(\mathbf{r})\rangle. \quad (26)$$

This last relation makes explicit the strong coupling that exists between the electrostatic potential and all the other physicochemical contributions to the free energy, and the chemical equilibrium through the average of the local charge density. Because we are modeling a volumetric hydrogel, periodic boundary conditions are imposed to the electrostatic potential, which guarantees electroneutrality.

At this point, the thermodynamic potential can be expressed in terms of the position-dependent osmotic pressure, $\pi(\mathbf{r})$, the electrostatic potential, the densities of the different mobile species in the homogeneous bath solution, and some other input quantities that must be provided by a molecular model of the APCN, which include the pK_a of the ionizable polymer ($pK_a = -\log_{10}K_a$), the volume fraction distributions of hydrophobic and hydrophilic polymer and the local density of ionizable polymer. Each of these polymer distributions must be given for each conformation of the network. The independent variables of a single calculation of the free energy are the bath pH, c and the total volume fraction of polymer, ϕ_G . Given pH and c , and using the self-ionization of water described by $K_w = [OH^-][H^+] \propto \exp(-\beta\mu_{OH^-}^0 - \beta\mu_{H^+}^0)$, the bath densities of all the mobile species can be obtained from imposing the incompressibility and charge neutrality constraints to the bath solution (see Section 1.2). Lastly, the quantities $\pi(\mathbf{r})$ and $\Psi(\mathbf{r})$ are determined by

substituting the expressions for the local densities of free species and local volume fraction of both types of monomers into the incompressibility constraint (Eq. (6)) and the Poisson equation (Eq. (26)). The solution is then calculated numerically as described in Section 1.3; once $\pi(\mathbf{r})$ and $\Psi(\mathbf{r})$ are determined, any thermodynamic quantity can be derived from the free energy in a straightforward manner.

This theoretical approach as described so far is general and can be therefore applied to the study of any particular molecular architecture of ACPN. The molecular details of the polymer network enter the framework through the input set of conformations, $\{\alpha\}$, *via* the volume fraction distributions of hydrophobic and hydrophilic polymer, $\{\phi_H(\alpha, \mathbf{r})\}$ and $\{\phi_P(\alpha, \mathbf{r})\}$, and the density distribution of ionizable polymer, $\{\rho_{IP}(\alpha, \mathbf{r})\}$. In this work, we study the nanoscale behavior of a 1:1 network of permanently cross-linked hydrophobic:hydrophilic polymer chains, where one of the two types of monomers bears an acidic group. The molecular model used to describe such system is detailed in Section 2.

1.1 Exchange Chemical Potentials

Consider the free species composing the bath solution. The Helmholtz free energy and the fundamental equation of such system are expressed as:

$$F = -pV + \sum_{i \in \{w, +, -, H^+, OH^-\}} \tilde{\mu}_i N_i$$

$$dF = -SdT - pdV + \sum_{i \in \{w, +, -, H^+, OH^-\}} \tilde{\mu}_i dN_i, \quad (27)$$

where the index i runs over all of the molecular species in the system, and $\tilde{\mu}_i$ is the chemical potential of species i . Now, we impose two constraints to the system: the incompressibility constraint that can be mathematically expressed as:

$$V = \sum_{i \in \{w, +, -, H^+, OH^-\}} N_i v_i, \quad (28)$$

with v_i being the molecular volume of species i . Additionally, the system must be charge neutral, which implies:

$$\sum_{i \in \{+, -, H^+, OH^-\}} N_i q_i = 0, \quad (29)$$

where q_i is the electric charge of the molecular species i . Using both constraints, Eqs. (28) and (29), we obtain:

$$\begin{aligned} N_{H^+} &= - \sum_{i \in \{+, -, OH^-\}} \frac{q_i}{q_{H^+}} N_i \\ dN_{H^+} &= - \sum_{i \in \{+, -, OH^-\}} \frac{q_i}{q_{H^+}} dN_i, \end{aligned} \quad (30)$$

and

$$\begin{aligned} N_w &= \frac{V}{v_w} + \sum_{i \in \{+, -, OH^-\}} (v_{H^+} q_i - v_i q_{H^+}) \frac{N_i}{v_w q_{H^+}} \\ dN_w &= \frac{dV}{v_w} + \sum_{i \in \{+, -, OH^-\}} (v_{H^+} q_i - v_i q_{H^+}) \frac{dN_i}{v_w q_{H^+}}. \end{aligned} \quad (31)$$

Now, we can re-express the free energy and fundamental equation, Eq. (27), using the expressions given by Eqs. (30) and (31), in the following way:

$$\begin{aligned} F &= - \left(p - \frac{\tilde{\mu}_w}{v_w} \right) V + \sum_{i \in \{+, -, OH^-\}} \left[\tilde{\mu}_i - \tilde{\mu}_{H^+} \frac{q_i}{q_{H^+}} + \frac{\tilde{\mu}_w}{v_w q_{H^+}} (v_{H^+} q_i - v_i q_{H^+}) \right] N_i \\ dF &= -SdT - \left(p - \frac{\tilde{\mu}_w}{v_w} \right) dV + \sum_{i \in \{+, -, OH^-\}} \left[\tilde{\mu}_i - \tilde{\mu}_{H^+} \frac{q_i}{q_{H^+}} + \frac{\tilde{\mu}_w}{v_w q_{H^+}} (v_{H^+} q_i - v_i q_{H^+}) \right] dN_i \end{aligned} \quad (32)$$

Therefore, defining the exchange chemical potential of species i as follows:

$$\mu_i = \tilde{\mu}_i - \tilde{\mu}_{H^+} \frac{q_i}{q_{H^+}} + \frac{\tilde{\mu}_w}{v_w q_{H^+}} (v_{H^+} q_i - v_i q_{H^+}), \quad (33)$$

and the system osmotic pressure as

$$\Pi = p - \frac{\tilde{\mu}_w}{v_w} \quad (34)$$

we obtain:

$$F = -\Pi V + \sum_{i \in \{+, -, OH^-\}} \mu_i N_i$$

$$dF = -SdT - \Pi dV + \sum_{i \in \{+, -, OH^-\}} \mu_i dN_i, \quad (35)$$

which means that the number of independent thermodynamic variables has been reduced by two, the number of constraints. $F = F(T, V, N_+, N_-, N_{OH^-})$ and the relevant conjugated variables are S , Π , μ_+ , μ_- , and μ_{OH^-} , respectively.

The self ionization of water imposes an additional constraint, which can be expressed as

$$dN_w = dN_{OH^-} + dN_{H^+}, \quad (36)$$

which leads to:

$$\left(\frac{\partial F}{\partial N_{OH^-}} \right)_{T, V, N_+, N_-} = \left(\frac{\partial F}{\partial N_w} \right)_{T, V, N_+, N_-} - \left(\frac{\partial F}{\partial N_{H^+}} \right)_{T, V, N_+, N_-}, \quad (37)$$

but F does not depend explicitly on N_w and N_{H^+} , which implies that both $\left(\frac{\partial F}{\partial N_w} \right)_{T, V, N_+, N_-}$ and $\left(\frac{\partial F}{\partial N_{H^+}} \right)_{T, V, N_+, N_-}$ are identically zero. Therefore,

$$\mu_{OH^-} = \left(\frac{\partial F}{\partial N_{OH^-}} \right)_{T, V, N_+, N_-} = 0. \quad (38)$$

In summary, for the bath solution we have:

$$F = -\Pi V + \mu_+ N_+ + \mu_- N_-$$

$$dF = -SdT - \Pi dV + \mu_+ dN_+ + \mu_- dN_-. \quad (39)$$

1.2 Bath Solution

Consider the bath solution in equilibrium with the APCN, which contains water, protons, hydroxyl ions, and salt ions. The relevant thermodynamic potential of the bath solution per unit volume is given by:

$$\beta \frac{W}{V} = \sum_{\gamma \in \{w, +, -, H^+, OH^-\}} \rho_\gamma^b \left[\ln(\rho_\gamma^b v_\gamma) - 1 \right] + \sum_{\gamma \in \{H^+, OH^-\}} \rho_\gamma^b \beta \mu_\gamma^0 - \sum_{\gamma \in \{+, -\}} \rho_\gamma^b \beta \mu_\gamma, \quad (40)$$

where we have used that the electrostatic energy is identically zero, the reason being twofold: first, the electrostatic potential is constant, $\Psi(\mathbf{r}) = \Psi_b$, and secondly, the bath solution charge density, ρ_q , is zero everywhere. Both reasons are a consequence of the homogeneity of the system. In particular, because the bath density of each species is independent of position, the satisfaction of the global charge neutrality constraint requires:

$$0 = \rho_q = \sum_{\gamma \in \{+, -, H^+, OH^-\}} \rho_\gamma^b q_\gamma. \quad (41)$$

Another condition imposed to the bath solution is the incompressibility constraint, which is expressed as:

$$\sum_{\gamma \in \{w, +, -, H^+, OH^-\}} \rho_\gamma^b v_\gamma = 1. \quad (42)$$

Because the system is homogeneous the incompressibility constraint is a single equation, as opposed to the APCN where the local constraint results in separate equation at each point in space. Thus, the density of the free species in the bath solution can be determined by optimizing the following function:

$$\Phi = \beta \frac{W}{V} + \beta \pi_b \left(\sum_{\gamma \in \{w, +, -, H^+, OH^-\}} \rho_\gamma^b v_\gamma - 1 \right), \quad (43)$$

where π_b is the Lagrange multiplier conjugated with the incompressibility constraint. Minimization of Φ with respect to each ρ_γ^b yields:

$$\rho_w^b v_w = e^{-\beta \pi_b v_w}, \quad (44)$$

$$\rho_\gamma^b v_w = e^{-\beta \pi_b v_\gamma - \beta \mu_\gamma^0}, \text{ for } \gamma \in \{H^+, OH^-\}, \quad (45)$$

$$\rho_\gamma^b v_w = e^{-\beta \pi_b v_\gamma + \beta \mu_\gamma}, \text{ for } \gamma \in \{+, -\}. \quad (46)$$

The last two equations can be re-expressed in the following way:

$$\rho_\gamma^b v_w = \left(\rho_w^b v_w \right)^{v_\gamma/v_w} e^{-\beta \mu_\gamma^0}, \text{ for } \gamma \in \{H^+, OH^-\}, \quad (47)$$

$$\rho_\gamma^b v_w = \left(\rho_w^b v_w \right)^{v_\gamma/v_w} e^{\beta \mu_\gamma}, \text{ for } \gamma \in \{+, -\}, \quad (48)$$

from where the standard chemical potentials of the protons and hydroxyl, and the chemical potentials of salt ions can be obtained:

$$e^{-\beta \mu_\gamma^0} = \frac{v_w \rho_\gamma^b}{(v_w \rho_w^b)^{v_\gamma/v_w}}, \text{ for } \gamma \in \{H^+, OH^-\}, \quad (49)$$

$$e^{\beta \mu_\gamma} = \frac{v_w \rho_\gamma^b}{(v_w \rho_w^b)^{v_\gamma/v_w}}, \text{ for } \gamma \in \{+, -\}. \quad (50)$$

Therefore, we can now determine the bath density of each species using the two aforementioned constraints, pK_w , and the pH and salt concentration, c of this solution: $\rho_{H^+}^b$ and $\rho_{OH^-}^b$ can be obtained from pH and pK_w , which is:

$$\rho_{H^+}^b = N_A [H^+] = N_A 10^{-pH} \quad (51)$$

$$\rho_{OH^-}^b = N_A [OH^-] = N_A 10^{pH - pK_w}, \quad (52)$$

where $[H^+] = 10^{-pH}$ and $[OH^-] = 10^{pH - pK_w}$ are given in M=mol/L. The number density of salt ions is, a priori, given by $N_A c$; however, the satisfaction of the charge neutrality constraint requires

the inclusion of additional salt ions; that is:

$$\rho_{H^+}^b q_{H^+} + \rho_{OH^-}^b q_{OH^-} + N_{Ac} (q_+ + q_-) + \delta q_c = 0, \quad (53)$$

where δq_c is the additional density of electric charge. Solving the last equation for δq_c yields ρ_+^b and ρ_-^b , depending on the sign of the additional electric charge:

$$\begin{aligned} \rho_+^b &= N_{Ac} + \frac{\delta q_c}{q_+}, \text{ and } \rho_-^b = N_{Ac} & \text{if } \delta q_c \geq 0 \\ \rho_+^b &= N_{Ac}, \text{ and } \rho_-^b = N_{Ac} + \frac{\delta q_c}{q_-} & \text{if } \delta q_c < 0. \end{aligned} \quad (54)$$

Finally, ρ_w^b is obtained by solving Eq. (42). All bath densities are known at this point, which allows the determination of $\mu_{H^+}^0$ and $\mu_{OH^-}^0$ using Eq. (49), and of μ_+ and μ_- using Eq. (50).

1.3 Numerical Solution

To obtain results from the theory, the nonlinear integro-differential equations described in Section 1 must be solved numerically. To this end, the volume of the system is divided in cubic cells of length $\delta = 0.5$ nm, and in the equations, sums over cells replace integrals over the volume, and finite differences substitute derivatives. Then, the incompressibility constraint, Eq. (6), is rewritten as:

$$\boxed{\langle \phi_H(i, j, k) \rangle + \langle \phi_P(i, j, k) \rangle + \sum_{\gamma \in \{w, +, -, H^+, OH^-\}} \rho_\gamma(i, j, k) v_\gamma = 1}, \quad (55)$$

which gives an equation for each cell (i, j, k) , where the discrete position vector is now described by the three integers i, j, k that are respectively the x-, y- and z-direction indexes; i, j , and k take values from 1 to n_x, n_y and n_z , respectively, so that the total number of cells spanning the system

volume is $n_x n_y n_z$. In Eq. (55), the discrete densities of the free species are:

$$\rho_w(i, j, k) = \frac{1}{v_w} \exp(-\beta \pi(i, j, k) v_w), \quad (56)$$

$$\rho_\gamma(i, j, k) = \frac{\rho_\gamma^b}{(v_w \rho_w^b)^{v_\gamma/v_w}} \exp(-\beta \pi(i, j, k) v_\gamma - \beta \Psi(i, j, k) q_\gamma), \quad (57)$$

$$\text{with } \gamma \in \{H^+, OH^-, +, -\}.$$

Moreover, in their discrete form, the ensemble average local volume fraction of hydrophobic and hydrophilic polymer are respectively:

$$\langle \phi_H(i, j, k) \rangle = \sum_{\alpha} P(\alpha) \phi_H(\alpha, i, j, k) \text{ and} \quad (58)$$

$$\langle \phi_P(i, j, k) \rangle = \sum_{\alpha} P(\alpha) \phi_P(\alpha, i, j, k), \quad (59)$$

where $\{\phi_H(\alpha, i, j, k); \forall(\alpha, i, j, k)\}$ and $\{\phi_P(\alpha, i, j, k); \forall(\alpha, i, j, k)\}$ are respectively the discrete volume fraction distribution of hydrophobic and hydrophilic polymer, which are both inputs provided by the molecular model. The probability density function of network conformations is now given by:

$$P(\alpha) = \frac{1}{Q} \exp \left(-\beta U_{\text{vdw}}(\alpha) - \delta^3 \sum_{i,j,k} [\phi_H(\alpha, i, j, k) + \phi_P(\alpha, i, j, k)] \beta \pi(i, j, k) \right) \\ \times \exp \left(-\delta^3 \sum_{i,j,k} \rho_{IP}(\alpha, i, j, k) [\beta \Psi(i, j, k) q_{IP} + \ln f_d(i, j, k)] \right), \quad (60)$$

where δ^3 is the volume of a cell, and $\sum_{i,j,k}$ runs over all the system cells. The discrete density distribution of ionizable polymer $\{\rho_{IP}(\alpha, i, j, k); \forall(\alpha, i, j, k)\}$ is another input defined by the molecular model. In addition, the discrete form of the Poisson equation, Eq. (26), is

$$\epsilon \left[\frac{\partial^2 \Psi}{\partial x^2}(i, j, k) + \frac{\partial^2 \Psi}{\partial y^2}(i, j, k) + \frac{\partial^2 \Psi}{\partial z^2}(i, j, k) \right] = -\langle \rho_q(i, j, k) \rangle, \quad (61)$$

where the second derivatives of the electrostatic potential are replaced by finite differences, which yields

$$\begin{aligned}\frac{\partial^2 \Psi}{\partial x^2}(i, j, k) &= \frac{1}{\delta^2} [\Psi(i+1, j, k) + \Psi(i-1, j, k) - 2\Psi(i, j, k)] \\ \frac{\partial^2 \Psi}{\partial y^2}(i, j, k) &= \frac{1}{\delta^2} [\Psi(i, j+1, k) + \Psi(i, j-1, k) - 2\Psi(i, j, k)] \\ \frac{\partial^2 \Psi}{\partial z^2}(i, j, k) &= \frac{1}{\delta^2} [\Psi(i, j, k+1) + \Psi(i, j, k-1) - 2\Psi(i, j, k)].\end{aligned}\quad (62)$$

Full periodic boundary conditions are imposed to the electrostatic potential, which can be expressed as $\Psi(i + l_x n_x, j + l_y n_y, k + l_z n_z) = \Psi(i, j, k)$, where l_x , l_y and l_z are arbitrary integer numbers. This condition is particularly important when calculating the second derivatives at the different boundary planes of the calculation box: we need to use $\Psi(0, j, k) = \Psi(n_x, j, k)$ to calculate $\frac{\partial^2 \Psi}{\partial x^2}(1, j, k)$, and $\Psi(n_x + 1, j, k) = \Psi(1, j, k)$ to obtain $\frac{\partial^2 \Psi}{\partial x^2}(n_x, j, k)$, and analogous relations must be considered to compute $\frac{\partial^2 \Psi}{\partial y^2}$ and $\frac{\partial^2 \Psi}{\partial z^2}$ at the corresponding boundary cells. The discrete local density of charge is

$$\langle \rho_q(i, j, k) \rangle = f_d(i, j, k) \langle \rho_{IP}(i, j, k) \rangle q_{IP} + \sum_{\gamma \in \{+, -, H^+, OH^-\}} \rho_\gamma(i, j, k) q_\gamma, \quad (63)$$

where the ensemble average density of ionizable polymer is, after discretization, given by

$$\langle \rho_{IP}(i, j, k) \rangle = \sum_{\alpha} P(\alpha) \rho_{IP}(\alpha, i, j, k). \quad (64)$$

For the local degree of dissociation, we obtain:

$$\frac{f_d(i, j, k)}{1 - f_d(i, j, k)} = \frac{K_a^0}{v_w \rho_{H^+}^b} \left(v_w \rho_w^b \right)^{v_{H^+}/v_w} \exp(-\beta \Psi(i, j, k) q_{IP}). \quad (65)$$

In sum, at given bath pH and salt concentration, and polymer volume fraction, the unknowns remaining are $\pi(i, j, k)$ and $\Psi(i, j, k)$ for each cell (i, j, k) . These quantities can be obtained by solving the system of nonlinear coupled equations given by Eqs. (55) and (61). The number of

equations to be solved (and of unknowns) is twice the number of cells, which increases with decreasing polymer volume fraction. In this work, the total number of equations ranges from 10^3 to 4×10^5 , for the largest and lowest volume fractions considered, respectively. The number of terms in each equation is roughly of the same order of magnitude as the number of molecular conformations of the network included in the calculation (2×10^4 , in this case). These equations are numerically solved using Jacobian-Free Newton method.

2 Amphiphilic Polymer Co-Network Model

In our formalism, the different conformations of the polymer network, given by the positions of all the monomers, must be specified, which requires the definition of a molecular model of the APCN. We have considered a regular architecture of the network that is shown in Fig. S1, where monodisperse polymer chains are inter-connected at six-coordinated nodal monomers (cross-links). Cross-

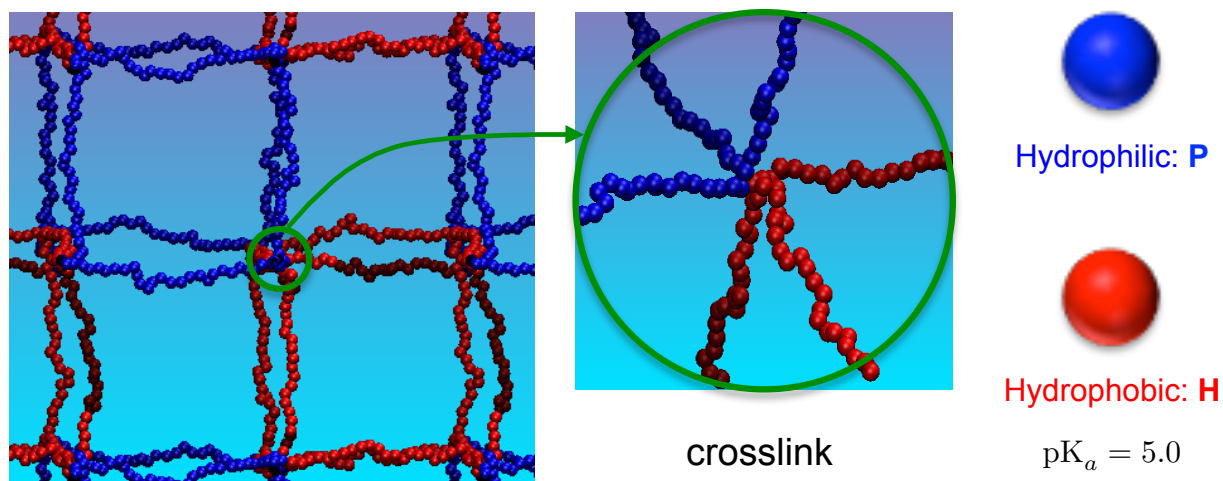


Figure S1: Schematic representation of the highly swollen ($\phi_G = 0.003$) amphiphilic polymer co-network.

links are connected to three hydrophobic and three hydrophilic polymer chains, each containing 25 monomers (excluding the nodes). In our calculations, a box of volume L^3 having 8 cross-links is considered, and full periodic boundary conditions are imposed; the periodicity of the interconnected molecule is also taken into account. Thus, $N_H = N_P = 304$ are the total number of hydropho-

bic and hydrophilic monomers in the box, respectively. All monomers, including the nodes, are spherical and have the same diameter (segment length), which is taken as $l_H = l_P \equiv l_M = 0.5$ nm. Then, the molecular volumes of the monomers are $v_H = v_P = \frac{\pi}{6} l_M^3 = 0.0655$ nm³. The total volume fraction of polymer is given by $\phi_G = \frac{(N_H v_H + N_P v_P)}{L^3}$. Different cubic box sizes with side lengths between 4.03 and 28.75 nm (ϕ_G between 0.609 and 0.0017) were considered. For each volume fraction, a large set ($\sim 10^4$) conformations are generated using Molecular Dynamics simulations (see Section 2.1). The theory requires the input of $\phi_H(\alpha, \mathbf{r})$, $\phi_P(\alpha, \mathbf{r})$ and $\rho_{IP}(\alpha, \mathbf{r})$ for each molecular conformation of the network. Considering the discretization of the volume described in Section 1.3, these distributions are obtained by counting the total number of monomers of each type that occupy a particular cell for the given conformation. If $n_H(\alpha, i, j, k)$, $n_P(\alpha, i, j, k)$ and $n_{IP}(\alpha, i, j, k)$ are respectively the number of hydrophobic, hydrophilic and ionizable monomers within the volume δ^3 of the cell given by (i, j, k) when the network is in conformation α , then the following relations are fulfilled:

$$\phi_H(\alpha, i, j, k) = n_H(\alpha, i, j, k) \frac{v_H}{\delta^3}, \quad (66)$$

$$\phi_P(\alpha, i, j, k) = n_P(\alpha, i, j, k) \frac{v_P}{\delta^3}, \quad (67)$$

$$\rho_{IP}(\alpha, i, j, k) = \frac{n_{IP}(\alpha, i, j, k)}{\delta^3}. \quad (68)$$

These quantities also satisfy $N_H = \sum_{i,j,k} n_H(\alpha, i, j, k)$ and $N_P = \sum_{i,j,k} n_P(\alpha, i, j, k)$ for each configuration.

P(n)/H(n) denotes a hydrophilic/hydrophobic monomer that is not ionizable, while P(i)/H(i) refers to a monomer that contains an acidic group. In this work, we consider the cases where either the hydrophilic or the hydrophobic monomer is ionizable; namely, H(i)-P(n) and H(n)-P(i) networks. In the first case, the local density of ionizable polymer is given by $\rho_{IP}(\alpha, \mathbf{r}) v_H = \phi_H(\alpha, \mathbf{r})$, while in the second case we have $\rho_{IP}(\alpha, \mathbf{r}) v_P = \phi_P(\alpha, \mathbf{r})$.

The pairwise attractive energy between hydrophobic monomers is given by

$$\beta u_{HH}(r) = \begin{cases} \frac{\left[\left(\frac{l_H}{r_c}\right)^6 - \left(\frac{l_H}{r}\right)^6\right]}{\left[1 - \left(\frac{l_H}{r_c}\right)^6\right]} & \text{if } r \leq r_c \\ 0 & \text{if } r > r_c. \end{cases} \quad (69)$$

Note that the contact between two hydrophobic monomers that are not chemically bonded lowers the energy by $u_{HH}(l_H) = -k_B T$. Water affinity of hydrophilic monomers is model by setting $u_{PP}(r) \equiv 0$, and we also use $u_{HP}(r) \equiv 0$.

The electric charge of an ionizable monomer is either zero or $q_{IP} = -e$, where e is the absolute value of the electron charge. The acid-base equilibrium constant is taken $pK_a = 5$, and the water dissociation equilibrium constant is $pK_w = 14$. The aqueous medium is assumed to have constant dielectric constant, $\epsilon(\mathbf{r}) \equiv \epsilon_w \epsilon_0$, with $\epsilon_w = 78.5$ being the relative dielectric constant of water at room temperature, and ϵ_0 denoting the vacuum permittivity. The monovalent salt is sodium chloride, and salt ions are described by $v_+ = v_- = 0.0335 \text{ nm}^3$ and $q_+ = -q_- = e$. For the rest of the mobile species in the solution, the values used are $v_{H^+} = v_{OH^-} = v_w = 0.03 \text{ nm}^3$, $q_{H^+} = -q_{OH^-} = e$.

2.1 MD simulations

The specification of conformations of the network molecule, which is needed for the evaluation of our theory, is obtained from Molecular Dynamics simulations using GROMACS 4.5.3.^{S2,S3} The force field used in the MD simulations has been described previously.^{S4} Non-bonded hydrophilic monomers interact *via* a repulsive (shifted) Lennard-Jones potential given by:

$$U_{rep}(r) = \begin{cases} 4\epsilon \left[\left(\frac{\sigma}{r}\right)^{12} - \left(\frac{\sigma}{r}\right)^6 + \frac{1}{4} \right] & \text{if } r \leq 2^{1/6}\sigma \\ 0 & \text{if } r > 2^{1/6}\sigma, \end{cases} \quad (70)$$

where r is the distance between the two monomers. $U_{rep}(r)$ is also used to describe the non-bonding interaction between a hydrophobic and a hydrophilic monomer. Non-bonded pairs of hydrophobic monomers, on the other hand, interact with a Lennard-Jones potential with a $-\epsilon$ well:

$$U_{att}(r) = 4\epsilon \left[\left(\frac{\sigma}{r} \right)^{12} - \left(\frac{\sigma}{r} \right)^6 \right]. \quad (71)$$

All neighboring monomers along a chain interact using $U_{bond}(r) = U_{rep}(r) + U_{FENE}(r)$, where the FENE potential is given by:

$$U_{FENE}(r) = \begin{cases} -\frac{kR_0^2}{2} \ln \left[1 - \left(\frac{r}{R_0} \right)^2 \right] & \text{if } r \leq R_0 \\ \infty & \text{if } r > R_0. \end{cases} \quad (72)$$

In this case, r represents the distance between chemically bonded monomers.

We set $\sigma = 0.575$ nm and $\epsilon = k_B T$; $R_0 = 1.5\sigma$ and $k = 30 \frac{\epsilon}{\sigma^2}$ in order to avoid any bond crossing.^{S4} The distance between bonded monomers was found to be larger than 0.87σ for all simulations at different volume fractions. As such, we set this value as the segment length l_M . For each volume fraction, a 10 ns long NVT MD simulation is performed at room temperature using a Berendsen thermostat and a 1 fs timestep. For the non-bonded interactions we use a spherical cutoff of 2σ . During the simulation time, one configuration is recorded every picosecond, which results in 10^4 conformations.

As pH increases, the hydrophobic chains increase their affinity for water. To describe this behavior, we also consider the case where the interaction between non-bonded hydrophobic monomers is purely repulsive, that is, hydrophobic monomers interact with $U_{rep}(r)$ instead of $U_{att}(r)$. Therefore, in total, we consider 2×10^4 conformations of the network.

3 Free Energy Correction

The theory requires the input of the complete set of network conformations for each volume fraction. The free energy term, $-k_B \sum_{\alpha} P(\alpha) \ln P(\alpha)$, represents the exact conformational entropy of the hydrogel if all possible molecular configurations of the network are included in the sum. It is, however, only possible to include a finite number of conformations in practice. To calculate the conformational entropy, we define $-\sum_{\alpha} P(\alpha) \ln P(\alpha) = -\sum_{\tilde{\alpha}} P(\tilde{\alpha}) \ln P(\tilde{\alpha}) + \beta \Delta_{\alpha} F$, where $\{\tilde{\alpha}\}$ is a finite set of conformations, large enough to describe the network's conformational degree of freedom properly, and $\Delta_{\alpha} F$ is the correction needed as a result of this truncation of the conformational space. It is important to mention that the main contribution to the conformational entropy comes from the term $-k_B \sum_{\tilde{\alpha}} P(\tilde{\alpha}) \ln P(\tilde{\alpha})$ and not from the correction. The network conformations included in $\{\tilde{\alpha}\}$ are generated using Molecular Dynamics simulations as described in Section 2.1. At fixed volume fraction, $\Delta_{\alpha} F$ represents only an additive constant to the free energy, in which case the correction has no relevance. However, this correction needs to be considered when comparing thermodynamic states having different volume fractions because of the different dimensions of their conformational space. For a polymer volume fraction ϕ_G , the correction due to the truncation of the conformational space is exactly expressed as:

$$\beta \Delta_{\alpha} F(\phi_G) = \ln \left(\frac{\Omega(\phi_G)}{\Omega(\phi_G^0)} \frac{\Omega_t(\phi_G^0)}{\Omega_t(\phi_G)} \right), \quad (73)$$

where ϕ_G^0 is the volume fraction of a reference state. $\Omega(\phi_G)$ and $\Omega_t(\phi_G)$ give the number of conformations included in the calculation at ϕ_G and the total number of conformations with that volume fraction, respectively; $\Omega(\phi_G^0)$ and $\Omega_t(\phi_G^0)$ are defined identically for the reference state. Assuming that the polymer chains within the network are independent, the correction to the free energy can be approximated by:

$$\beta \Delta_{\alpha} F(\phi_G) \approx \ln \left(\frac{\Omega(\phi_G)}{\Omega(\phi_G^0)} \right) + n_{chains} \ln \left(\frac{\int P_{1,free}(R) P_{node}(R, \phi_G^0) d\mathbf{R}}{\int P_{1,free}(R) P_{node}(R, \phi_G) d\mathbf{R}} \right), \quad (74)$$

where n_{chains} is the number of polymer chains in the network, $P_{1,free}(R)$ is the probability of a free chain having end-to-end distance R (considering the two cross-links), and $P_{node}(R, \phi_G)$ denotes the probability that the nodes connecting the chain are separated by a distance R given that the polymer volume fraction is ϕ_G . The derivation of Eqs. (73) and (74) has been described elsewhere.^{S1} In this work, $P_{1,free}(R)$ is obtained by performing a MD simulation of the free chain under the same conditions described in Section 2.1; the chain includes two additional monomers representing the cross-links, which allows for the proper comparison with network chains. $P_{node}(R, \phi_G)$ is obtained through a histogram of distances between the end-groups (nodes) of all chains, for all of the conformations in $\{\tilde{\alpha}\}$ at that particular volume fraction. In both cases, once a large number of configurations has been generated, the criterion to stop the generation of more network configurations hinges on the condition that adding more conformations would not modify the corresponding probability any further.

4 Additional Results

In this section, we present additional results supporting those discussed in the article. We begin by describing the deprotonation of the pendant acidic units on the H(i)-P(n) architecture. Consider the isolated acid groups in a dilute solution: the equilibrium conditions of the acid-base reaction, $AH \rightleftharpoons A^- + H^+$, are described by:

$$K_a = \frac{[A^-][H^+]}{[AH]}, \quad (75)$$

where $K_a = 10^{-pK_a}$ is the equilibrium constant given in molar units. Under the assumption of ideal solution, the degree of dissociation, which is the fraction of deprotonated acid groups, can be written as

$$f_{ideal} = \frac{[A^-]}{[AH] + [A^-]} = \frac{1}{1 + \frac{[H^+]}{K_a}}. \quad (76)$$

Then, given the pK_a of the acid, f_{ideal} depends only on the pH of the solution. In a hydrogel, the acid groups are part of the interconnected polymer network, which imposes a constraint that

modifies the equilibrium conditions with respect to those of the ideal solution. In the formalism described throughout Section 1, the degree of dissociation is locally defined independently of the density of ionizable polymer; therefore, in order to quantify the state of charge of the network, we introduce the average degree of dissociation, which is weighted by the ensemble average local density of ionizable polymer:

$$\langle f_d \rangle = \frac{\int_V f_d(\mathbf{r}) \langle \rho_{IP}(\mathbf{r}) \rangle d\mathbf{r}}{\int_V \langle \rho_{IP}(\mathbf{r}) \rangle d\mathbf{r}}. \quad (77)$$

In Fig. S2A, f_{ideal} and $\langle f_d \rangle$ are shown as a function of pH for the H(i)-P(n) network at different c and constant volume fraction.

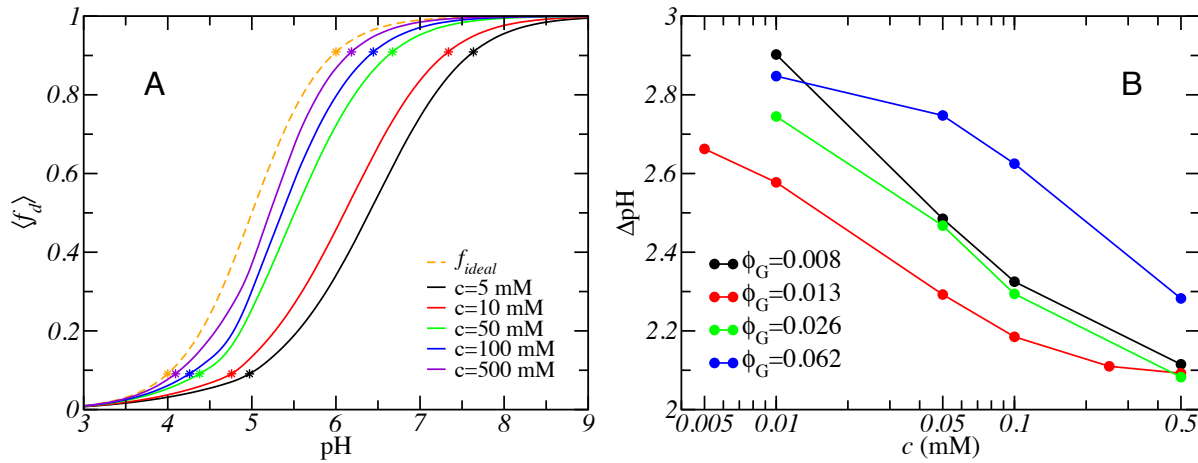


Figure S2: (A) Ensemble average degree of dissociation, $\langle f_d \rangle$, vs. pH at different salt concentrations and $\phi_G = 0.013$. The orange dashed line corresponds to the degree of dissociation of the isolated acid group in dilute solution. The stars are placed at the values $\langle f_d \rangle = \frac{1}{11}$ and $\langle f_d \rangle = \frac{10}{11}$ of each curve. (B) ΔpH as a function of the ionic strength at different polymer volume fractions. Both panels correspond to the H(i)-P(n) network.

To quantitatively describe the transition from the uncharged ($\langle f_d \rangle \sim 0$) to the fully dissociated regime ($\langle f_d \rangle \sim 1$) as a function of pH, we define the width of this transition as $\Delta pH = pH_1 - pH_0$, with $\langle f_d \rangle_{pH=pH_0} = \frac{1}{11} \approx 0.1$, and $\langle f_d \rangle_{pH=pH_1} = \frac{10}{11} \approx 0.9$. In the ideal solution, ΔpH is exactly 2. The values of pH_0 and pH_1 for the different cases presented are marked in Fig. S2A using stars. Figure S2B shows ΔpH as a function of the salt concentration at different polymer volume fractions of the H(i)-P(n) architecture. Within the range of salt concentrations considered, $\Delta pH > 2$, which indicates that deprotonation in this APCN occurs in a wider range of pH than in the dilute solution

of isolated acid groups. At constant volume fraction, the width of the deprotonation transition decreases with increasing ionic strength, while the dependence of ΔpH on the polymer volume fraction at constant c is not monotonic.

We have shown in the article that, for the H(i)-P(n) structure, isosurfaces of density of charge are correlated with those of density of hydrophobic polymer; that is, regions of high density of hydrophobic polymer are also regions of relatively high density of charge. This is not surprising since in this architecture the hydrophobic monomers bear the ionizable groups. However, in Fig. S3 we

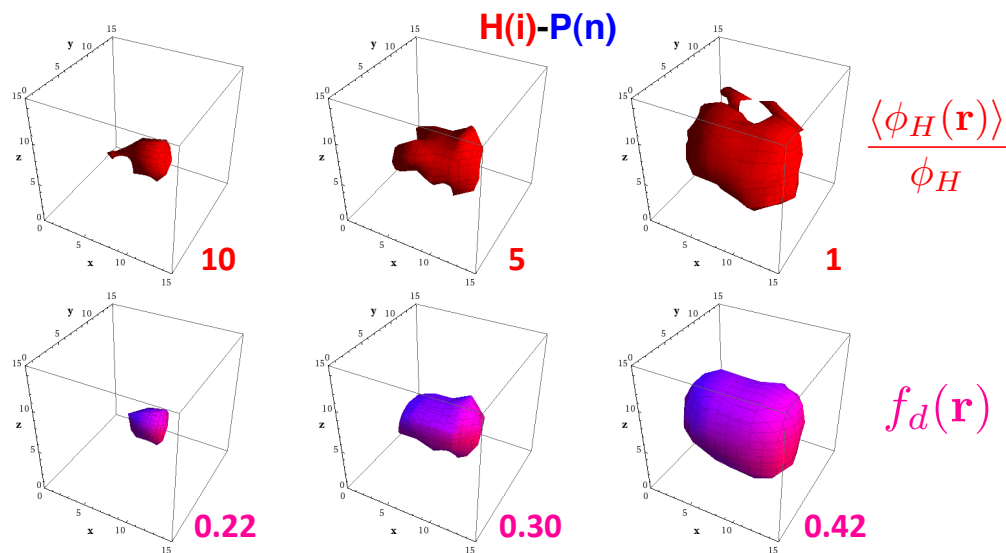


Figure S3: Surfaces of constant volume fraction of hydrophobic polymer (top) and constant local degree of dissociation (bottom) for the H(i)-P(n) network at $c = 100$ mM, pH 5 and $\phi_G = 0.013$, which correspond to the same conditions of Figs. 8 and 9 of the article. The Cartesian coordinates are in nm.

see that there is an inverse correlation between the volume fraction of hydrophobic polymer and the local degree of dissociation. Namely, as the value of the isosurface of density of hydrophobic polymer increases, the local degree of dissociation on the surface decreases. Therefore, even though the total electric charge increases with the amount of ionizable polymer, the aggregation of hydrophobic monomers clearly disfavors charge separation.

The presence of the hydrophobic aggregate within the H(n)-P(i) network is clearly observed in the localized and high magnitude isosurfaces of volume fraction of such polymer shown in Fig. S4. At low pH, these isosurfaces are almost identical in both architectures, the H(i)-P(n) and the H(n)-

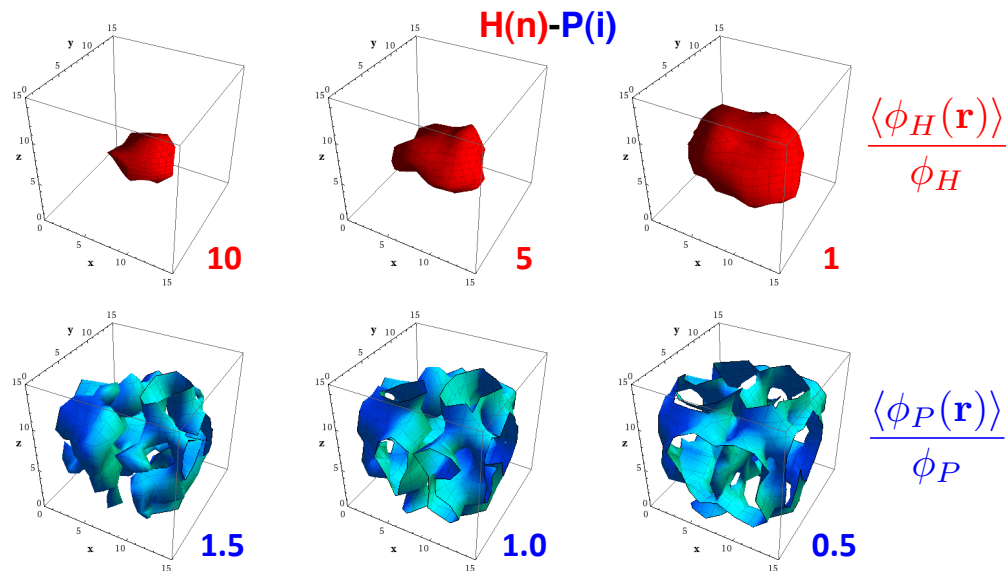


Figure S4: Isosurfaces of volume fraction of hydrophobic (top) and hydrophilic (bottom) monomers for the H(n)-P(i) network at $c = 100$ mM, pH 5 and $\phi_G = 0.013$, which are the same conditions as Fig. 10 of the article. The constant value of the different surfaces for both types of polymer can be directly compared because $\phi_H = \phi_P = \frac{\phi_G}{2}$. The Cartesian coordinates are in nm.

P(i), and likewise for the hydrophilic polymer. This can be observed by comparing the surfaces shown in Fig. S4 and those presented in Fig. 8 of the article. At higher pH, the increase in the electric charge of the hydrophobic polymer leads to swelling of the aggregate in the H(i)-P(n), while aggregate formation is less sensitive to pH (at constant volume fraction) in the H(n)-P(i) structure that has the hydrophilic polymer bearing the pendant ionizable groups.

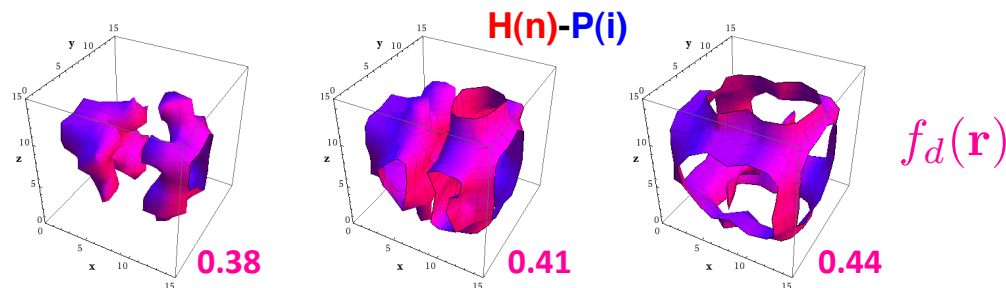


Figure S5: Isosurfaces of local degree of dissociation of the hydrophilic polymer in the H(n)-P(i) network at $c = 100$ mM, pH 5 and $\phi_G = 0.013$, which are the same conditions as Fig. 10 of the article and Fig. S4 of this SI.

In Fig. S5, surfaces of constant local degree of dissociation for the H(n)-P(i) architecture are

shown at the same conditions of Fig. S4. A comparison between Figs. S4 and S5 shows that, similarly to what was found for the H(i)-P(n) architecture, the local degree of dissociation in the H(n)-P(i) structure is inversely correlated with the density of ionizable polymer, which are the hydrophilic units in this case. However, the fact that these isosurfaces, as well as those of density of ionizable polymer, are less localized in the latter architecture leads to a higher average degree of dissociation as compared to the H(i)-P(n) structure, as discussed in the article.

If the volume of the APCN is not constraint, then the optimal polymer volume fraction of the unconstrained hydrogel, ϕ_G^0 , is that which minimizes the free energy:

$$\left. \frac{\partial F}{\partial \phi_G} \right|_{\phi_G = \phi_G^0} = 0. \quad (78)$$

The last equation is valid in the range $\phi_G^{max} > \phi_G^0 > \phi_G^{min}$, where ϕ_G^{min} and ϕ_G^{max} are respectively the minimum and maximum possible volume fractions given by the molecular structure of the network.

The optimal volume fraction of both APCNs studied are shown in Fig. S6 as a function of pH at

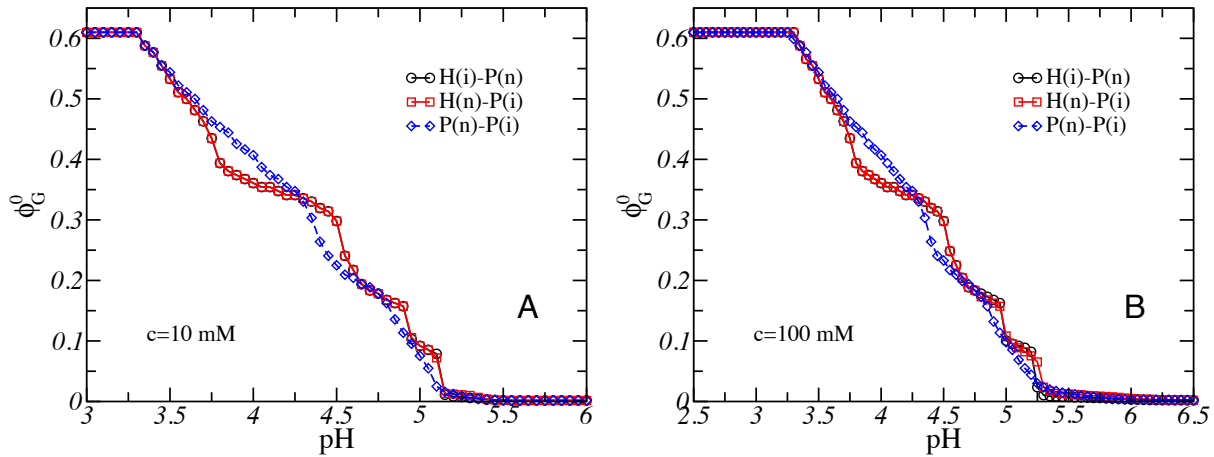


Figure S6: Swelling behavior of the different APCNs studied. Optimal polymer volume fraction vs. pH at $c = 10$ mM (A) and $c = 100$ mM (B). The swelling of a purely hydrophilic hydrogel, P(n)-P(i), having the same number of ionizable units and similar molecular structure as the APCNs is also displayed.

two different salt concentrations. These results demonstrate that although at the nanometer scale the APCNs studied show significantly different behaviors, their macroscopic swelling transition

are almost identical.

In addition, ϕ_G^0 vs. pH is also displayed in Fig. S6 for a hydrogel where both the ionizable and the neutral monomers are hydrophilic. This architecture, termed P(n)-P(i), has the same number of ionizable units and the same molecular structure as the APCNs considered. An interesting feature of both panels is that, as pH increases in the region $\phi_G^0 > 0.4$, a sharper response of the APCNs is observed as compared to that of the P(n)-P(i) hydrogel. In this range of pH, where ϕ_G^0 is still high, swelling leads to a better packing of the aggregate, which increases the net attractive interactions between the hydrophobic monomers, thus decreasing the system free energy. A more stable aggregate in the region $0.4 > \phi_G^0 > 0.3$ is also suggested by the near-zero slope of $\phi_G^0(\text{pH})$ in this range. Overall, however, these differences between the swelling transition of the purely hydrophilic network and those of the APCNs are relatively small, and significant changes in the optimal volume fraction are not observed, which indicates that the swelling behavior of the polymer network depends mainly on the number and localization of the acid groups within the network.

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