Supporting Information (SI):

P22 viral capsids as nanocomposite high-relaxivity MRI contrast agents

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The additional figures provide supplementary data for further reference to accompany the manuscript. This material is available free of charge via the Internet at http://pubs.acs.org.

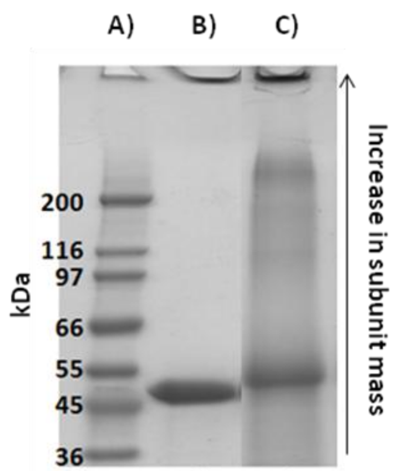

Figure S1. SDS-PAGE gel shows evidence of mass increase after modification. A) SigmaMarker Wide Ladder (MW 6,500-200,000 Da). B) P22 WB migrates at ~46.6kDa. C) P22-AACC-Gd migrates at ~49kDa). Higher molecular weight species are suggestive of inter-subunit cross-linking within the P22 capsid.

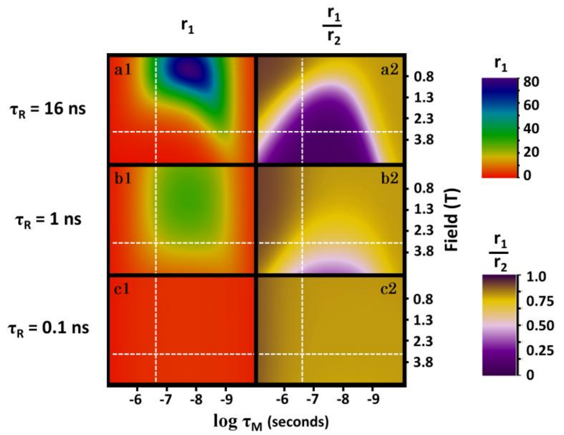

Figure S2. Contour plots of relaxivity for P22-AACC-Gd at variable field strengths and log τ_M values. The "intersection point" of the horizontal and vertical white lines represents a field strength of 3T and τ_M = 533ns (the established value for P22-AACC-Gd). The system was evaluated at three different τ_R values. a1-2) r_1 (a1) and r_1/r_2 (a2) contour plots for τ_R = 16ns (the established value for P22-AACC-Gd). b1-2) r_1 (b1) and r_1/r_2 (b2) contour plots for τ_R = 1ns. c1-2) r_1 (a1) and r_1/r_2 (a2) contour plots for τ_R = 0.1ns. The 2D plots reveal optimal performance of this system for the given "intersection point" occurs when τ_R = 1ns, with r_1 = 13.0mM^{-1}sec^{-1}, r_1/r_2 = 0.78.

Eqn. S1 (Relaxivity Equations):[1]

Analytical equation containing the decay constant, T_1, for the recovery of the net nuclear spin magnetization for a sample placed in a magnetic field which has be tilted out of equilibrium:

$$M_z(t) = M_{z\ Equilibrium}\left(1 - e^{\frac{-t}{T_1}}\right)$$

- $M_z(t)$ — nuclear spin magnetization in the z axis at time t in units of seconds
- $M_{z\ Equilibrium}$ — equilibrium state of the nuclear spin magnetization in the z axis (maximum magnetization)
- T_1 — decay constant for the recovery of spin in units of seconds

Observed T_1 of a specific sample type with a contrast agent present:

$$T_{1\ Observed} = \left[\frac{1}{T_{1\ Sample}} + (r_1)[Contrast\ Agent]\right]^{-1}$$

- r_1 — relaxivity of a contrast agent in units of mM^{-1} $seconds^{-1}$
- $[Contrast\ Agent]$ — concentration of the contrast agent in units of mM

Solomon-Bloembergen-Morgan (SBM) model for PRE:

Relaxivity of contrast agent including the dipolar, scalar and Currie relaxation mechanisms:

$$r_1 = \frac{q \cdot [Contrast\ Agent]}{[Water]} \left[\frac{1}{T_{1M} + \tau_M}\right]$$

$$r_1 = \frac{q \cdot [Contrast\ Agent]}{[Water]} \left[\frac{1}{\left(\frac{1}{T_{1M}^{dipolar}} + \frac{1}{T_{1M}^{scalar}} + \frac{1}{T_{1M}^{currie}}\right) + \tau_M}\right]$$

$[Water] = 55.6 Molar$	concentration of water in units of (moles / liter), (fixed value)
q	number of inner sphere waters that bind to the Gd ion, (fitting parameter)
$T_{1M}^{dipolar}$	dipolar contribution to the relaxation time
T_{1M}^{scalar}	scalar contribution to the relaxation time
T_{1M}^{currie}	Currie contribution to the relaxation time
τ_M	residence time for the Gd bound water molecule, (fitting parameter)

Relaxivity of contrast agent considering only the dipolar relaxation mechanism (the dipolar mechanism was only considered in the fitting of the NMRD profiles in this work):

$$r_1 = \frac{q \cdot [Contrast\ Agent]}{[Water]} \left[\frac{1}{T_{1M}^{dipolar} + \tau_M}\right]$$

SBM analytical description of the dipolar relaxation time:

$$T_{1M}^{dipolar} = \frac{2C_{dd}}{15 r_{1s}^6} [3J(\omega_1, \tau_{d1}) + 7J(\omega_s, \tau_{d2})]$$

Prefactor for relaxation:

$$C_{dd} = \gamma_I^2 \gamma_S^2 \hbar^2 S(S+1) \left(\frac{\mu_0}{4\pi}\right)^2$$

$\gamma_I = 2.675 \cdot 10^8$	nuclear gyromagnetic ratio (second^{-1} Tesla^{-1})
$\gamma_S = -1.760859778 \cdot 10^{11}$	electromagnetic gyromagnetic ratio (second^{-1} Tesla^{-1})
$\hbar = 1.054571628 \cdot 10^{-34}$	Plank's constant (Joules · second)
$S = 7/2$	spin quantum number for the Gd ion
$\mu_0 = 4\pi \cdot 10^{-7}$	magnetic permeability of free space (Newton · Amps^{-2})
$r_{1s}^6 = 3 \cdot 10^{-10}$	distance between the nuclear and the electronic spin (meters),(fixed value)

Spectral density function:

$$J(\omega, \tau) = \frac{\tau}{1 + \omega^2 \tau^2}$$

ω	Larmor frequency of nuclear or electric spin
τ	correlation time where τ is either τ_{d1} or τ_{d2}

Correlation times in units of seconds:

$$\tau_{d1} = \left(\frac{1}{\tau_R} + \frac{1}{\tau_M} + \frac{1}{T_{1e}}\right)^{-1}$$

and

$$\tau_{d2} = \left(\frac{1}{\tau_R} + \frac{1}{\tau_M} + \frac{1}{T_{2e}}\right)^{-1}$$

τ_R	rotational correlation time for the Gd ion, (fitting parameter)
T_{1e}	longitudinal electronic relaxation rate
T_{2e}	transverse electronic relaxation rate

Electronic relaxation time (longitudinal and transverse) in units of seconds:

$$T_{1e} = \left[\frac{2\Delta^2}{50}(4S(S+1)-3)\left(\frac{\tau_v}{1+\omega_S^2\tau_v^2} + \frac{4\tau_v}{1+4\omega_S^2\tau_v^2}\right)\right]^{-1}$$

and

$$T_{2e} = \left[\frac{\Delta^2}{50}(4S(S+1)-3)\left(3\tau_v + \frac{5\tau_v}{1+\omega_S^2\tau_v^2} + \frac{2\tau_v}{1+4\omega_S^2\tau_v^2}\right)\right]^{-1}$$

$\tau_v = 1.4 \cdot 10^{-11}$	correlation time for instantaneous distortions of the metal complex polyhedron in units of seconds, (fixed value in the SBM fit)
$\Delta^2 = 9 \cdot 10^{18}$	mean square fluctuation of the zero-field splitting in units of seconds^{-2}, (fixed value in the SBM fit)

References:

(1) Liepold, L.; Abedin, M.; Buckhouse, E.; Frank, J.; Young, M.; Douglas, T. Supramolecular Protein Cage Composite MR Contrast Agents with Extremely Efficient Relaxivity Properties. *Nano Lett.* **2009**, *9* (12), 4520-4526.