SUPPLEMENTAL INFORMATION for

Stoichiometry and energetics of poly(amidoamine) dendrimer-phospholipid interactions

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RECEIVED DATE

TITLE RUNNING HEAD Stoichiometry and Energetics of PAMAM and phospholipids

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FIGURES

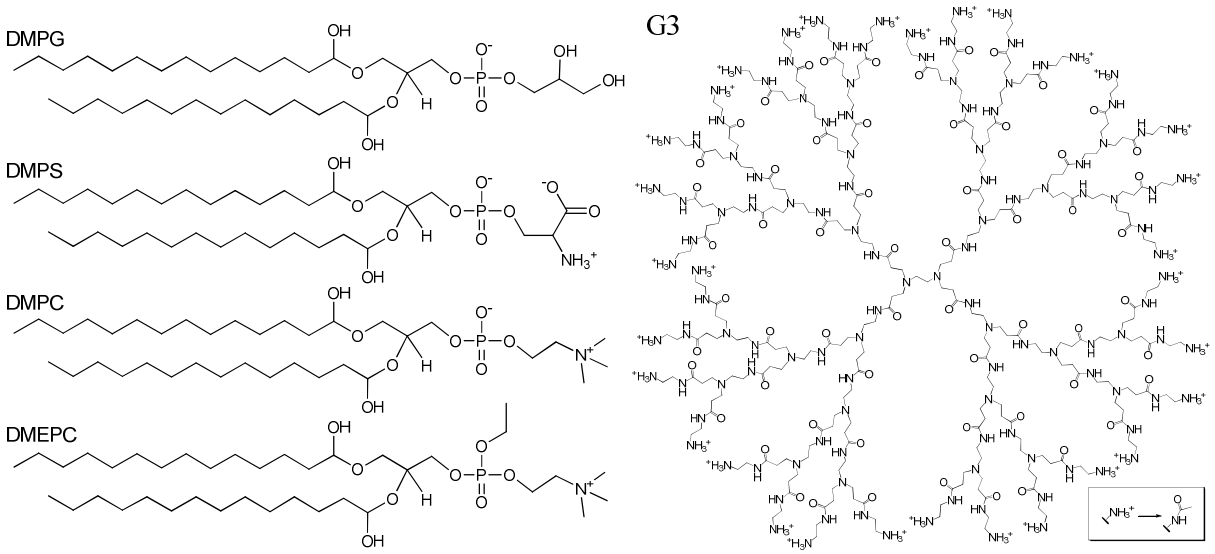

Figure S1: Molecular structure of the phosopholipids and PAMAM dendrimer used in this study. The PAMAM dendrimer contains protonated primary amines at pH 7.4. To reduce the total charge on the dendrimer, the terminal amines may be acetylated, as shown in the inset.[1]

Table S1: Lipid and dendrimer properties.

Lipid	Net Charge (*e*)	T_m (°C)
DMPG	-1	23
DMPS	-1	35
DMPC	0	23
DMEPC	+1	24
PAMAM Dendrimer	**Mass (kD)**[a]	**Dendrimer Charge (*e*)**[b]
G5-Ac(100%)	32	0
G3	6.9	31
G5-Ac(40%)	29	70
G5	27	112
G6	46	187
G7	106	450
G8	260	1090
G9	428	1880

[a] Determined by gas phase chromatography with 5% uncertainty.

[b] Equal to the number of primary amines per dendrimer at pH 7, as determined by acid-base titrations with 5% uncertainty.[2]

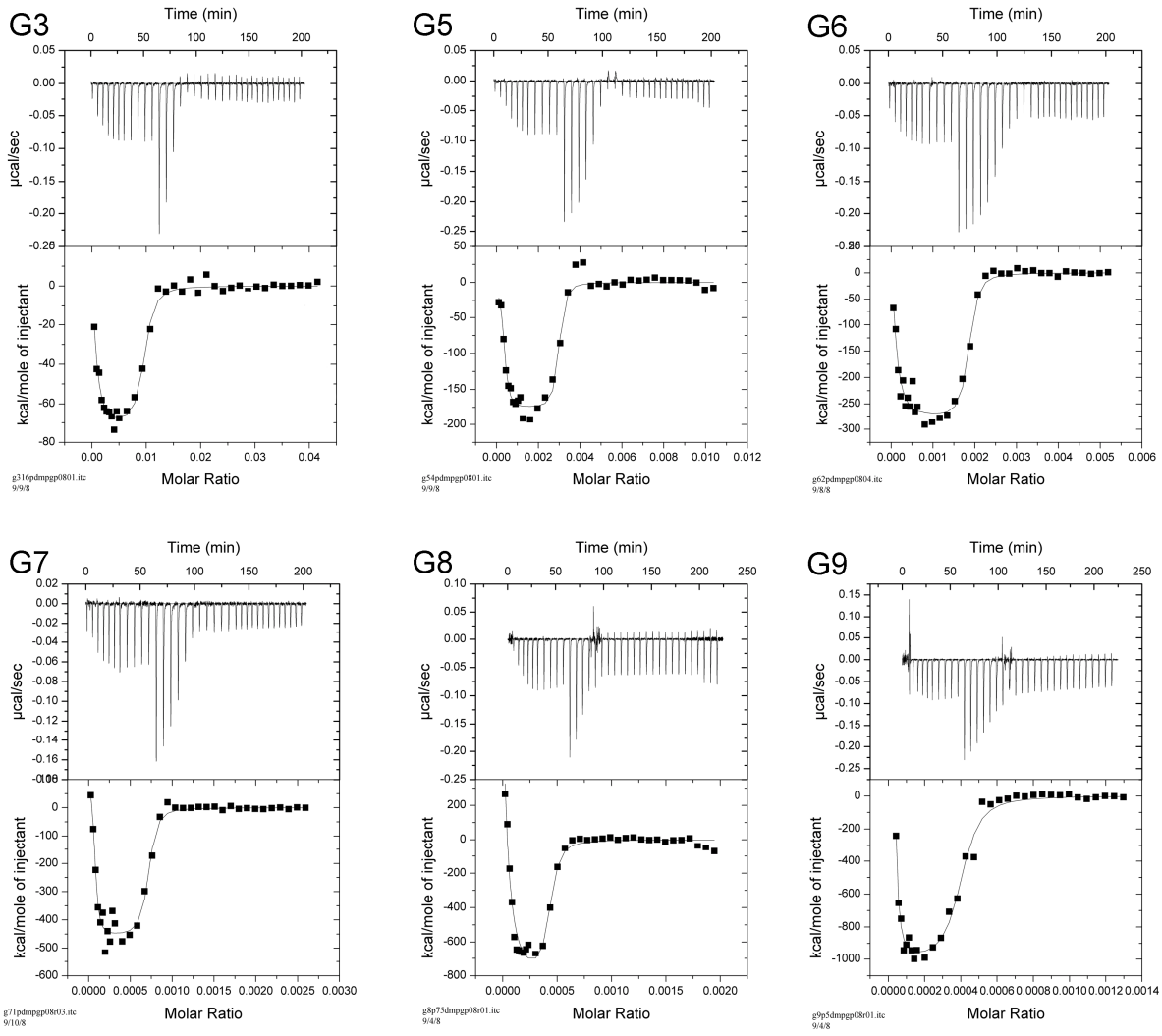

Figure S2: Power vs. time data and ΔH vs. molar ratio from ITC for PAMAM dendrimers titrated into DMPG SUVs at 50°C in PBS.

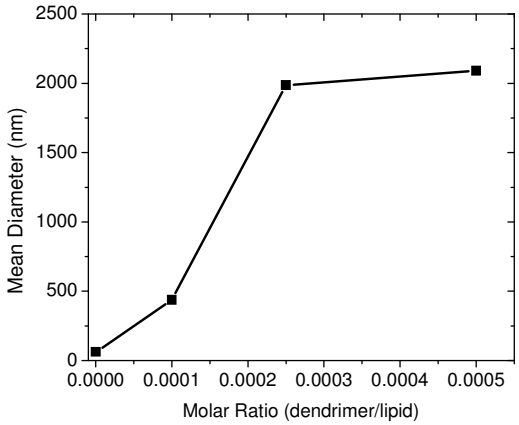

Figure S3: Mean diameter of G5-DMPS mixtures as measured with dynamic light scattering (DLS). DMPS was prepared as SUVs and G5 was titrated into the sample to the indicated molar ratio. This data was collected at 50 °C in PBS. Similar data has been obtained for G3, G5, G8 in DMPG (not shown). The flocculation and aggregation at higher dendrimer/lipid ratios yields particle sizes too large for DLS analysis, as visible by eye.

Dynamic light scattering (DLS) was performed on a Nanosizer ZS (Malvern Instruments Ltd.). Samples were prepared in a semi-micro cuvette to a volume of 0.5 mL and varying molar ratios. Samples were in PBS, stirred and 50 °C for > 5 min before measurement, and 50 °C during measurement, to replicate ITC conditions. All samples of dendrimers and lipids were observed to aggregate as the dendrimer/lipid molar ratio increased until the DLS was unable to determine accurately the average particle size due to the aggregates. The molar ratios at which DLS was unable to determine the average particle size were approximately n_L.

Table S2: Stoichiometric comparison of ITC results and proposed dendrimer-lipid models

PAMAM Dendrimer	n_D^{-1}	n_L^{-1}	Flattened-dendrimer model [A,B]	Dendrimer-encased vesicle model [B,C]
	(lipids/dendrimer)			
G3	76	140	***70 - 110***	1100 - 1200
G5	240	460	***110 - 170***	1300 - 1500
G6	410	860	170 - 270	1600 - 1900
G7	1200	2300	390 - 610	***1900 - 2200***
G8	1600	2700	690 - 1100	***2300 - 2900***
G9	1800	3800	1100 - 1700	***3000 - 3800***

[A] Assuming a lipid density of 0.58 nm^2/lipid/monolayer and the maximum dendrimer extension on the surface equals that observed on mica under water.[3]

[B] Numbers in bold and italics indicate a general agreement between the model and the ITC-determined stoichiometries.

[C] Analogous to an estimate by Mecke et al.[4] with the minimum dendrimer radius equal to that observed in simulations.

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