Supporting Information

"The biomolecular corona of liposomes in circulating biological media"

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Increase in size of the nanoparticle-protein corona is due to particle agglomeration

The simplest theoretical models of particle coagulation are based on effective collisions between rigid spheres in Brownian diffusion. Agglomeration is driven by Van der Waals-London interactions and can be described in terms of collision rates and efficiencies. It is expected that the time evolution of particle concentration follows a non-increasing trend, due to the clustering of k > 1 units and the subsequent formation of larger k-fold particles. Although, in general, the clustering process defines a nonlinear dynamical system in the k-fold particle concentrations, it can be regarded as a sphere-packing problem (R. M'Hallah, A. Alkandari, and N. Mladenovic, Computers & Operations Research 40, 2013, 603). The dense sphere-packing conditions determine size ratios $\rho_k = r_k / R$ and locations of k identical units of radius r_k in a larger sphere of radius R (Figure S1).

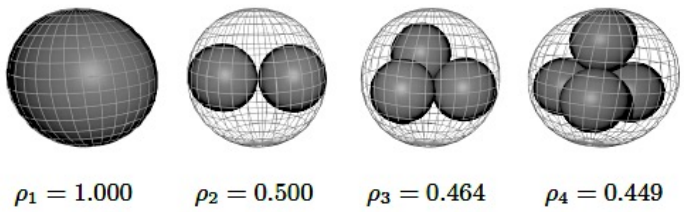

Figure S1: Schematic picture of the dense sphere packing problem and corresponding size ratio ρ_k for k = 1, 2, 3 and 4.

DLS experiments provide the size of liposome-protein corona systems under static and dynamic conditions, as functions of the incubation time. Measurements are based on the peak mean value of the size distribution by intensity and lead to the average hydrodynamic diameter at time t, i.e. $D_H(t)$. The comparison of $D_H(t)$ with the bare liposome's reference size $D_H(0)$ and the theoretical predicted size ratios ρ_k allowed us to estimate the k elementary units in aggregates and the thickness of the protein corona as follows. At a given time t the elementary unit's size d_k is estimated.

$$d_k = \rho_k D_H \quad (\mathbf{1})$$

for all the k-values that yield $d_k > D_H(0)$. Then, for each possible elementary unit, we evaluated the thickness s_k of the protein layer adsorbed on it:

$$s_k = \frac{1}{2}[d_k - D_H(0)] \quad (\mathbf{2})$$

The imposed constraint on the d_k values prevents negative values of the corona thickness. Hence, the maximum acceptable k value defines the possible number of elementary units in aggregates. Table S1 summarizes the results in the plateau region (t ≥ 15 min).

Table S1. Estimation of the corona thickness s_k of elementary units clustered in k-fold aggregates. Results are obtained from the measured average size within the plateau region (t ≥ 15 min). Dynamic vs. static incubations resulted in the same number of units within aggregates as well virtually identical corona thickness. * Dynamic incubation seemed to produce aggregates made of up to five units, while static incubation did not. We cannot exclude that such discrepancy is merely due to intrinsic low resolution of the DLS technique.

	s_2(nm)	s_3(nm)	s_4(nm)	s_5(nm)
Static incubation	10.9 ±2.74	9.24±1.23	9.69±1.38	< 0*
Dynamic incubation	11.32±3.91	14.15±3.63	11.44±3.52	11.27*

The intrinsic limit of the DLS technique (e.g. low spatial resolution) coupled with the complexity of the studied systems (nanoparticles interact with more than 3700 plasma proteins) result to large sample heterogeneity as demonstrated by the observed high polydispersity index in the plateau region. As a result, the proposed approach should not be intended as a rigorous method to measure the thickness of the protein corona at a specific incubation time, neither the relative abundance of monomers and aggregates. However, this approach can provide a rough estimation about the largest number of units within nanoparticle-protein agglomerates that is compatible with the dense sphere-packing model. The model provides an estimation of the he thickness of the protein corona as well.

Of note, the values we obtained (Figure S1) are in very good agreement with those reported in the literature (e.g. Monopoli et al., *JACS*, 2011, 133, 2525-2534).

Table S2. The full list of the most abundant corona proteins identified onto the surface of multicomponent liposomes following 90 min dynamic incubation with fetal bovine serum**.**

DYNAMIC			
#	**Identified Proteins**	**RPA (%)**	**St. Dev. (%)**
1	Apolipoprotein A-II	16.56657	1.68724113
2	Serum albumin	6.63396218	1.59572343
3	Antitrypsin	5.35977265	1.53071812
4	Alpha-2-HS-glycoprotein	5.10242438	0.59931002
5	Hemoglobin fetal subunit beta	4.53700053	0.20976655
6	Apolipoprotein C-III	3.75269568	0.49741892
7	Apolipoprotein C-II	3.20560565	0.47147474
8	Apolipoprotein A-I	2.9118297	0.90065018
9	Hemoglobin subunit beta	2.87382547	0.17274616
10	Hemoglobin subunit alpha	2.33824	0.5831613
11	Apolipoprotein E	2.05562431	0.04493812
12	Alpha-2-macroglobulin	1.75244864	0.04476972
13	Clusterin	1.66121609	0.1666323
14	Hyaluronan-binding protein 2	1.4802315	0.13631126
15	Inter-alpha-trypsin inhibitor heavy chain H3	1.2919873	0.48252524
16	Apolipoprotein A-IV	0.93375068	0.2706122
17	Prothrombin	0.87806505	0.04778798
18	Apolipoprotein D	0.87314592	0.11131315
19	C4b-binding protein alpha chain	0.83674051	0.07999817
20	Protein AMBP	0.82699146	0.27046823
21	Complement C4 (Fragments)	0.78635811	0.19828212
22	Tubulin alpha-4A chain	0.74096506	0.026992
23	Tubulin beta-5 chain	0.71463635	0.02961606
24	Tubulin alpha-1B chain	0.70899449	0.03971631
25	Tubulin beta-4B chain	0.69771076	0.03518322
26	Alpha-2-antiplasmin	0.69583013	0.05236128
27	Complement C3	0.66374894	0.16438488
28	Serotransferrin	0.64616242	0.06670824
29	Tubulin beta-4A chain	0.64317272	0.02564826
30	Alpha-1-acid glycoprotein	0.60915799	0.07244501
31	Kininogen-1	0.56554936	0.04532105
32	60S acidic ribosomal protein P2	0.56418659	0.0507826
33	Myosin light polypeptide 6	0.54206163	0.08815348
34	Lumican	0.54007606	0.13064264
35	Metallothionein-1A	0.5328429	0.1969921
36	Glyceraldehyde-3-phosphate dehydrogenase	0.50672315	0.05365686
37	Alpha-fetoprotein	0.47151827	0.01955942
38	Kininogen-2	0.44426287	0.03537956
39	Inter-alpha-trypsin inhibitor heavy chain H4	0.43696805	0.05433582
40	Fibromodulin	0.4264201	0.04760935
41	Hemopexin	0.39601559	0.03194078
42	Transthyretin	0.38787828	0.02879103
43	Vitamin D-binding protein	0.38499526	0.03261775
44	Fetuin-B	0.38049794	0.02454643
45	Beta-2-glycoprotein 1	0.37117539	0.02642046

46	Actin, cytoplasmic 2	0.36716905	0.05493137
47	14-3-3 protein zeta/delta	0.35933313	0.07186976
48	Tubulin beta-6 chain	0.34039258	0.05398401
49	Ras-related protein Rap-1b	0.33582535	0.01096801
50	Secreted phosphoprotein 24	0.33524131	0.03516896
51	Fibrinogen gamma-B chain	0.31970574	0.01617772
52	Fibrinogen alpha chain	0.31577608	0.01498474
53	Biglycan	0.31119816	0.02076211
54	Inter-alpha-trypsin inhibitor heavy chain H1	0.31095433	0.07011618
55	Cathelicidin-1	0.30821305	0.09688984
56	Gelsolin	0.29602383	0.15801589
57	Antithrombin-III	0.29113475	0.00922051
58	Fibrinogen beta chain	0.28741581	0.04897485
59	Plasminogen	0.28415992	0.00584528
60	Spleen trypsin inhibitor I	0.2820933	0.0553992
61	Galectin-3-binding protein	0.28057667	0.04142373
62	Pentraxin-related protein PTX3	0.26642145	0.02760222
63	14-3-3 protein theta	0.26194378	0.04113004
64	Microtubule-associated protein RP/EB family member 2	0.25922087	0.02713452
65	Thyroglobulin	0.2572666	0.03645859
66	Coagulation factor X	0.25302914	0.02850567
67	Nucleosome assembly protein 1-like 1	0.24239128	0.01937797
68	Protein NDRG2	0.23628327	0.02458802
69	Fibronectin	0.23611486	0.02678247
70	Inter-alpha-trypsin inhibitor heavy chain H2 (Fragments)	0.23507775	0.03838804
71	Appetite-regulating hormone	0.21699484	0.01771755
72	Vitamin K-dependent protein Z	0.21649021	0.01417189
73	Keratin, type II cytoskeletal 5	0.208958	0.04512363
74	Haptoglobin	0.20477884	0.03484026
75	Heat shock protein HSP 90-alpha	0.20354967	0.02033813
76	14-3-3 protein beta/alpha	0.20149521	0.02965929
77	Pigment epithelium-derived factor	0.19010635	0.03283398
78	Keratin, type I cytoskeletal 10	0.18977185	0.02215968
79	Heat shock protein HSP 90-beta	0.18353058	0.02370994
80	Alpha-S1-casein	0.18053971	0.02437565
81	14-3-3 protein epsilon	0.17833484	0.01213214
82	14-3-3 protein gamma	0.16791268	0.05599328
83	Decorin	0.16455442	0.0087958
84	Nucleosome assembly protein 1-like 4	0.16241735	0.00799619
85	Adenylyl cyclase-associated protein 1	0.153031	0.12288266
86	Coagulation factor IX (Fragment)	0.15205029	0.05100706
87	Proteasome subunit alpha type-5	0.14827981	0.08961534
88	Proteasome subunit alpha type-2	0.14827981	0.07429411
89	Collectin-11	0.14776316	0.03324501
90	Vitamin K-dependent protein C (Fragment)	0.14749976	0.00689867
91	Resistin	0.14532079	0.13941826
92	Serpin A3-1	0.1430908	0.01156348
93	Proteasome subunit alpha type-1	0.14104665	0.08720085

94	Proteasome subunit beta type-1	0.13743007	0.08183388
95	Proteasome subunit alpha type-7	0.13097189	0.09342949
96	ADP-ribosylation factor 4	0.12985247	0.04566347
97	Heat shock protein beta-1	0.12822423	0.01046946
98	Thrombospondin-1	0.12802696	0.01077717
99	Coagulation factor XIII A chain (Fragment)	0.12673757	0.01529705
100	Proteasome subunit alpha type-6	0.1253748	0.09028017
101	Sulfotransferase 1A1	0.12445293	0.0244253
102	Tubulin alpha-1C chain	0.12224043	0.08646772
103	Aggrecan core protein	0.1215524	0.00613969
104	Elongation factor 1-alpha 1	0.12035981	0.0106384
105	Histone H4	0.11967594	0.06396948
106	Adenosylhomocysteinase	0.11753887	0.00831125
107	Transforming protein RhoA	0.11112766	0.0120891
108	Proteasome subunit alpha type-4	0.11024336	0.07835739
109	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A	0.10994405	0.04091694
110	Complement component C9	0.10768077	0.01832552
111	Carboxypeptidase B2	0.10746411	0.00271388
112	Protein HP-20 homolog	0.10746411	0.02901863
113	Endoplasmin	0.1073181	0.04098517
114	ADP-ribosylation factor 1	0.10298644	0.02532953
115	Serum amyloid A-4 protein	0.10029984	0.07256591
116	Serpin A3-7	0.10003308	0.01721034
117	Keratin, type I cytoskeletal 17	0.09978811	0.03058386
118	Galactokinase	0.09850877	0.02814173
119	60S acidic ribosomal protein P0	0.09679672	0.010348
120	Proteasome subunit beta type-2	0.0940311	0.0666783
121	Adiponectin	0.0940311	0.00511462
122	Cofilin-1	0.0940311	0.01851748
123	Plasma serine protease inhibitor	0.09194152	0.00295511
124	Tropomyosin alpha-1 chain	0.09118167	0.05936117
125	Alpha-1B-glycoprotein	0.09054847	0.02188801
126	Suprabasin	0.08743243	0.03086247
127	60S acidic ribosomal protein P1	0.08619517	0.06740718
128	Proteasome subunit beta type-3	0.08585448	0.0625391
129	Peroxiredoxin-2	0.08548282	0.04231184
130	Factor XIIa inhibitor	0.08498965	0.03440507
131	Keratin, type II cytoskeletal 75	0.08446861	0.01477981
132	Proteasome subunit beta type-6	0.08318136	0.03688203
133	Coagulation factor V	0.08270205	0.02405034
134	Cartilage oligomeric matrix protein	0.08256389	0.00842664
135	Osteomodulin	0.08251709	0.01957006
136	Neurexin-1	0.08059808	0.01088199
137	Thrombospondin-4	0.07895064	0.00331917
138	Thioredoxin	0.07835925	0.05863869
139	CMP-N-acetylneuraminate-poly-alpha-2,8-sialyltransferase	0.07797701	0.04063989
140	Argininosuccinate synthase	0.07767786	0.00764853

141	Calpain small subunit 1	0.07723983	0.02644291
142	L-lactate dehydrogenase B chain	0.07624143	0.02490035
143	Glutathione peroxidase 3	0.0759482	0.02343812
144	Hyaluronan and proteoglycan link protein 1	0.07522488	0.02840455
145	Apolipoprotein C-IV	0.07388158	0.02513087
146	Coagulation factor VII	0.07292208	0.02588875
147	Monocyte differentiation antigen CD14	0.0728741	0.04829117
148	26S protease regulatory subunit 8	0.0715454	0.0236628
149	CD9 antigen	0.07146364	0.03488034
150	Ubiquitin-like modifier-activating enzyme 1	0.07092176	0.00982452
151	GTP-binding nuclear protein Ran	0.07052332	0.02879103
152	26S proteasome non-ATPase regulatory subunit 5	0.07052332	0.01645202
153	Insulin-like growth factor-binding protein 2	0.06914051	0.02564731
154	Heat shock cognate 71 kDa protein	0.06754347	0.01123775
155	Lipopolysaccharide-binding protein	0.06617003	0.00651541
156	Tubulin alpha-1D chain	0.06394115	0.09042644
157	Small glutamine-rich tetratricopeptide	0.06360927	0.00391118
158	General vesicular transport factor p115	0.0626874	0.04478604
159	Selenoprotein P	0.0626874	0.00886534
160	Gamma-glutamyl hydrolase	0.0626874	0.03385507
161	Myocilin	0.06154763	0.00418779
162	Complement factor B	0.06084365	0.01025892
163	Phosphoglycerate kinase 1	0.06059782	0.08569826
164	Regucalcin	0.05983797	0.0120891
165	Conglutinin	0.05938806	0.01049843
166	Myosin-10	0.0558438	0.00290349
167	GTP-binding protein SAR1a	0.05556383	0.03963675
168	Thyroxine-binding globulin	0.05519217	0.00867261
169	Insulin-like growth factor-binding protein 6	0.05265742	0.03835731
170	Ras-related protein Rab-1B	0.05128969	0.03774819
171	Heat shock 70 kDa protein 1A	0.05104545	0.01329801
172	Mannose-binding protein C	0.05063213	0.05695397
173	Corticosteroid-binding globulin	0.05014992	0.01845467
174	Prostaglandin E synthase 3	0.04949005	0.03499475
175	Histidine-rich glycoprotein (Fragments)	0.04915262	0.01317379
176	Proteasome subunit beta type-4	0.04863678	0.03971176
177	Clathrin heavy chain 1	0.04701555	0.00786647
178	Dynactin subunit 2	0.04701555	0.01599237
179	Integrin-linked protein kinase	0.04609368	0.01303726
180	Complement factor H	0.04567225	0.00414033
181	Microtubule-associated protein RP/EB family member 1	0.04388118	0.06205736
182	Proteasome subunit alpha type-3	0.0436573	0.03114316
183	26S protease regulatory subunit 7	0.04221804	0.0143605
184	Proteasome subunit beta type-7	0.04074681	0.02906695
185	Follistatin-related protein 1	0.04029904	0.02868507
186	Estrogen sulfotransferase	0.04029904	0.05699145
187	Proteasome subunit beta type-5	0.03890942	0.02863656
188	Phosphatidylinositol-glycan-specific phospholipase D	0.03842131	0.00623276

189	Calpain-2 catalytic subunit	0.03761244	0.01585686
190	Prenylcysteine oxidase-like	0.03656765	0.01128502
191	Fermitin family homolog 3	0.03588029	0.01525386
192	Prosaposin	0.03566697	0.03006926
193	Transgelin-2	0.03419313	0.04835638
194	Cullin-associated NEDD8-dissociated protein 1	0.03387885	0.010348
195	Versican core protein	0.03354623	0.006131
196	Exportin-2	0.03248347	0.01190638
197	Acylamino-acid-releasing enzyme	0.0313437	0.00492519
198	Matrix Gla protein	0.0313437	0.02216334
199	Microfibrillar-associated protein 5	0.02969403	0.02424508
200	BOLA class I histocompatibility antigen, alpha chain BL3-7	0.02910486	0.00837696
201	Alpha-actinin-1	0.02830062	0.01008357
202	Neural cell adhesion molecule 1	0.02800926	0.01995654
203	26S proteasome non-ATPase regulatory subunit 2	0.02726902	0.02012353
204	Beta-2-microglobulin	0.02686603	0.0379943
205	26S protease regulatory subunit 10B	0.02564485	0.0276996
206	Complement C1q subcomponent subunit B	0.02531607	0.01844102
207	Serum amyloid A protein	0.02507496	0.01773067
208	LIM and SH3 domain protein 1	0.02507496	0.00886534
209	Elongation factor 2	0.02474503	0.00979853
210	Actin, alpha cardiac muscle 1	0.02462719	0.03482811
211	Keratin, type II cytoskeletal 79	0.02431839	0.00397118
212	Complement component C7	0.02426609	0.00495329
213	Serpin H1	0.02400794	0.00848809
214	Myosin regulatory light chain 12B	0.02350777	0.01759161
215	Ras-related protein Rab-11B	0.02350777	0.01919402
216	Vitamin K-dependent protein S	0.02256746	0.00614209
217	Junction plakoglobin	0.02178769	0.01547011
218	Elongation factor 1-delta	0.02123283	0.03002775
219	F-actin-capping protein subunit alpha-1	0.01994599	0.02820789
220	Proteasome activator complex subunit 1	0.01945471	0.02751311
221	CD44 antigen	0.01880622	0.01449117
222	Cysteine and glycine-rich protein 1	0.01791069	0.01266477
223	Keratin, type II cuticular Hb1	0.01709656	0.02417819
224	Protein S100-A1	0.01709656	0.02417819
225	Calreticulin	0.01567185	0.00554084
226	Metalloproteinase inhibitor 3	0.01567185	0.01108167
227	ATPase inhibitor, mitochondrial	0.01567185	0.02216334
228	Nucleobindin-1	0.01538691	0.02176037
229	Desmoglein-1	0.01511214	0.00712393
230	Cation-independent mannose-6-phosphate receptor	0.01470304	0.00476255
231	Angiotensin-converting enzyme	0.01415522	0.01000925
232	Proteasome subunit beta type-8	0.01253748	0.00886534
233	D-3-phosphoglycerate dehydrogenase	0.01175389	0.01662251
234	Cathelicidin-4	0.01175389	0.01662251
235	Pantetheinase	0.01154768	0.01016924
236	Beta-casein	0.01128373	0.01595761

237	Calmodulin	0.01106248	0.01564471
238	Keratin, type II cytoskeletal 7	0.01084974	0.01534385
239	Alpha-actinin-4	0.01074641	0.01519772
240	cAMP-dependent protein kinase type II-alpha regulatory subunit	0.0104479	0.01477556
241	Eukaryotic initiation factor 4A-I	0.01022077	0.00764853
242	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2	0.01016552	0.00718811
243	L-lactate dehydrogenase A chain	0.01016552	0.01437622
244	Pulmonary surfactant-associated protein B	0.00917377	0.01297366
245	von Willebrand factor (Fragment)	0.00912923	0.00516427
246	Retinol-binding protein 4	0.00895534	0.01266477
247	Ras-related C3 botulinum toxin substrate 1	0.00895534	0.01266477
248	Prolargin	0.00854828	0.00604455
249	Alpha-enolase	0.00800265	0.00565873
250	Flotillin-1	0.00800265	0.01131745
251	Primary amine oxidase, liver isozyme	0.00774374	0.00681937
252	Leukocyte cell-derived chemotaxin 1	0.00762414	0.01078217
253	Platelet-activating factor acetylhydrolase	0.00752249	0.0053192
254	High mobility group protein B1	0.00752249	0.0106384
255	CD97 antigen	0.00705233	0.0099735
256	Alcohol dehydrogenase class-3	0.00705233	0.0099735
257	Chloride intracellular channel protein 1	0.00696527	0.00985037
258	Dentin matrix acidic phosphoprotein 1	0.00683863	0.00483564
259	Sphingomyelin phosphodiesterase	0.00681385	0.00963624
260	26S protease regulatory subunit 6B	0.00600199	0.00848809
261	Peroxisomal biogenesis factor 19	0.00569885	0.0080594
262	Golgi phosphoprotein 3-like	0.00569885	0.0080594
263	Annexin A5	0.00522395	0.00738778
264	Fatty acid synthase	0.00512897	0.00301986
265	Oncoprotein-induced transcript 3 protein	0.00462448	0.00654
266	Asporin	0.00447767	0.00633238
267	Integrin beta-1	0.00427414	0.00302227
268	Coagulation factor XII	0.00421035	0.00595433
269	DnaJ homolog subfamily A member 2	0.00408831	0.00578174
270	Flotillin-2	0.00400132	0.00565873
271	cGMP-specific 3',5'-cyclic phosphodiesterase	0.00379924	0.00537293
272	Solute carrier family 2, facilitated glucose transporter member 3	0.00348263	0.00492519
273	Calpain-1 catalytic subunit	0.00344016	0.00486512
274	T-complex protein 1 subunit beta	0.00329934	0.00466597
275	T-complex protein 1 subunit zeta	0.00324245	0.00458552
276	T-complex protein 1 subunit alpha	0.00313437	0.00443267
277	Catalase	0.00313437	0.00443267
278	T-complex protein 1 subunit gamma	0.00308299	0.00436
279	Collagen alpha-2(I) chain	0.00291569	0.00206171
280	WD repeat-containing protein 1	0.00284943	0.0040297
281	Cytoplasmic dynein 1 intermediate chain 2	0.00276562	0.00391118
282	P-selectin	0.00264876	0.00374592

283	Hepatocyte growth factor-like protein	0.00235078	0.0033245
284	Dynamin-1-like protein	0.00226581	0.00320434
285	Lysyl oxidase homolog 4	0.00223884	0.00316619
286	ATP-dependent 6-phosphofructokinase, liver type	0.0022125	0.00312894
287	Transitional endoplasmic reticulum ATPase	0.00211306	0.00298832
288	Glycogen phosphorylase, liver form	0.00193879	0.00274186
289	Transportin-1	0.00184375	0.00260745
290	AP-1 complex subunit beta-1	0.00177417	0.00250906

Table S3. The full list of the most abundant corona proteins identified onto the surface of multicomponent liposomes following 90 min static incubation with fetal bovine serum**.**

STATIC			
#	**Identified Proteins**	**RPA (%)**	**St. Dev. (%)**
1	Apolipoprotein A-II	12.3567218	0.14996388
2	Serum albumin	6.504891	0.37342348
3	Alpha-2-HS-glycoprotein	5.57976748	0.07109987
4	Hemoglobin fetal subunit beta	4.19459411	0.06665642
5	Antitrypsin	4.02282626	0.18021309
6	Inter-alpha-trypsin inhibitor heavy chain H3	3.66536467	0.23611399
7	Apolipoprotein C-II	3.54040905	0.1238941
8	Apolipoprotein C-III	3.31672308	0.07153029
9	Alpha-2-macroglobulin	1.98126455	0.07983118
10	Protein AMBP	1.88184974	0.05064872
11	Complement C4 (Fragments)	1.73020119	0.07968195
12	Apolipoprotein E	1.71578284	0.02027434
13	Hemoglobin subunit alpha	1.67995881	0.03665784
14	Hyaluronan-binding protein 2	1.65587337	0.12272239
15	Clusterin	1.62871823	0.06786407
16	Apolipoprotein A-I	1.60925347	0.13756868
17	Hemoglobin subunit beta	1.16663806	0.37877708
18	Lumican	1.0290346	0.04655878
19	C4b-binding protein alpha chain	0.96897053	0.01658899
20	Prothrombin	0.91658017	0.00676005
21	Tubulin beta-5 chain	0.7856777	0.02539729
22	Serotransferrin	0.75273989	0.02682197
23	Tubulin beta-4B chain	0.74664836	0.00959927
24	Tubulin alpha-4A chain	0.73646679	0.02505484
25	Tubulin beta-4A chain	0.69913437	0.00865267
26	Tubulin alpha-1B chain	0.68555895	0.01964336
27	Alpha-2-antiplasmin	0.66642994	0.02724884
28	Alpha-fetoprotein	0.61482902	0.01764891
29	Alpha-1-acid glycoprotein	0.6123697	0.01043399
30	Fibromodulin	0.56630042	0.04768386
31	60S acidic ribosomal protein P2	0.55857216	0.02645551
32	Apolipoprotein D	0.51715904	0.04881919
33	Inter-alpha-trypsin inhibitor heavy chain H1	0.51579893	0.01855761
34	Complement C3	0.50272629	0.01541327
35	Glyceraldehyde-3-phosphate dehydrogenase	0.4972942	0.02185648
36	Apolipoprotein A-IV	0.49131988	0.00966653
37	Vitamin D-binding protein	0.48666617	0.0113199
38	Inter-alpha-trypsin inhibitor heavy chain H2 (Fragments)	0.46665522	0
39	Fetuin-B	0.45185643	0.00279049
40	Myosin light polypeptide 6	0.44419588	0.0429339
41	Proteasome subunit alpha type-1	0.42988845	0.02226938
42	Hemopexin	0.42586368	0.02431121
43	Proteasome subunit alpha type-4	0.42423202	0.01655047
44	Proteasome subunit alpha type-7	0.40302042	0.00428539
45	Proteasome subunit alpha type-5	0.39486211	0.04101934

46	Kininogen-1	0.38734228	0.03130198
47	Beta-2-glycoprotein 1	0.36841202	0.03586408
48	Heat shock protein HSP 90-alpha	0.36434044	0.01346636
49	Galectin-3-binding protein	0.36401844	0.050207
50	Tubulin beta-6 chain	0.35296104	0.02050406
51	Plasminogen	0.34591226	0.01171981
52	Cathelicidin-1	0.34409931	0.00666616
53	Proteasome subunit alpha type-2	0.33938562	0.03604458
54	Spleen trypsin inhibitor I	0.323959	0.0327248
55	Tropomyosin alpha-3 chain	0.323959	0.01259578
56	Ras-related protein Rap-1b	0.3232244	0.03475602
57	Proteasome subunit beta type-2	0.32094075	0.03258014
58	Proteasome subunit beta type-5	0.31890545	0.0149184
59	Inter-alpha-trypsin inhibitor heavy chain H4	0.31359897	0.00235276
60	Thyroglobulin	0.31306363	0.00824043
61	Actin, cytoplasmic 2	0.30908333	0.02267616
62	14-3-3 protein zeta/delta	0.30908333	0.05797169
63	Kininogen-2	0.30741451	0.02220205
64	Secreted phosphoprotein 24	0.30249588	0.02274036
65	Metallothionein-1A	0.29696242	0.0346384
66	Prothymosin alpha	0.29696242	0.0346384
67	Proteasome subunit alpha type-6	0.28282135	0.02036546
68	Tropomyosin alpha-1 chain	0.28025024	0.01924037
69	Proteasome subunit beta type-1	0.27738248	0.03026281
70	Heat shock protein HSP 90-beta	0.2698729	0.0109146
71	Collectin-11	0.2636299	0.00742251
72	Nucleosome assembly protein 1-like 1	0.26208112	0.00961408
73	Proteasome subunit beta type-3	0.26191716	0.005217
74	Gelsolin	0.25034927	0.0257008
75	Fibrinogen alpha chain	0.24820739	0.02601446
76	14-3-3 protein theta	0.23938807	0.02999773
77	Microtubule-associated protein RP/EB family member 2	0.23848719	0.01621499
78	Antithrombin-III	0.2382226	0.00230752
79	Serpin A3-1	0.23793883	0.0090361
80	Protein NDRG2	0.23495927	0.01846014
81	Biglycan	0.23433769	0.01999849
82	Pentraxin-related protein PTX3	0.23231754	0.01873412
83	Proteasome subunit beta type-6	0.21537933	0.00799348
84	Coagulation factor X	0.21443	0.00786606
85	Fibrinogen gamma-B chain	0.21381294	0.01498686
86	14-3-3 protein gamma	0.21211601	0.04535231
87	14-3-3 protein beta/alpha	0.20908578	0.03927625
88	Fibrinogen beta chain	0.20811382	0.00598993
89	Tropomyosin beta chain	0.20568825	0.02908871
90	Endoplasmin	0.20381582	0.01710507
91	14-3-3 protein epsilon	0.19895019	0.00827524
92	Complement component C9	0.19432564	0.03440331
93	Nucleobindin-1	0.19283274	0.01573213

94	Proteasome subunit alpha type-3	0.18484395	0.02386004
95	Osteomodulin	0.18354528	0.00489759
96	Pigment epithelium-derived factor	0.17707076	0.0090361
97	Cartilage oligomeric matrix protein	0.17279695	0.00387154
98	Appetite-regulating hormone	0.16969281	0.04884095
99	Complement C1q subcomponent subunit B	0.16969281	0.03230525
100	Vitamin K-dependent protein Z	0.16574646	0.02691048
101	Coagulation factor V	0.16424083	0.00915593
102	Nucleosome assembly protein 1-like 4	0.15812284	0.00272707
103	Proteasome subunit beta type-4	0.15798986	0.02866626
104	Neural cell adhesion molecule 1	0.15705611	0.01547673
105	Alpha-1B-glycoprotein	0.15555174	0.02142872
106	Serpin A3-7	0.15525087	0.005106
107	Fibronectin	0.15378411	0.00361091
108	Factor XIIa inhibitor	0.15337619	0.01615263
109	Haptoglobin	0.15272353	0.02013137
110	Complement factor B	0.15072714	0.02050552
111	Protein HP-20 homolog	0.14949128	0.02060159
112	Keratin, type II cytoskeletal 5	0.14814452	0.03618774
113	Proteasome subunit beta type-7	0.1470671	0.0039997
114	Transthyretin	0.14317831	0.03436672
115	Proteasome subunit beta type-8	0.14141067	0.01442112
116	Decorin	0.13999657	0.01374669
117	Histone H4	0.13883957	0.01889367
118	Tubulin beta-2B chain	0.13745118	0.09739244
119	Coagulation factor IX (Fragment)	0.13719844	0.005106
120	Thrombospondin-1	0.13444892	0.00788618
121	ADP-ribosylation factor 4	0.13333006	0.03568301
122	Elongation factor 1-alpha 1	0.13236039	0.00415661
123	Calmodulin	0.12976509	0.01411658
124	Coagulation factor XIII A chain (Fragment)	0.12911409	0.03651898
125	Tubulin alpha-1C chain	0.12896653	0.09157125
126	Keratin, type I cytoskeletal 10	0.12187029	0.01745323
127	Corticosteroid-binding globulin	0.12067044	0.0070548
128	Transforming protein RhoA	0.1195563	0.04363307
129	Vitamin K-dependent protein C (Fragment)	0.1181195	0.01882211
130	Hyaluronan and proteoglycan link protein 1	0.11666381	0.01199909
131	Adenosylhomocysteinase	0.11489617	0.01802639
132	CMP-N-acetylneuraminate-poly-alpha-2,8-sialyltransferase	0.11174892	0.0134114
133	Retinol-binding protein 4	0.10908823	0.02618417
134	Insulin-like growth factor-binding protein 2	0.10730575	0.00933724
135	Insulin-like growth factor-binding protein 6	0.10520954	0.00479964
136	60S acidic ribosomal protein P0	0.10481026	0.01058744
137	Complement C1q subcomponent subunit A	0.10442634	0.02569543
138	Peroxiredoxin-2	0.10412968	0.02834051
139	Gamma-glutamyl hydrolase	0.10134432	0.0088185
140	Follistatin-related protein 1	0.09696732	0.01814092

141	Small glutamine-rich tetratricopeptide	0.09482833	0.01964945
142	Suprabasin	0.09228907	0.00917594
143	Calreticulin	0.09191694	0.01249906
144	Aggrecan core protein	0.09036487	0.00562522
145	Cysteine and glycine-rich protein 1	0.08888671	0.01511744
146	Argininosuccinate synthase	0.08853538	0.01355416
147	Complement C1s subcomponent	0.08705021	0.00412294
148	Thyroxine-binding globulin	0.08669089	0.005217
149	ADP-ribosylation factor 1	0.0848464	0.0692768
150	Galactokinase	0.08282625	0.00285693
151	Ubiquitin-like modifier-activating enzyme 1	0.08268929	0.00970034
152	Myocilin	0.08176108	0.00577211
153	Keratin, type I cytoskeletal 17	0.08138329	0.01489544
154	Sulfotransferase 1A1	0.07985544	0.01538319
155	Adiponectin	0.07831976	0.00799348
156	Heat shock protein beta-1	0.07713309	0.00545413
157	Vitamin K-dependent protein S	0.07692741	0.00973168
158	Integrin-linked protein kinase	0.07652813	0.02317203
159	Conglutinin	0.0759152	0.00835437
160	Prostaglandin E synthase 3	0.0759152	0.00631531
161	Vimentin	0.07541903	0.00769742
162	26S protease regulatory subunit 7	0.07272549	0.01529272
163	Complement factor H	0.07211944	0.01347004
164	Adenine phosphoribosyltransferase	0.07211944	0.01587331
165	Thrombospondin-4	0.07123896	0.00113199
166	60S acidic ribosomal protein P1	0.07070534	0.05291103
167	Tubulin alpha-1D chain	0.06957405	0.09839257
168	Regucalcin	0.06941979	0.01889367
169	Selenoprotein P	0.06599165	0.01162285
170	CD44 antigen	0.06575596	0.00299977
171	Elongation factor 1-delta	0.06568754	0.01773766
172	Ras-related protein Rab-1B	0.06556313	0.00545413
173	Calpain small subunit 1	0.0636348	0
174	Carboxypeptidase B2	0.06233613	0.00734638
175	Acylamino-acid-releasing enzyme	0.06075422	0.00740685
176	Collectin-43	0.05989158	0.01222532
177	Histidine-rich glycoprotein (Fragments)	0.05977815	0.00721514
178	Plasma serine protease inhibitor	0.05844975	0.00961408
179	CD9 antigen	0.05769555	0.01730534
180	Complement component C7	0.0574766	0.00223474
181	Serpin A3-4	0.0571791	0.0026085
182	26S protease regulatory subunit 8	0.05349012	0.00690144
183	L-lactate dehydrogenase B chain	0.05274236	0.006486
184	26S proteasome non-ATPase regulatory subunit 2	0.04836245	0.00549868
185	Dynactin subunit 2	0.04820818	0.00721514
186	Heat shock cognate 71 kDa protein	0.04660577	0.00585438
187	Heat shock 70 kDa protein 1A	0.04484739	0.00342831
188	Phosphatidylinositol-glycan-specific phospholipase D	0.04470402	0.00341361

189	Myosin-10	0.044461	0.00240117
190	Prolargin	0.0424232	0.022322
191	Apolipoprotein C-IV	0.0424232	0.05999547
192	Ferritin light chain	0.0424232	0.02399819
193	Alpha-actinin-1	0.04118757	0.00708618
194	Neurexin-1	0.04040305	0.0051504
195	Oncoprotein-induced transcript 3 protein	0.04033682	0.00786826
196	General vesicular transport factor p115	0.03928074	0.00777719
197	Mannose-binding protein C	0.03915988	0
198	Keratin, type II cytoskeletal 75	0.03882802	0.02883331
199	Ferritin heavy chain	0.03636274	0.03568301
200	T-complex protein 1 subunit gamma	0.03616404	0.00786826
201	Prosaposin	0.03510886	0.00620643
202	Versican core protein	0.03462651	0.00116928
203	Protein disulfide-isomerase	0.03423627	0.00759006
204	Glucosidase 2 subunit beta	0.03393856	0.00692768
205	Glutathione peroxidase 3	0.03263323	0.02442048
206	WD repeat-containing protein 1	0.03213879	0.01192171
207	cAMP-dependent protein kinase type II-alpha regulatory subunit	0.03205309	0.00961408
208	Angiotensin-converting enzyme 2	0.03193144	0.00682723
209	GTP-binding nuclear protein Ran	0.0318174	0.01499887
210	Dermatopontin	0.0318174	0.02291115
211	Prenylcysteine oxidase-like	0.03142459	0.005879
212	Junction plakoglobin	0.03104137	0.0110477
213	Elongation factor 1-gamma	0.03054471	0.00831322
214	Elongation factor 2	0.03036608	0.00550556
215	Cation-independent mannose-6-phosphate receptor	0.02992764	0.00157321
216	78 kDa glucose-regulated protein	0.02946056	0.0088185
217	BOLA class I histocompatibility antigen, alpha chain BL3-7	0.02828213	0.00285693
218	Thioredoxin	0.02828213	0.01999849
219	Matrix Gla protein	0.02828213	0.03999698
220	Primary amine oxidase, liver isozyme	0.02595302	0.00615327
221	Complement component C6	0.02585795	0.00412032
222	Peroxisomal biogenesis factor 19	0.02571103	0.00727218
223	Clathrin heavy chain 1	0.02563068	0.00062495
224	Chloride intracellular channel protein 1	0.02513968	0.02351601
225	Sphingomyelin phosphodiesterase	0.02459316	0.01516024
226	Beta-2-microglobulin	0.02424183	0.01714156
227	ATP-dependent 6-phosphofructokinase, liver type	0.02395663	0.00423497
228	Pantetheinase	0.02381653	0.00556958
229	Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A	0.0221906	0.0048841
230	Olfactomedin-like protein 3	0.02213384	0.01807221
231	Asporin	0.02020152	0.00571385
232	CD81 antigen	0.01957994	0
233	Keratin, type II cytoskeletal 79	0.0190173	0.01615792
234	Annexin A5	0.01885476	0.00666616
235	26S protease regulatory subunit 10B	0.01735495	0.0081812
236	Regakine-1	0.01696928	0.02399819

237	Elongation factor 1-beta	0.01696928	0.02399819
238	Neuroendocrine secretory protein 55	0.0157123	0.01175801
239	Microfibril-associated glycoprotein 4	0.01462869	0.01094711
240	Serpin H1	0.01444194	0.005106
241	Ras-related protein Rab-11B	0.01414107	0.01999849
242	Collagen alpha-1(I) chain	0.01403933	0.01217756
243	Platelet-activating factor acetylhydrolase	0.01357542	0.01269865
244	BOLA class I histocompatibility antigen, alpha chain BL3-6	0.01272696	0.01039152
245	Proteasome subunit beta type-10	0.01170295	0.00827524
246	Leukocyte cell-derived chemotaxin 1	0.01146573	0.01621499
247	Galectin-1	0.01131285	0.01599879
248	Eukaryotic initiation factor 4A-I	0.01106692	0.0090361
249	LIM and senescent cell antigen-like-containing domain protein 2	0.01087774	0.00814016
250	Calpain-2 catalytic subunit	0.0106058	0.00299977
251	Ras-related protein Rab-8A	0.0106058	0.01499887
252	Alpha-actinin-4	0.00969673	0.01371325
253	Methylosome protein 50	0.00917258	0.006486
254	Myosin regulatory light chain 12B	0.00848464	0.01199909
255	Insulin-like growth factor II	0.00848464	0.01199909
256	Alcohol dehydrogenase class-3	0.00848464	0.00599955
257	Desmoglein-1	0.00833313	0.00876936
258	Transportin-1	0.00831827	0.00117638
259	UDP-glucose 6-dehydrogenase	0.00771331	0.00577211
260	Tetranectin	0.00771331	0.01090827
261	26S proteasome non-ATPase regulatory subunit 5	0.00757557	0.01071348
262	Alpha-enolase	0.00722097	0.005106
263	Drebrin-like protein	0.00707053	0.00499962
264	Coagulation factor VII	0.00692624	0.00489759
265	Coagulation factor XI	0.00606046	0.00453523
266	Transitional endoplasmic reticulum ATPase	0.00571998	0
267	Mimecan	0.00499096	0.00705829
268	SPARC	0.00484837	0.00685662
269	Glycogen phosphorylase, liver form	0.00437353	0.00327285
270	Lysyl oxidase homolog 4	0.0040403	0.00285693
271	Membrane primary amine oxidase	0.00399277	0.00564663
272	Cytoplasmic dynein 1 intermediate chain 2	0.00374322	0.00529372
273	26S protease regulatory subunit 6B	0.00361049	0.005106
274	Glycogen phosphorylase, brain form	0.00353527	0.00499962
275	Coronin-1A	0.00332731	0.00470553
276	Lipopolysaccharide-binding protein	0.00314246	0.00444411
277	Collagen alpha-2(XI) chain	0.00295976	0.00241663
278	Glypican-1	0.00278185	0.00393413
279	Fatty acid synthase	0.00277679	0.00199952
280	Collagen alpha-2(I) chain	0.0026309	0.00186032
281	CD97 antigen	0.00212116	0.00299977
282	Hepatocyte growth factor-like protein	0.00212116	0.00299977

283	Integrin beta-1	0.00192833	0.00272707
284	von Willebrand factor (Fragment)	0.0016475	0.00232992
285	Myosin light chain kinase, smooth muscle	0.00131545	0.00186032
286	Cullin-associated NEDD8-dissociated protein 1	0.00124774	0.00176457

Table S4. List of the unique proteins bound to MC liposomes following 90 min incubation with fetal bovine serum under dynamic and static incubation.

DYNAMIC				STATIC			
#	Identified Proteins	RPA (%)	St. Dev. (%)	#	Identified Proteins	RPA (%)	St. Dev. (%)
1	Alpha-S1-casein	0.18	0.02	1	Tropomyosin alpha-3 chain	0.32	0.01
2	Adenylyl cyclase-associated protein 1	0.15	0.09	2	Prothymosin alpha	0.30	0.03
3	Resistin	0.14	0.08	3	Tropomyosin beta chain	0.21	0.03
4	Serum amyloid A-4 protein	0.10	0.07	4	Tubulin beta-2B chain	0.14	0.09
5	Cofilin-1	0.09	0.02	5	Complement C1q subcomponent subunit A	0.10	0.03
6	Monocyte differentiation antigen CD14	0.07	0.05	6	Complement C1s subcomponent	0.087	0.004
7	Phosphoglycerate kinase 1	0.06	0.08	7	Vimentin	0.075	0.008
8	GTP-binding protein SAR1a	0.05	0.04	8	Adenine phosphoribosyltransferase	0.07	0.02
9	Microtubule-associated protein RP/EB family member 1	0.04	0.06	9	Collectin-43	0.06	0.01
10	Estrogen sulfotransferase	0.04	0.06	10	Serpin A3-4	0.057	0.003
11	Fermitin family homolog 3	0.035	0.008	11	Ferritin light chain	0.04	0.02
12	Transgelin-2	0.034	0.007	12	Ferritin heavy chain	0.04	0.04
13	Exportin-2	0.032	0.009	13	Protein disulfide-isomerase	0.034	0.008
14	Microfibrillar-associated protein 5	0.03	0.02	14	Glucosidase 2 subunit beta	0.034	0.007
15	Serum amyloid A protein	0.025	0.009	15	Dermatopontin	0.03	0.02
16	LIM and SH3 domain protein 1	0.025	0.009	16	Elongation factor 1-gamma	0.031	0.008
17	Actin, alpha cardiac muscle 1	0.024	0.008	17	78 kDa glucose-regulated protein	0.029	0.009
18	F-actin-capping protein subunit alpha-1	0.02	0.02	18	Complement component C6	0.026	0.004
19	Proteasome activator complex subunit 1	0.019	0.009	19	Olfactomedin-like protein 3	0.02	0.02
20	Keratin, type II cuticular Hb1	0.017	0.009	20	CD81 antigen	0.02	0.00
21	Protein S100-A1	0.02	0.02	21	Regakine-1	0.02	0.02
22	Metalloproteinase inhibitor 3	0.02	0.01	22	Elongation factor 1-beta	0.02	0.02
23	ATPase inhibitor, mitochondrial	0.02	0.02	23	Neuroendocrine secretory protein 55	0.02	0.01
24	D-3-phosphoglycerate dehydrogenase	0.01	0.01	24	Microfibril-associated glycoprotein 4	0.01	0.01
25	Cathelicidin-4	0.01	0.01	25	Collagen alpha-1(I) chain	0.01	0.01
26	Beta-casein	0.01	0.01	26	BOLA class I histocompatibility antigen, alpha chain BL3-6	0.01	0.01
27	Keratin, type II cytoskeletal 7	0.01	0.01	27	Proteasome subunit beta type-10	0.012	0.008
28	Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-2	0.010	0.007	28	Galectin-1	0.01	0.02
29	L-lactate dehydrogenase A chain	0.01	0.01	29	LIM and senescent cell antigen-like-containing domain protein 2	0.011	0.008
30	Pulmonary surfactant-associated protein B	0.01	0.01	30	Ras-related protein Rab-8A	0.01	0.01
31	Ras-related C3 botulinum toxin substrate 1	0.01	0.01	31	Methylosome protein 50	0.009	0.006
32	Flotillin-1	0.01	0.01	32	Insulin-like growth factor II	0.01	0.01
33	High mobility group protein B1	0.007	0.004	33	UDP-glucose 6-dehydrogenase	0.008	0.006
34	Dentin matrix acidic phosphoprotein 1	0.007	0.005	34	Tetranectin	0.01	0.01
35	Golgi phosphoprotein 3-like	0.006	0.008	35	Drebrin-like protein	0.007	0.005
36	Coagulation factor XII	0.004	0.005	36	Coagulation factor XI	0.006	0.005
37	DnaJ homolog subfamily A member 2	0.004	0.006	37	Mimecan	0.005	0.007
38	Flotillin-2	0.004	0.006	38	SPARC	0.005	0.007
39	cGMP-specific 3',5'-cyclic phosphodiesterase	0.004	0.005	39	Membrane primary amine oxidase	0.004	0.006
40	Solute carrier family 2, facilitated glucose transporter member 3	0.003	0.005	40	Glycogen phosphorylase, brain form	0.004	0.005
41	Calpain-1 catalytic subunit	0.003	0.005	41	Coronin-1A	0.003	0.005
42	T-complex protein 1 subunit beta	0.003	0.005	42	Collagen alpha-2(XI) chain	0.003	0.002
43	T-complex protein 1 subunit zeta	0.003	0.004	43	Glypican-1	0.003	0.004
44	T-complex protein 1 subunit alpha	0.003	0.004	44	Myosin light chain kinase, smooth muscle	0.001	0.002
45	Catalase	0.003	0.004				
46	P-selectin	0.003	0.004				
47	Dynamin-1-like protein	0.002	0.003				
48	AP-1 complex subunit beta-1	0.002	0.002				