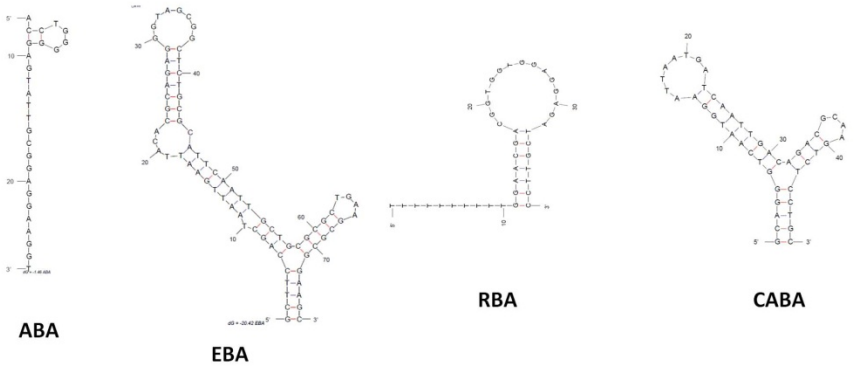

Figure S1. Mfold predicted structures of DNA aptamers used in this study. Notice that mfold did not predict the experimentally observed structures for ABA (pseudohelix) and RBA (G-quartet). Structures were folded at 25 °C, 5 mM NaCl, 1 mM $MgCl_2$, to mimic our experimental conditions.

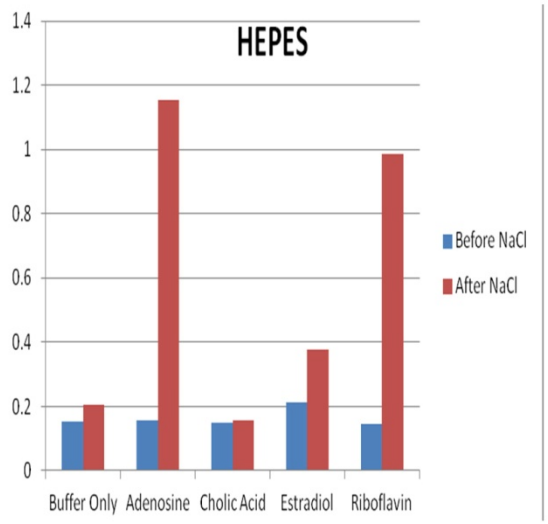

Figure S2. Citrate-stabilized AuNPs aggregation in the presence of different analytes. AuNPs were suspended in 10 mM HEPES, 1 mM $MgCl_2$, pH 7.4 (HEPES buffer). AuNPs aggregation degree before (blue bars) and after (red bars) NaCl addition a mixture of 90 µL AuNPs in HEPES buffer and 10 µL of 180 µM different analytes dissolved in HEPES buffer.

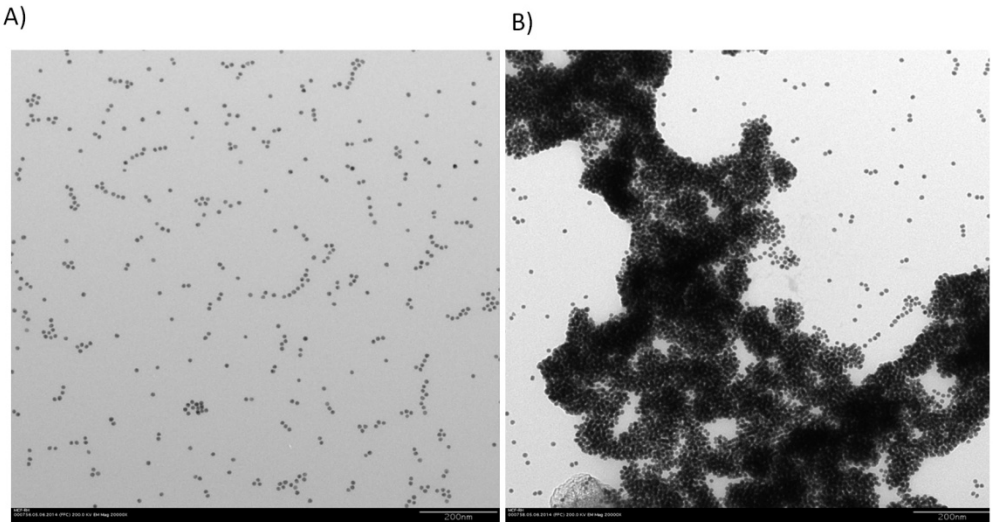

Figure S3. TEM images of ABA-AuNPs. Images showed the aggregation of ABA-AuNPs exposed to A): buffer and B) adenosine (20 μM), after addition of NaCl.

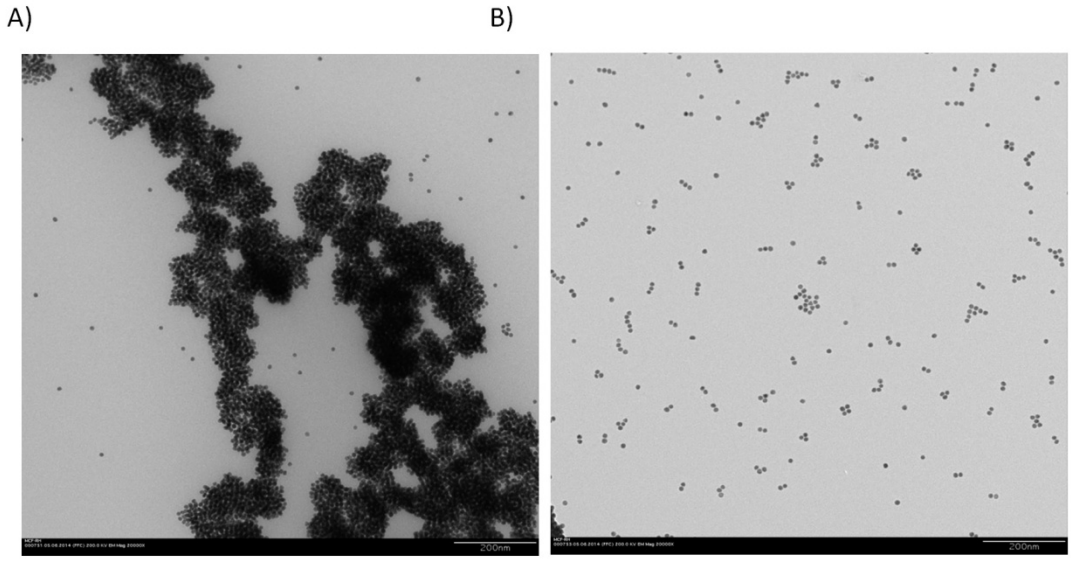

Figure S4. TEM images of CABA-AuNPs. Images showed the aggregation of CABA-AuNPs exposed to A): buffer and B) cholic acid (50 μM), after addition of NaCl.

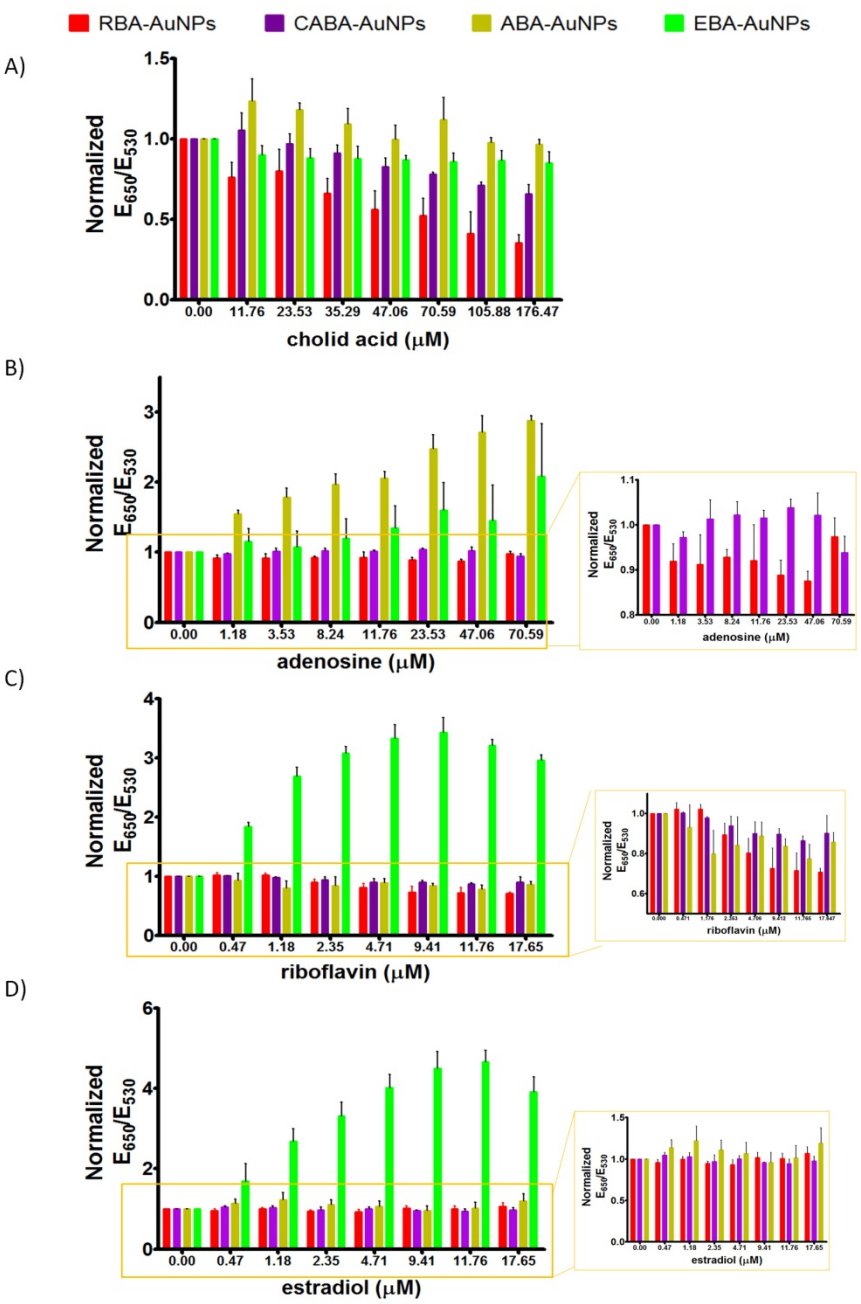

Figure S5. Fingerprint data analysis. The responses from the four Apt-AuNPs designed in this work were combined to obtain a fingerprint per analyte studied. Insets show the "stabilization effect" that allowed a more efficient analyte differentiation.

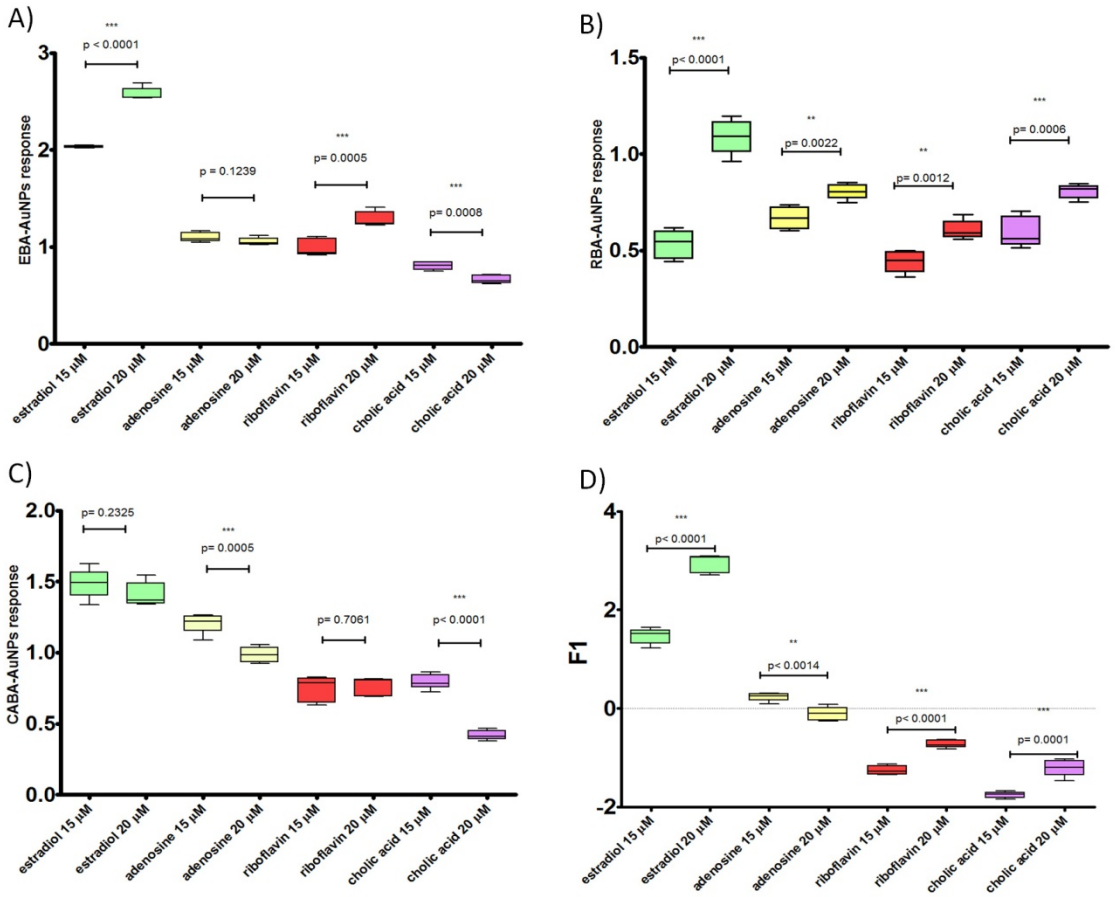

Figure S6. T-test analysis. The Apt- AuNPs response was further analyzed to determine the statistical differences of the output obtained with the analytes at different concentrations. The results are presented in Figure S6. Each plot shows the results of one Apt-AuNP exposed to each analyte at two different concentrations. These two values were analyzed using the t-test. It was observed that, in most cases, a statistically different response was obtained. Analysis of the output per Apt-AuNPs has limited practical relevance since it was established in this work that the combined response of the sensors provides a superior means for analyte identification and quantification. Therefore the PCA output was analyzed in a similar manner, comparing the first principal component of each sensor. Figure S6 D shows that in all cases the responses observed with different concentrations of the same target were significantly different, confirming the superior analytical performance when the Apt-AuNPs were used as cross-reactive sensors.

Table S1

CABA-AuNPs	peak 1			peak 2				
	size	**%**	**SD**	**size**	**%**	**SD**	**Zav**	**PDI**
blank no salt	15.76	93	5.95	368	6.8	120	16.74	0.191
blank + 300 mM NaCl	251.7	87.1	66.72	82.59	12.9	125.5	181	0.244
50 uM CA+ 300 mM NaCl	101.8	73.11	61.6	16.98	26.9	13.31	47.69	0.512

EBA-AuNPs	peak 1			peak 2			peak 3				
	size	**%**	**SD**	**size**	**%**	**SD**	**size**	**%**	**SD**	**Zav**	**PDI**
blank no salt	18.63	94.1	6.02	4.94	2.6	0.54	4152	3.3	1024	16.75	0.192
blank + 172 mM NaCl	88.66	50.3	28.27	16.57	41.3	3.24	1490	8.4	612.5	32.84	0.479
5 uM Est+ 172 mM NaCl	87.97	77.5	21.19	17.75	22.5	2.172				50.94	0.444

Apt-AuNP Size Analysis by Dynamic Light Scattering.

Apt-AuNPs were prepared as described in the experimental section. Samples were analyzed in a Zetasizer Nano Istrument (Malvern Instruments, Westborough, MA) utilized in backscatter mode (173 ° detection angle) with the temperature set at 20.0 °C. Apt-AuNPs (75 µL) were mixed with 10 µL of assay buffer (blank) or the analyte of interest in assay buffer and incubated for one minute. This was followed by NaCl addition (exact concentrations are listed on Table S1), and after another one-minute incubation, the size was determined by DLS.

Table S2. Data utilized for PCA analysis

	ABA	EBA	RBA	CABA
buffer 1	0.265957	0.239474	0.275401	0.501433
buffer 2	0.270053	0.248	0.268617	0.52149
buffer 3	0.281501	0.257979	0.308108	0.480114
buffer 4	0.284211	0.255937	0.272727	0.52071
buffer 5	0.265416	0.248021	0.259259	0.530259
estradiol 1	0.579387	0.667638	0.298343	0.74772
estradiol 2	0.574586	0.663768	0.312668	0.737805
estradiol 3	0.589385	0.649718	0.321716	0.742424
estradiol 4	0.555241	0.637883	0.296	0.697605
estradiol 5	0.571429	0.628571	0.290667	0.725076
adenosine 1	0.289817	0.267532	0.241558	0.511364
adenosine 2	0.299479	0.260982	0.221932	0.461957
adenosine 3	0.291777	0.264935	0.228792	0.495798
adenosine 4	0.263708	0.239401	0.23057	0.480226
adenosine 5	0.278947	0.253071	0.226221	0.5
riboflavin 1	0.219321	0.315508	0.155844	0.404372
riboflavin 2	0.220472	0.307278	0.158442	0.382514
riboflavin 3	0.218182	0.320955	0.159794	0.389503
riboflavin 4	0.223377	0.31383	0.158031	0.359673
riboflavin 5	0.227513	0.324397	0.159269	0.365854
cholic acid 1	0.186667	0.176966	0.232	0.2
cholic acid 2	0.189474	0.160105	0.233244	0.228495
cholic acid 3	0.187831	0.16	0.213542	0.223404
cholic acid 4	0.18617	0.163102	0.231608	0.213333
cholic acid 5	0.195187	0.16129	0.224	0.2

Table S3. Results of PCA analysis of the data of the four sensors (data shown in Table S1).

Observation	F1	F2	F3	F4
buffer 1	0.262	2.867	-0.323	-0.071
buffer 2	0.074	2.691	-0.363	-0.252
buffer 3	-0.228	1.789	-0.359	-0.039
buffer 4	-0.091	1.933	-0.419	-0.059
buffer 5	-0.172	2.103	-0.412	-0.160
15estradiol 1	0.945	-0.928	-1.196	-0.231
15estradiol 2	1.152	-0.682	-1.299	-0.007
15estradiol 3	1.173	-0.914	-1.244	0.165
15estradiol 4	1.334	-0.855	-1.277	-0.047
15estradiol 5	1.043	-0.659	-1.331	-0.353
20estradiol 1	4.087	-0.252	0.610	-0.204
20estradiol 2	4.066	-0.047	0.583	-0.257
20estradiol 3	4.137	0.078	0.722	-0.244
20estradiol 4	3.670	-0.183	0.605	-0.310
20estradiol 5	3.800	-0.267	0.737	-0.169
15adenosine 1	-0.089	0.306	-0.497	0.253
15adenosine 2	-0.088	0.428	-0.450	0.432
15adenosine 3	-0.248	0.271	-0.341	0.536
15adenosine 4	-0.050	0.182	-0.424	0.624
15adenosine 5	-0.087	0.544	-0.379	0.326
20adenosine 1	0.263	0.107	0.542	0.659
20adenosine 2	0.018	-0.128	0.683	0.423
20adenosine 3	0.155	-0.051	0.589	0.601
20adenosine 4	-0.114	0.053	0.517	0.670
20adenosine 5	0.063	-0.053	0.554	0.700
15riboflavin 1	-1.312	-0.905	-0.083	-0.551
15riboflavin 2	-1.447	-0.875	-0.141	-0.510
15riboflavin 3	-1.340	-0.753	-0.052	-0.020
15riboflavin 4	-1.320	-0.956	0.133	-0.270
15riboflavin 5	-1.275	-0.807	-0.109	-0.094
20riboflavin 1	-0.631	-0.980	0.058	0.278
20riboflavin 2	-0.730	-0.923	0.108	0.179
20riboflavin 3	-0.661	-0.930	0.033	0.178
20riboflavin 4	-0.786	-0.933	0.115	0.030
20riboflavin 5	-0.702	-0.942	0.095	0.016
15cholic acid 1	-1.775	0.389	0.434	-0.428
15cholic acid 2	-1.703	0.418	0.501	-0.233
15cholic acid 3	-1.804	0.163	0.517	-0.221
15cholic acid 4	-1.773	0.402	0.479	-0.312

15cholic acid 5	-1.819	0.301	0.561	-0.388
20cholic acid 1	-1.282	-0.158	0.247	-0.100
20cholic acid 2	-1.023	-0.211	0.288	0.018
20cholic acid 3	-1.274	-0.298	0.188	-0.008
20cholic acid 4	-1.336	-0.237	0.497	-0.402
20cholic acid 5	-1.081	-0.102	0.300	-0.149

Table S4. Results of PCA analysis of the data of the three sensors (without sensor ABA-AuNPs, data shown in Table S1).

	F1	F2	F3
buffer 1	0.581	19.388	0.788
buffer 2	0.312	17.148	2.579
buffer 3	0.044	7.433	0.631
buffer 4	0.143	8.592	0.907
buffer 5	0.093	10.313	1.755
15estradiol 1	1.697	3.276	5.957
15estradiol 2	2.612	2.189	3.165
15estradiol 3	2.589	3.400	1.119
15estradiol 4	3.018	3.069	3.485
15estradiol 5	2.170	2.013	9.554
20estradiol 1	10.564	0.199	0.237
20estradiol 2	10.640	0.016	0.059
20estradiol 3	10.700	0.011	0.237
20estradiol 4	8.234	0.094	0.003
20estradiol 5	8.601	0.178	0.605
15adenosine 1	0.073	0.111	0.029
15adenosine 2	0.088	0.273	0.774
15adenosine 3	0.009	0.094	2.000
15adenosine 4	0.103	0.016	2.668
15adenosine 5	0.065	0.537	0.348
20adenosine 1	0.008	0.061	10.202
20adenosine 2	0.077	0.003	6.445
20adenosine 3	0.004	0.000	9.319
20adenosine 4	0.056	0.031	10.050
20adenosine 5	0.011	0.000	11.237
15riboflavin 1	1.821	1.756	4.704
15riboflavin 2	2.039	1.664	4.465
15riboflavin 3	1.610	1.251	0.043
15riboflavin 4	2.022	1.875	0.692
15riboflavin 5	1.444	1.478	0.301

20riboflavin 1	0.444	2.276	1.223
20riboflavin 2	0.629	1.939	0.654
20riboflavin 3	0.481	2.035	0.491
20riboflavin 4	0.768	1.934	0.074
20riboflavin 5	0.631	2.000	0.040
15cholic acid 1	3.387	0.736	1.184
15cholic acid 2	3.134	0.816	0.078
15cholic acid 3	3.607	0.262	0.042
15cholic acid 4	3.380	0.777	0.362
15cholic acid 5	3.804	0.569	0.574
20cholic acid 1	1.720	0.010	0.009
20cholic acid 2	1.181	0.039	0.173
20cholic acid 3	1.622	0.120	0.025
20cholic acid 4	2.431	0.018	0.681
20cholic acid 5	1.351	0.000	0.034