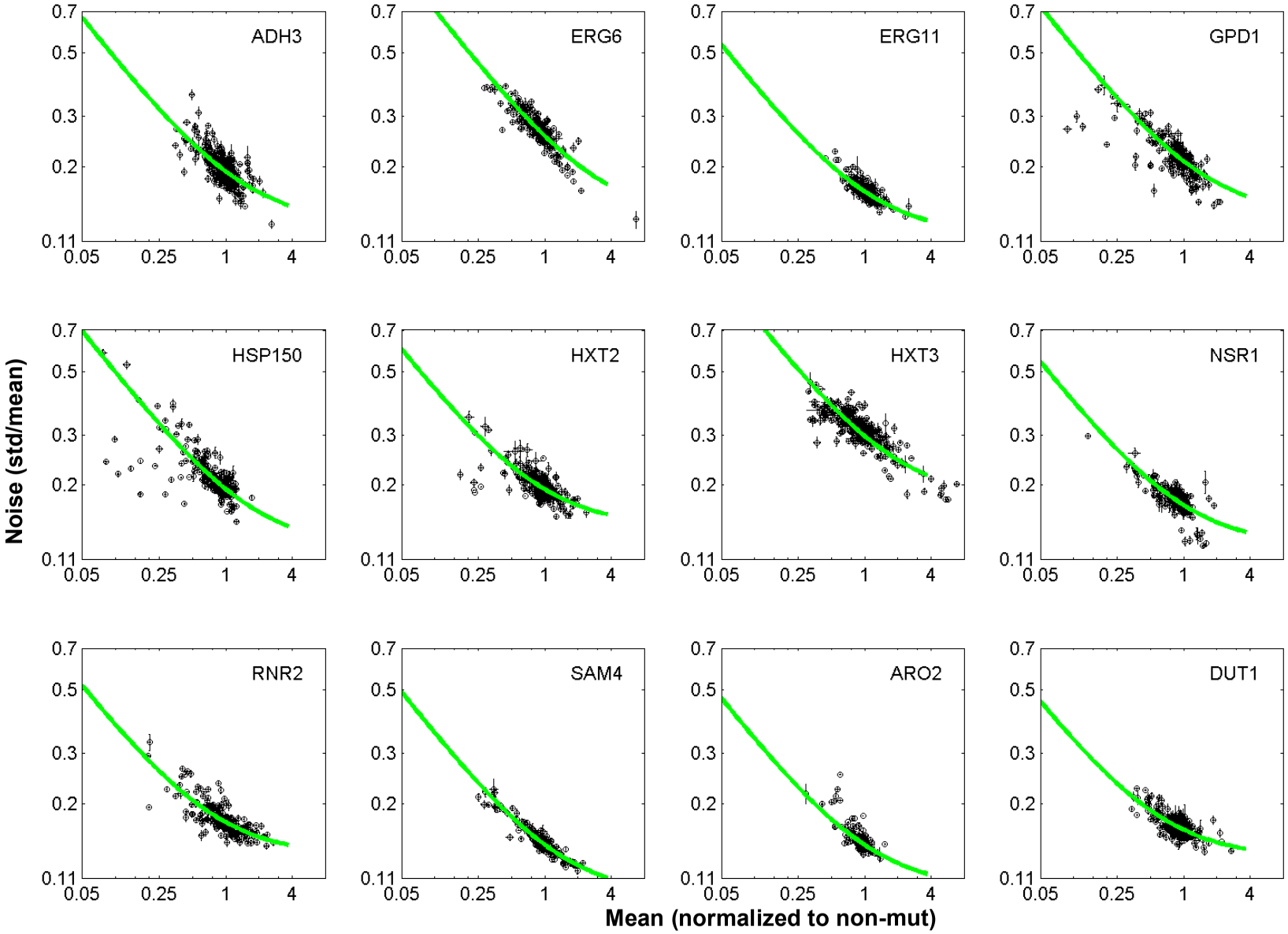

Figure S1 – Noise vs. mean for all promoter libraries
Each dot is the noise and mean values for all clones generated by mutagenesis of a promoter (name of each promoter is given in each figure), The thick gray line is a fit to the scaling law $\eta^2=b/m+\eta_{ext}^2$ (Methods). Error bars denote standard error between measurements. Data is provided as supplementary files.
Figure continues on next page.

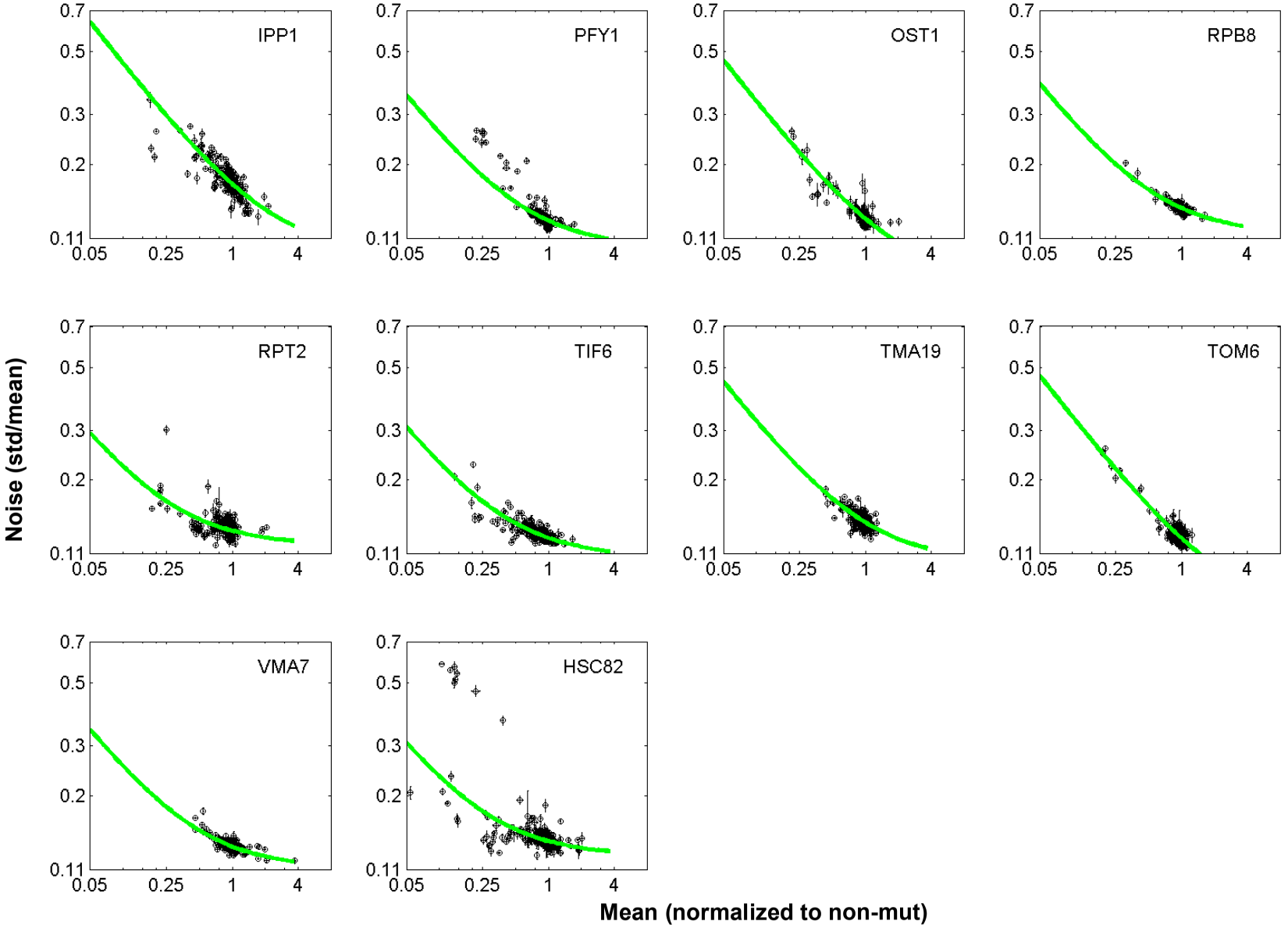

Figure S1 – Noise vs. mean for all promoter libraries
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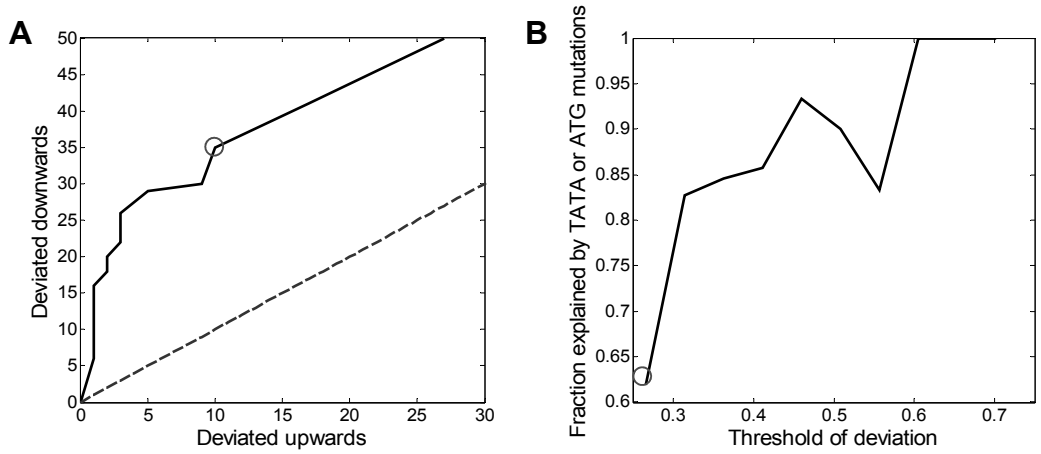

Figure S2 – Mutants that deviated from the noise-mean scaling
(A) - Total number of mutant colonies that deviated downwards (lower burst size) versus the number that deviated upwards (higher burst size) in all 21 promoters (excluding HSC82). The deviation was calculated as the log ratio between the actual noise level and the predicted noise level based on a fitted curve (Methods). Dashed gray line is the y=x line that is expected if there is no bias between upwards and downwards.
(B) – The fraction of colonies that deviated from the scaling, and that can be explained by a mutation in a TATA box or a generation of an out-of-frame ATG. The fraction is plotted against the threshold for defining deviation.
The circle is the data point detailed in Table I of the main text.

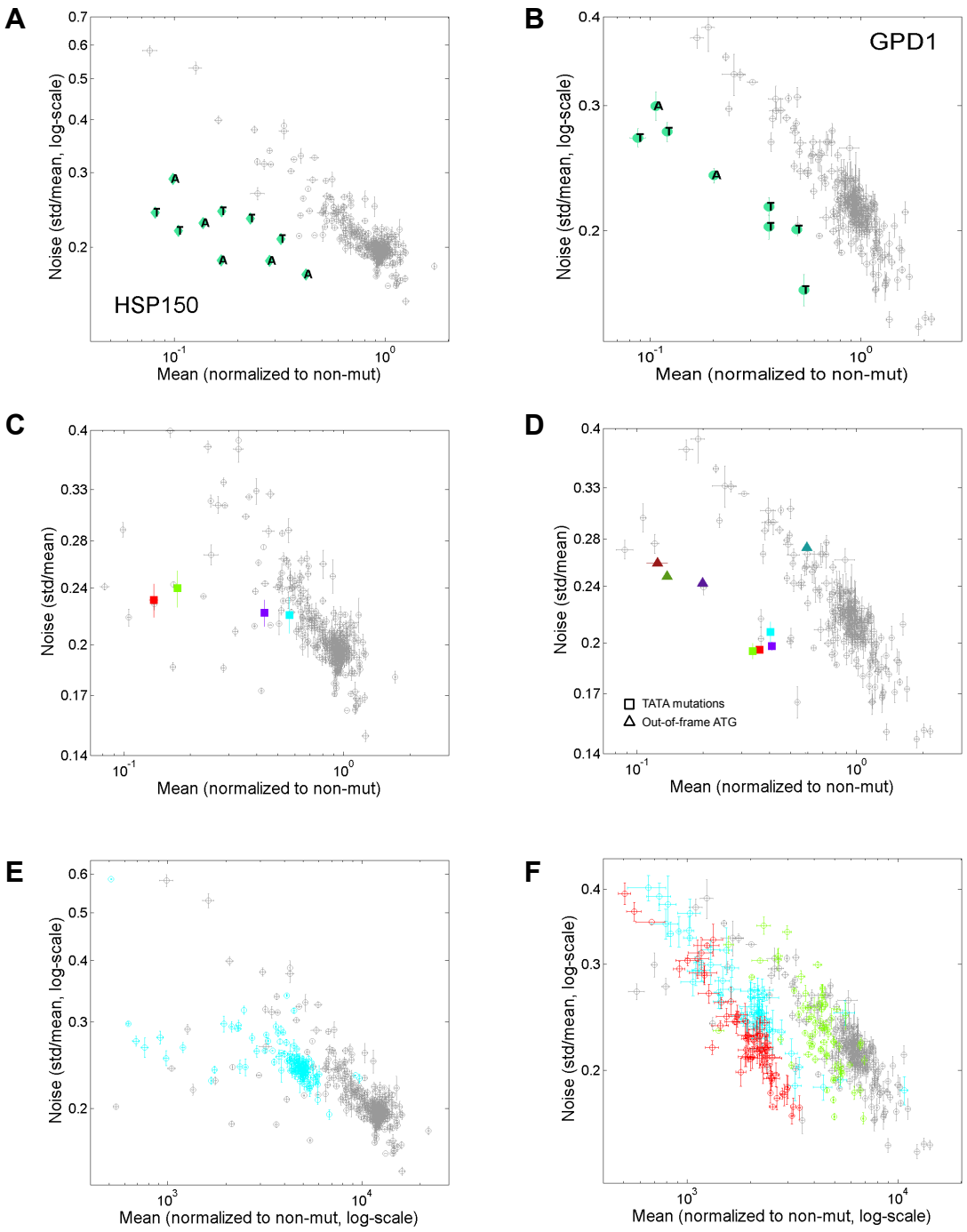

Figure S3 – Mutants that break the noise-mean scaling
(A-B) Noise vs. mean for the HSP150 and GPD1 promoter mutants,respectively, is shown in gray. Colonies that deviate from the noise-mean scaling are shown in green and labeled in T if their sequencing showed a mutation in the TATA, and A if they generated an upstream out-of-frame translation start site. (C-D) Squares: Specific promoter mutations of HSP150 and GPD1, respectively, that were designed in the TATA box (red `TATgAAAA` green `TATAgAAA` cyan `TATAAAcA` purple `TacAAAAA`). Triangles: generation of an out-of-frame ATG in different positions (triangles; red -13, green -23, blue -34, purple -43). (E-F) Some of the TATA mutants of HSP150 and GPD1, respectively, were subjected to further random mutagenesis and the resulting mean and noise of the clones are shown. Colors correspond to (C and D). Error bars are standard error of three biological repeats.

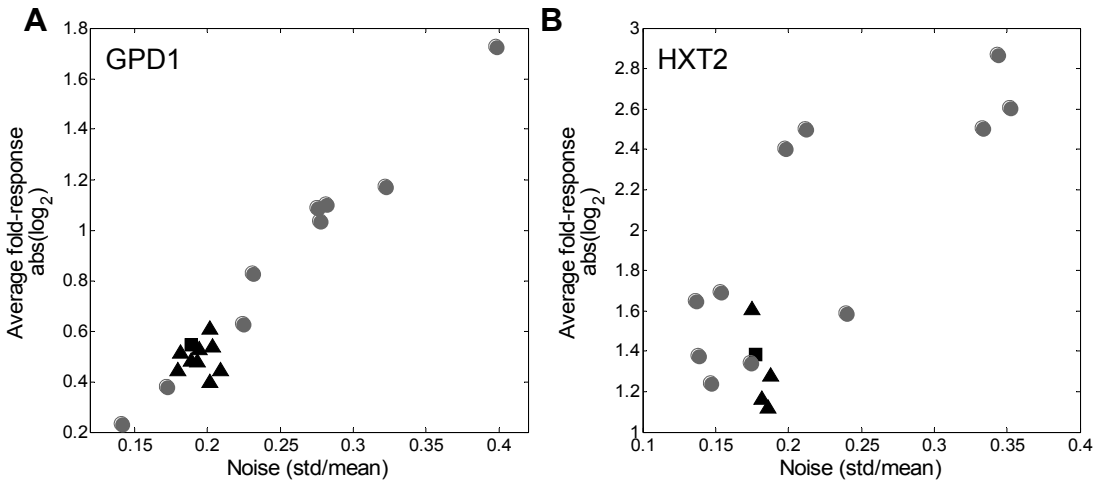

Figure S4 – Correlation between noise and responsiveness
(A-B) – The average fold-response over all conditions ("responsiveness") is plotted against the noise level of promoter mutants of GPD1 and HXT2 (A and B, respectively). Black triangles represent TATA mutants, grey circles represent control mutations and the black square is the original promoter.