Supplementary Material

Degree	No. of H(X ₁)	No. of $H(X_1, X_2)$	<i>No. of</i> H(X ₁ , X ₂ , X ₃)	No. of $H(X_1,,X_4)$	No. of $H(X_1,,X_5)$	No. of $H(X_1,,X_6)$
2 (<i>MI</i>)	2	1				
$3(\bar{\Delta}_3)$	1	2	1			
$4 (\overline{\Delta}_4)$	1	3	3	1		
$5(\bar{\Delta}_5)$	1	4	6	4	1	
6 $(\bar{\Delta}_6)$	1	5	10	10	5	1

Supplementary Table S1. Number of Entropy Terms of Increasing Size Necessary to Compute Mutual Information and Differential Interaction Information (Δ) of Up to Six Variables

A number of figures are included here that provide additional information about the relationships among the delta measures and the noise introduced in the simulated data set.



SUPPLEMENTARY FIG. S1. Detectability of the signal from the background measured with (a) Mutual Information, (b) $\bar{\Delta}_3$, and (c) $\bar{\Delta}_4$. Each curve is a difference between a background curve and a curve corresponding to the same tuple from Figure 5, divided by the standard deviation. The horizontal line corresponds to 2 standard deviations.



SUPPLEMENTARY FIG. S2. Distinction of the signal from the background measured for (a) Mutual Information, (b) $\overline{\Delta}_3$, and (c) $\overline{\Delta}_4$. Each curve is the log_{10} of the *P*-value after performing ANOVA test between the populations represented by a background curve and a curve corresponding to the same tuple in Figure 5.



SUPPLEMENTARY FIG. S3. Information gain over background as a function of amount of noise. Each point shows the difference between average *MI* of a selected pair and average *MI* of the background scaled by the standard deviation of *MI* of the selected pair. The analysis for three pairs is shown: (a) $\langle X_{17}, X_{19} \rangle$, (b) $\langle X_{12}, X_{19} \rangle$, (c) $\langle X_{11}, X_{19} \rangle$. The average values of *MI* were computed for each subset size and noise level as follows: we randomly selected 10 subsets and for each subset we seeded noise 100 times, and finally averaged across the resulting 1000 *MI* values. To compute the average background *MI*, we repeated this process for each non-informative pair and took the average across all these pairs. The horizontal line shows a 2 standard deviation level.



SUPPLEMENTARY FIG. S4. Information gain over background as a function of amount of noise. Three plots of the figure show average $\overline{\Delta}_3$ difference from the background for the three informative triplets, (a) $\langle X_{12}, X_{17}, X_{19} \rangle$, (b) $\langle X_{11}, X_{17}, X_{19} \rangle$, (c) $\langle X_{11}, X_{12}, X_{19} \rangle$. These plots are computed similarly to those in Figure S3.

SUPPLEMENTARY FIG. S5. Information gain over background as a function of amount of noise. The figure shows average $\overline{\Delta}_4$ difference from the background for the informative tuple $\langle X_{11}, X_{12}, X_{17}, X_{19} \rangle$. This plot is computed similarly to those in Figures S3 and S4.

