Dremi produces a line of fit based on binned conditional probabilities of P(Y|range of X). We could use a Kolmagrov-Smirnove test of this line against the line produced under the null hypothesis to determine if there is an interesting relationship between X and Y.

I like the density-dependant down-sampling employed by SPADE more than that employed by DREMI. It uses local neighborhoods to define the likelihood that every point might be down sampled rather than a bin of X values over which the joint distribution is normalized. However, this local uniformity my complicate trend finding in resulting down-sampled data is uniform. Could we do a weighted combination of these down sampling probabilities per sample point? This would make for easy preliminary work.

Data cleaning is an important step. You could be detecting non-biologically relevant trends between X and Y like RNA degradation, the rate of which has been shown to be both gene and sample dependant (http://www.nature.com/ncomms/2015/150803/ncomms8816/fig\_tab/ncomms8816\_F2.html)