Systematic binding variations on cDNA microarrays

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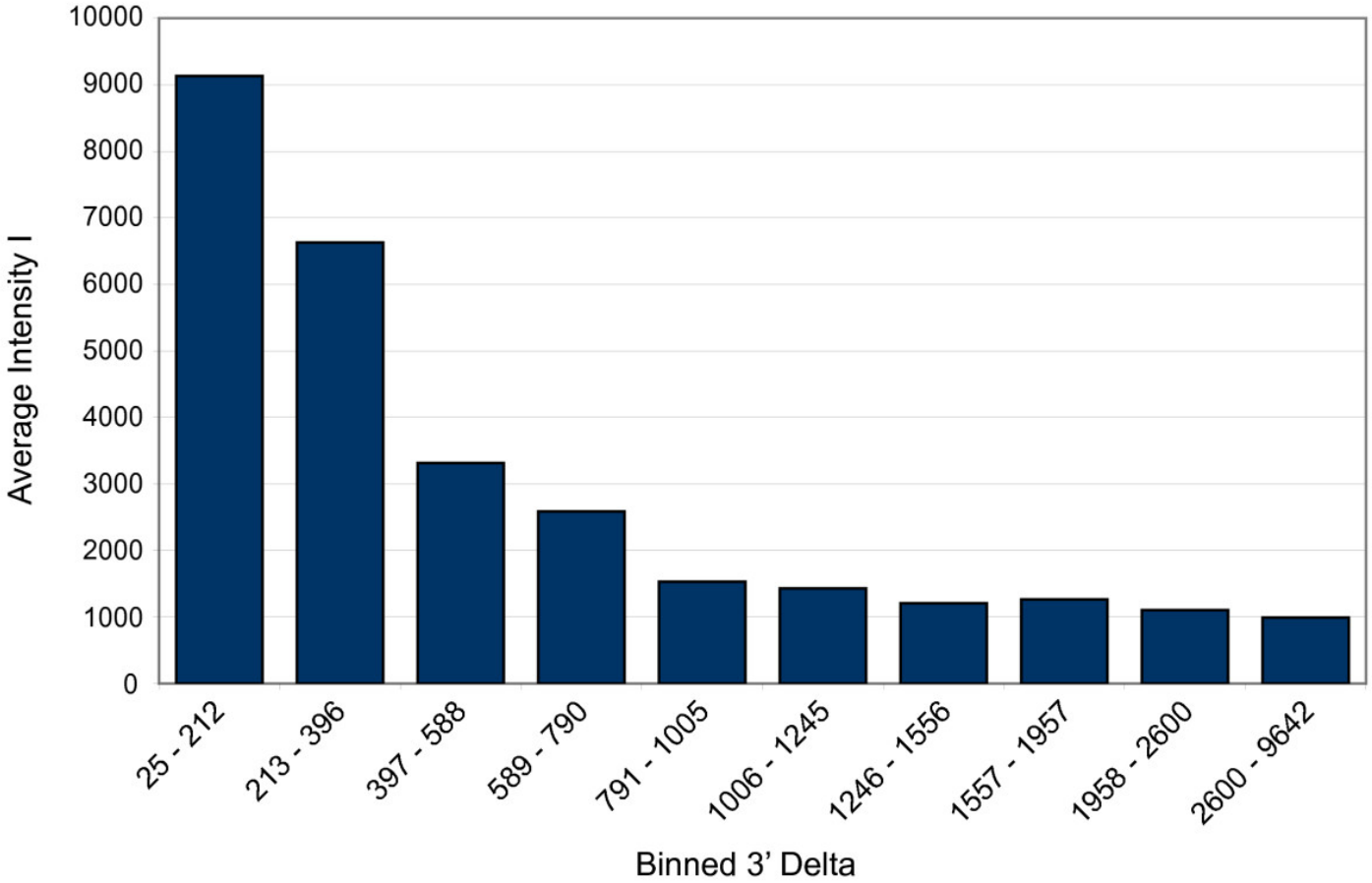
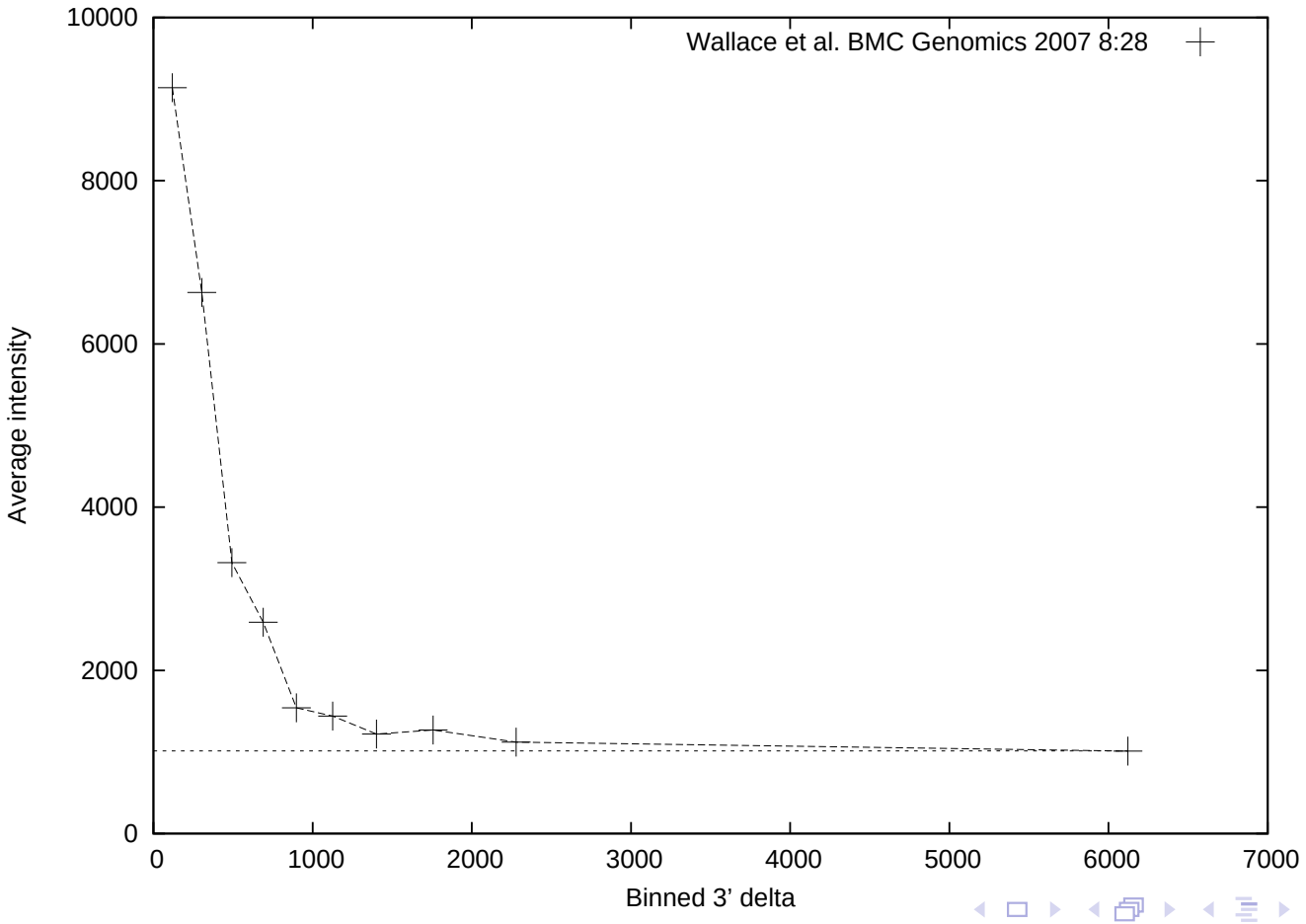
2007-06-21

A systematic variation in binding efficacy



Average binned signal channel intensities for 60-mer oligonucleotide probes increase with proximity to the 3’ UTR of gene transcripts [1].

A physicist’s view



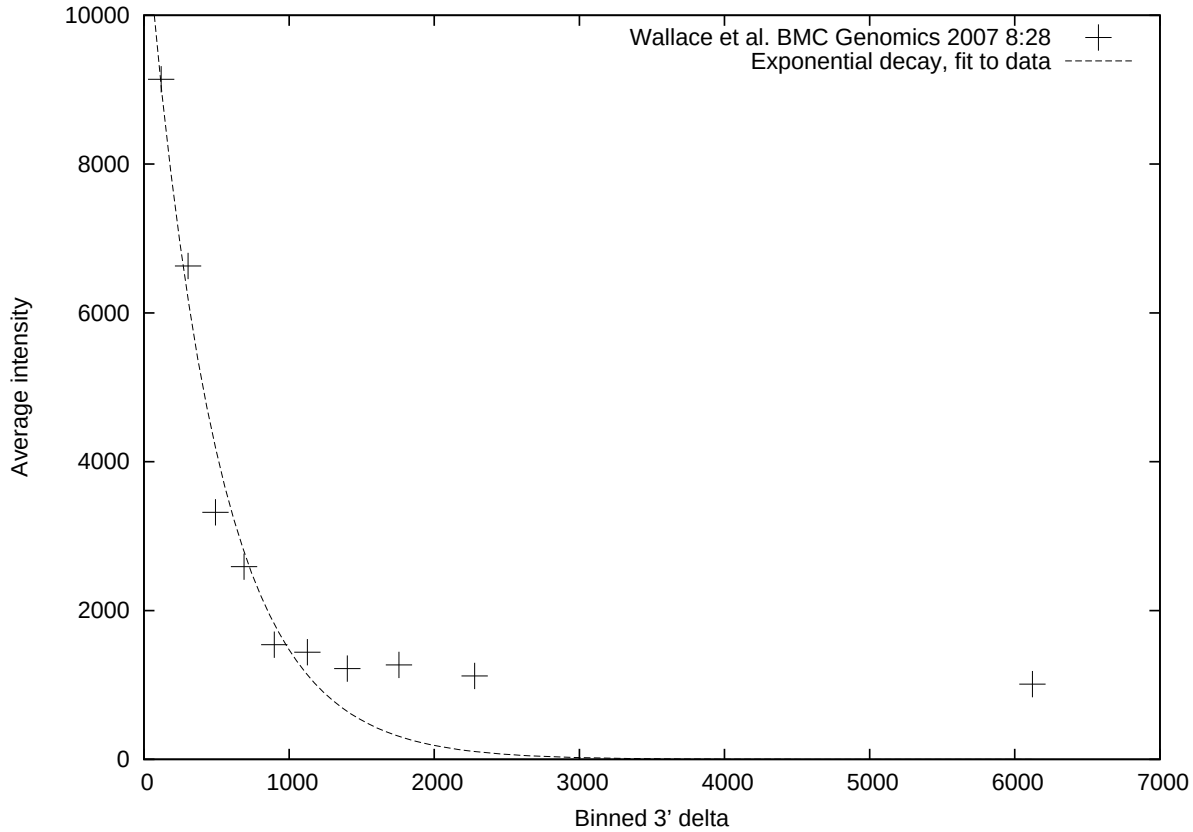
The “traditional” explanation

Human ER α gene structure and mapping of 4 Affymetrix oligonucleotide probe sets to the sequence of the ER gene. The reverse transcription reaction starts at the 3’ end of the cDNA, and the efficacy of the reaction drops off as it moves toward the 5’ end, therefore, probes close to the 3’ end give stronger signal and show the best correlation with the overlapping cDNA probe.

James Stec et al. *JMD 2005, Vol. 7, No. 3*.

I.e. exponential decay of the average intensity with increasing distance to the 3’ end of the gene transcripts.

The “traditional” explanation – illustrated



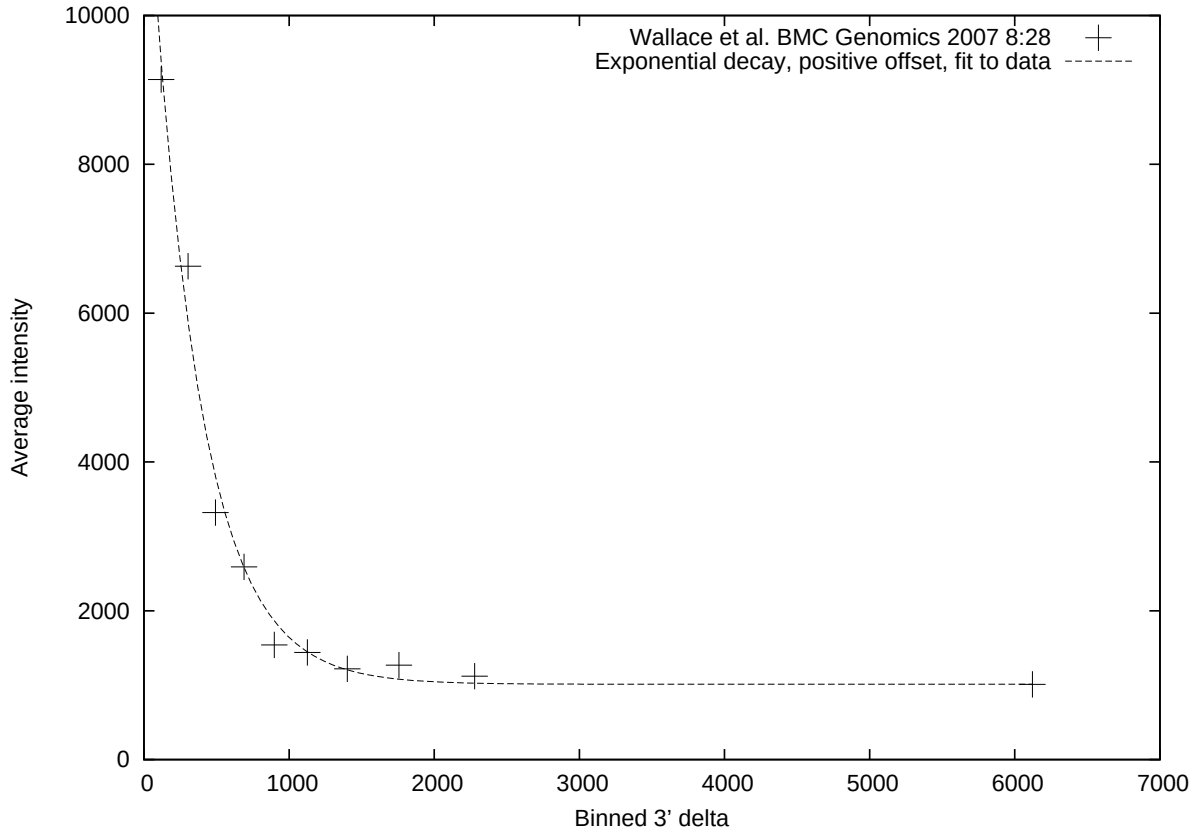
A physicist’s explanation

We need an explanation which takes into account that once the probe is separated some distance from the 3’ end of the gene transcript, the average intensity reaches a non-zero plateau.

My claim is that we see the effect of having to **bend** the part of the sample cDNA between the 3’ end and the probe.

- Bending will only require more energy up to a certain length (probe distance to the 3’ end).
- The samples can be forced to bend, because the array surface acts as an obstacle.

A physicist’s explanation – illustrated



Future work

Still quite a bit!

- Validate the result on non-binned data.
- Check the effect of inverting the probes (swapping the 3’ and 5’ ends).
- Use a model of the mecanical properties of cDNA molecules to calculate the magnitude of variation in average intensities, given the proposed explanation.

Contact

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Bibliography

James C. Wallace, Marcus J. Korth, Bryan Paeper, Sean C. Proll, Matthew J. Thomas, Charles L. Magness, Shawn P. Iadonato, Charles Nelson, and Michael G. Katze.
High-density rhesus macaque oligonucleotide microarray design using early-stage rhesus genome sequence information and human genome annotations.
BMC Genomics, 8(28), 2007.