Flanking sequences compensate for mutations in *Drosophila melanogaster* minimal enhancers

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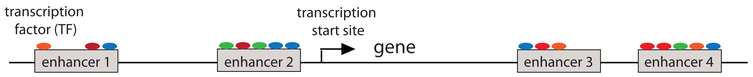
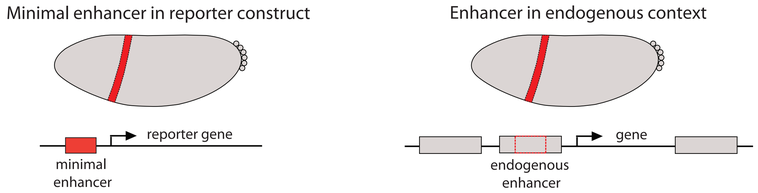
Abstract

Enhancers are non-coding DNA sequences that contain clusters of transcription factor binding sites (TFBS) and are important for transcriptional control of gene expression in animals. Much of our understanding about enhancers is based on experiments that test minimal enhancers, the shortest DNA fragments sufficient to drive the native expression pattern of a gene. Yet in an animal genome, minimal enhancers are only part of a large amount of intergenic DNA with additional TFBS. The role of these additional sequences in the function of an enhancer is unclear. We want to determine whether mutations have the same effect in a minimal enhancer as in a larger sequence of the enhancer (full). We mutated single TFBS in a minimal and a full sequence of a *Drosophila melanogaster* enhancer to determine the relative effects of these mutations on gene expression. We found that mutations that had a large effect on expression in the minimal enhancer did not significantly alter expression in the full enhancer. Our results suggest that additional sequences in the full enhancer are compensating for mutations in the minimal enhancer.

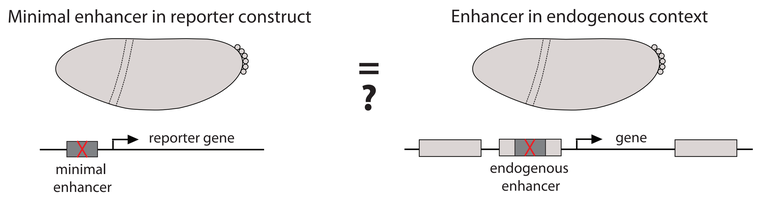
Enhancers control gene expression in animals.



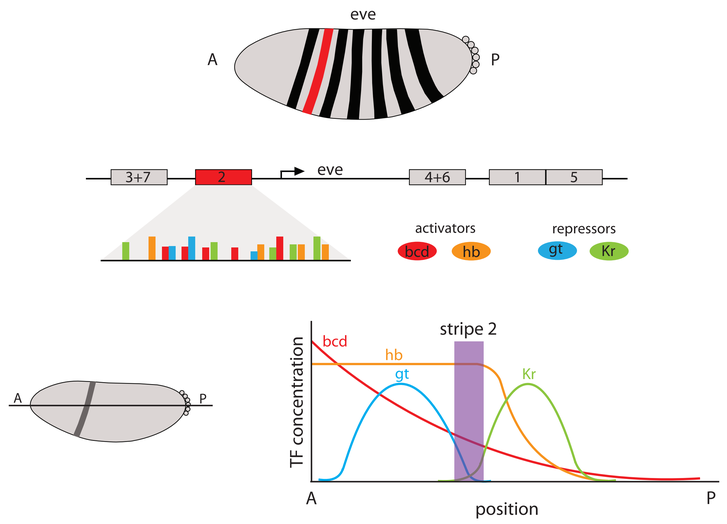
Minimal reporter constructs are used to study enhancers.



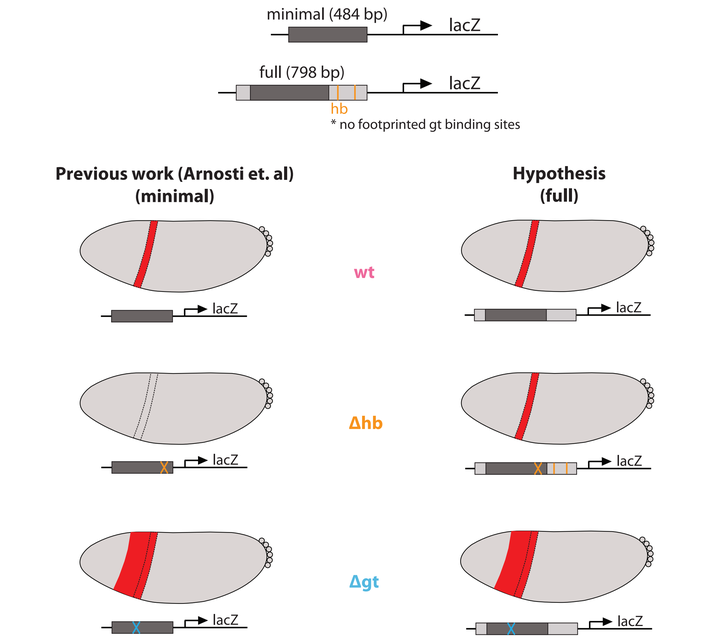
What are the effects of mutations in the endogenous context?



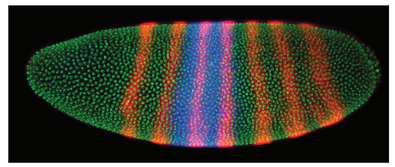
We focused on the *even-skipped* (*eve*) stripe 2 enhancer in *Drosophila melanogaster* embryos.



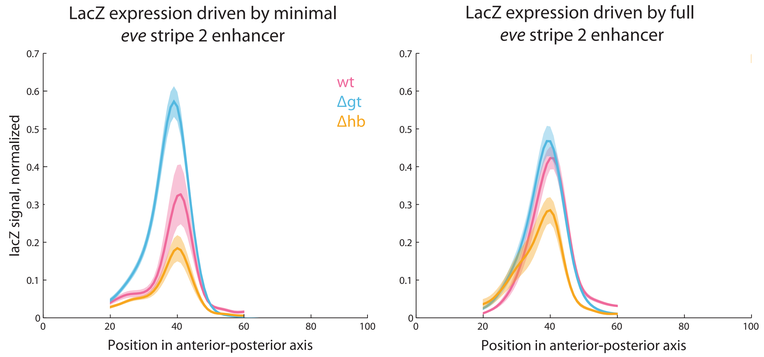
We mutated *eve* stripe 2 enhancers with and without flanking sequences. We expect flanking sequences to compensate for mutations if they contain binding sites.



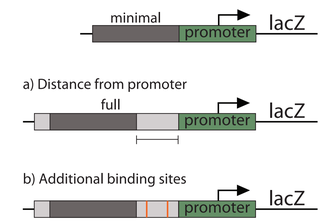
We measured the effect of enhancer mutations on *eve* stripe 2 expression quantitatively at cellular resolution.



We found that flanking sequences compensate for mutations even in the absence of footprinted binding sites.



We hope to identify the sequence features responsible for compensation.



Acknowlegments

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References

Arnosti, D. N., Barolo, S., Levine, M., Small, S. (1996). The eve stripe 2 enhancer employs multiple modes of transcriptional synergy. *Development 122* (*205-214*).