Genome Encoded Memory

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Early Acknowledgements

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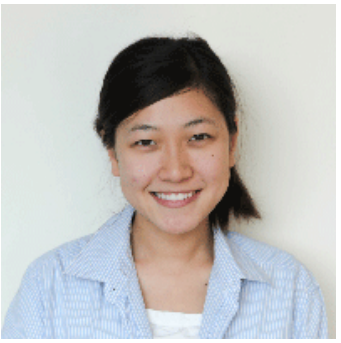
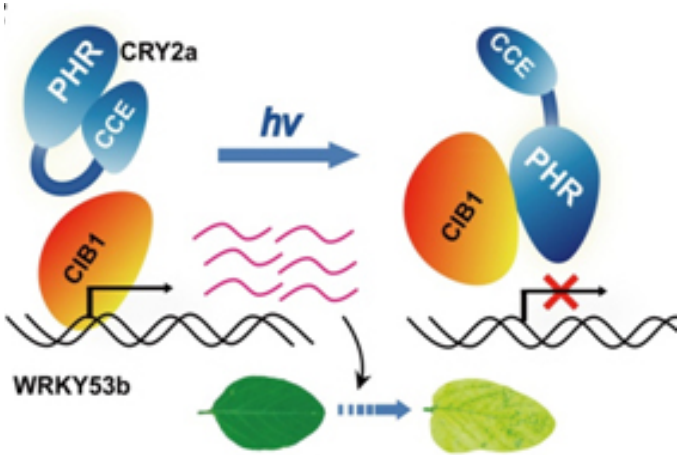


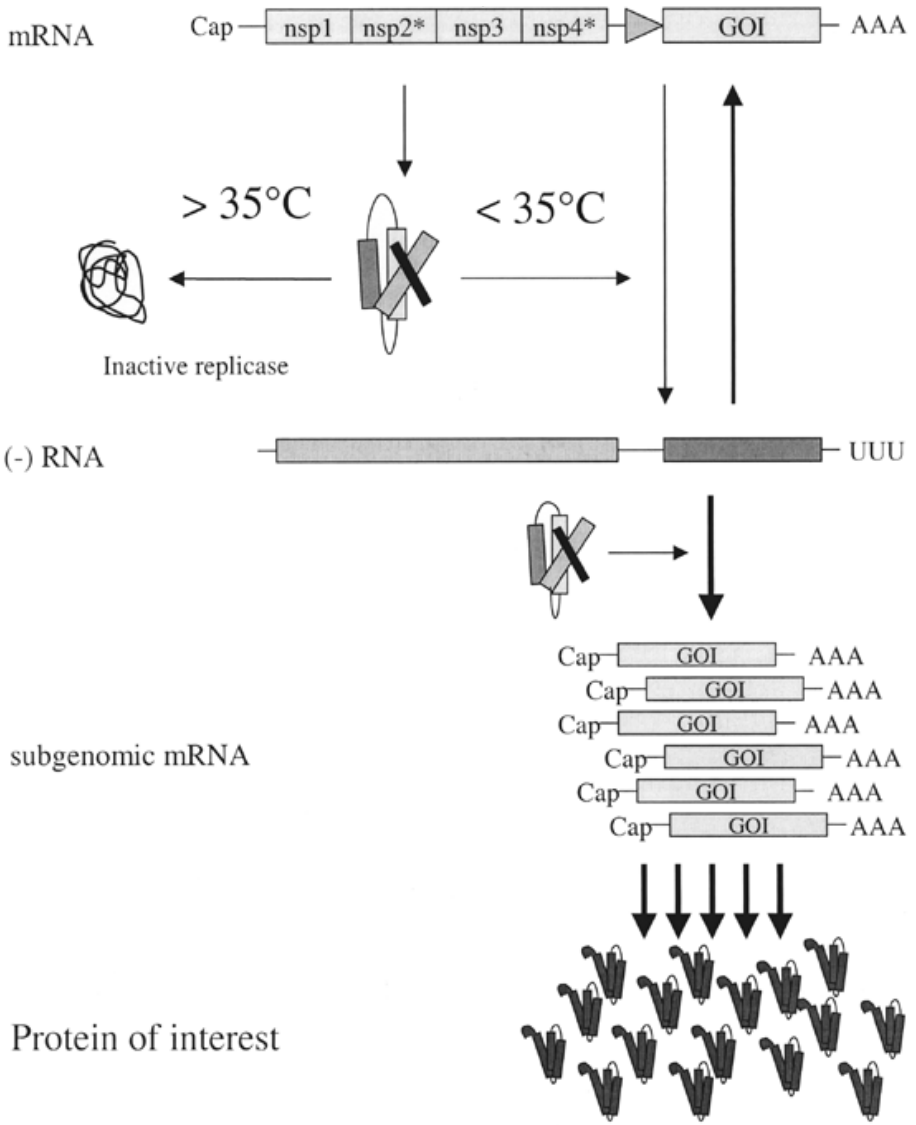



Biological Machinery as Sensors

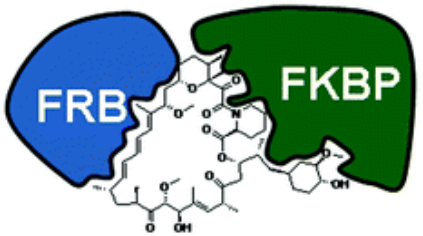
Light



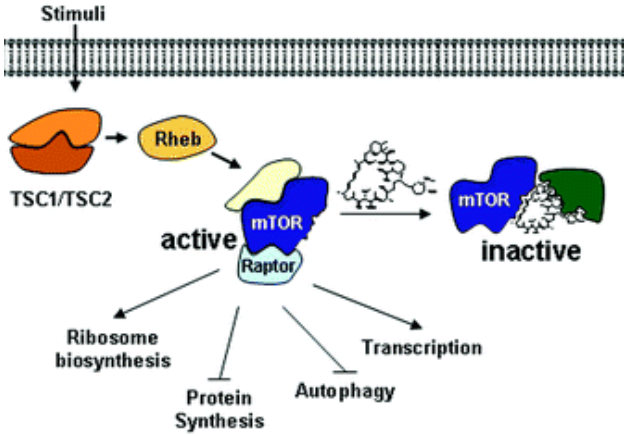
Temperature



Small Molecules

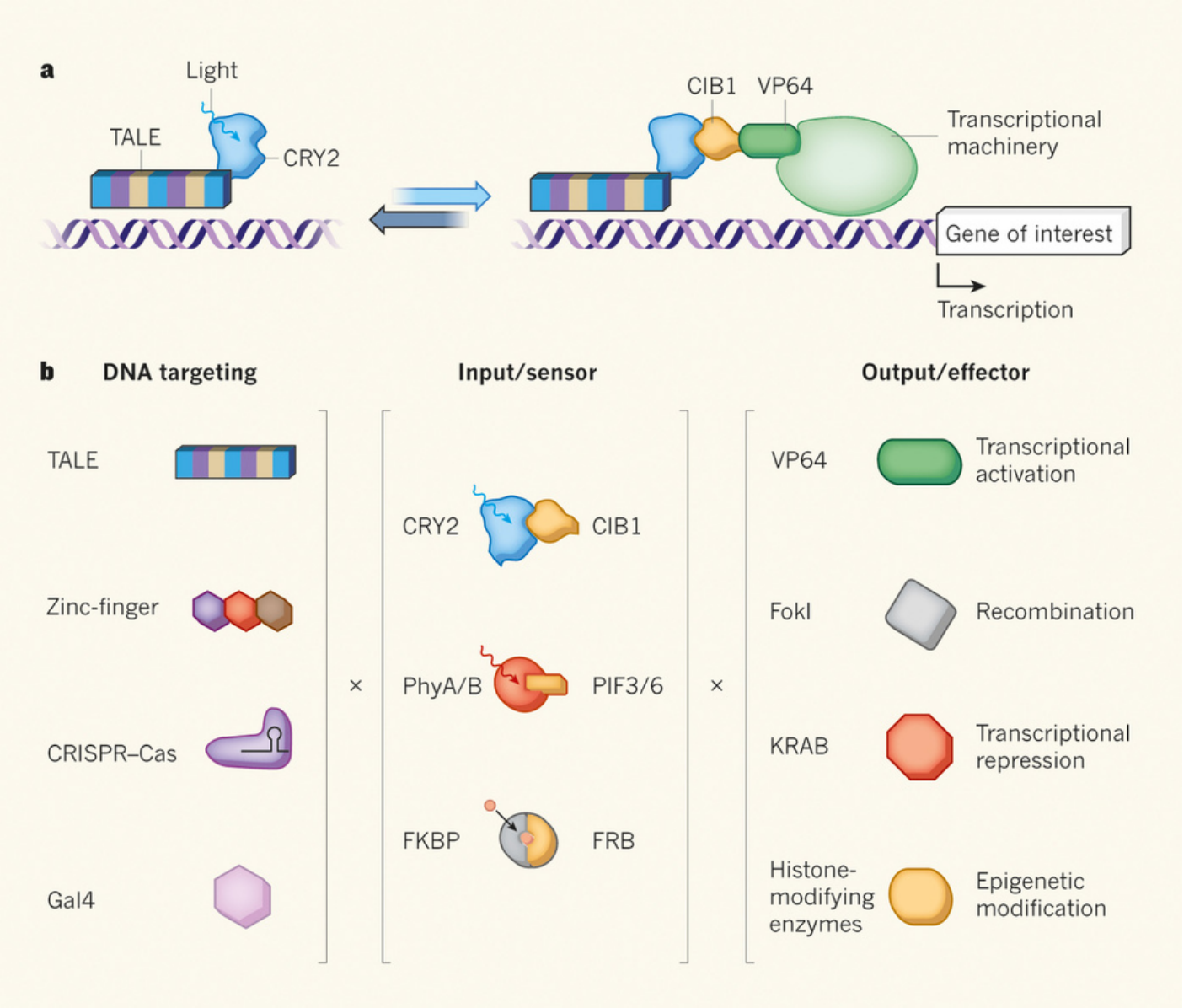


rapamycin 6



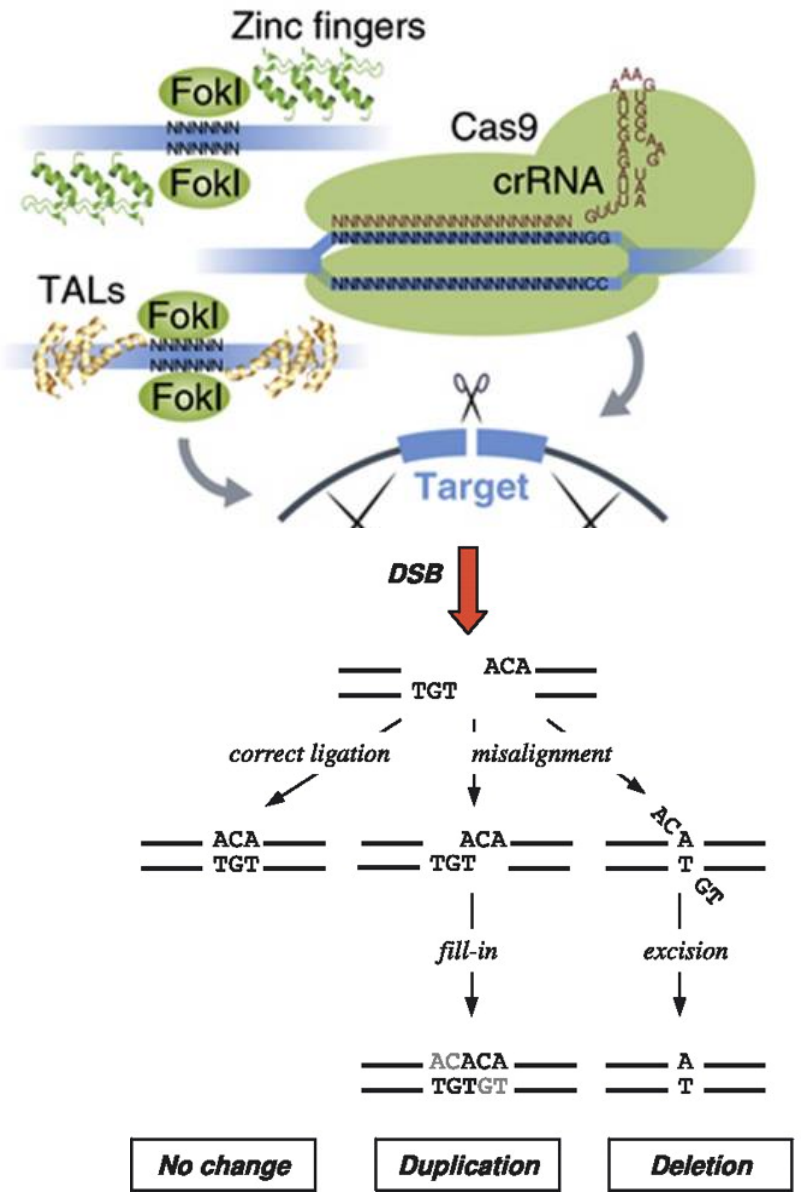
Clockwise from Right: Boorsma et al, Nature Biotech 2000; Pucheault Org Biomol Chem 2008; Meng et al, The Plant Cell 2013

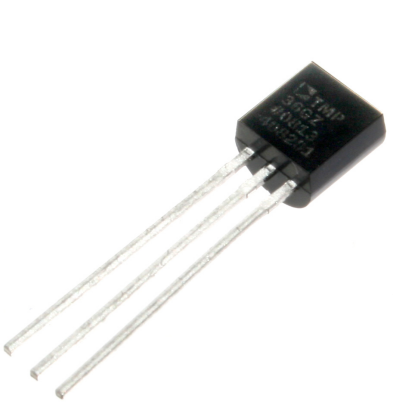
Molecules for DNA Modification



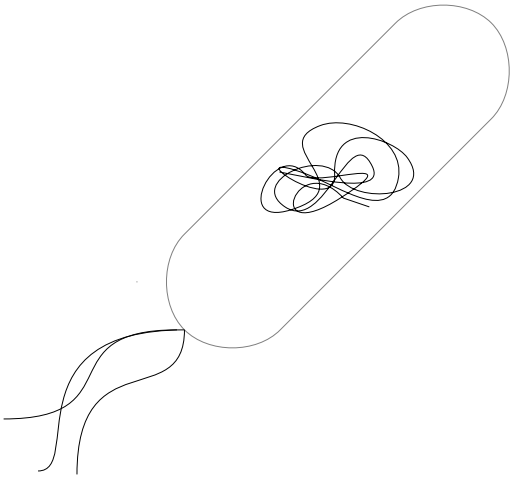
Moglich and Hegeman, Nature 2013

Genomic Mutation Write





vs



Cost per temperature sensor: $1

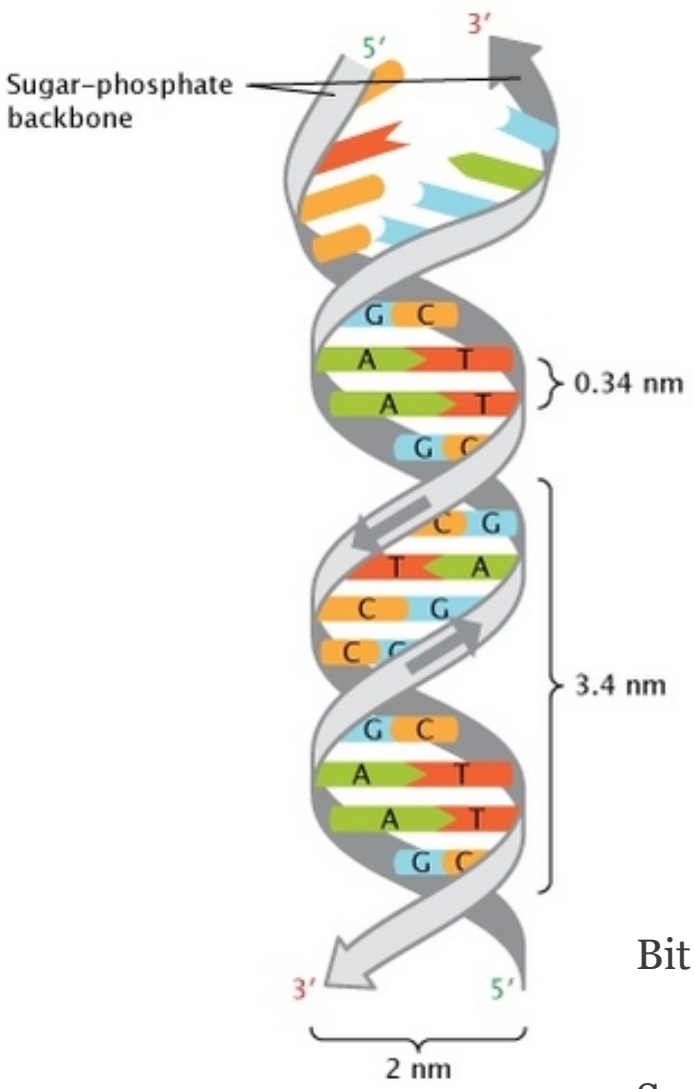
Cells grown in bioreactor: 10e10 cells

Cost of bioreactor run: $10,000

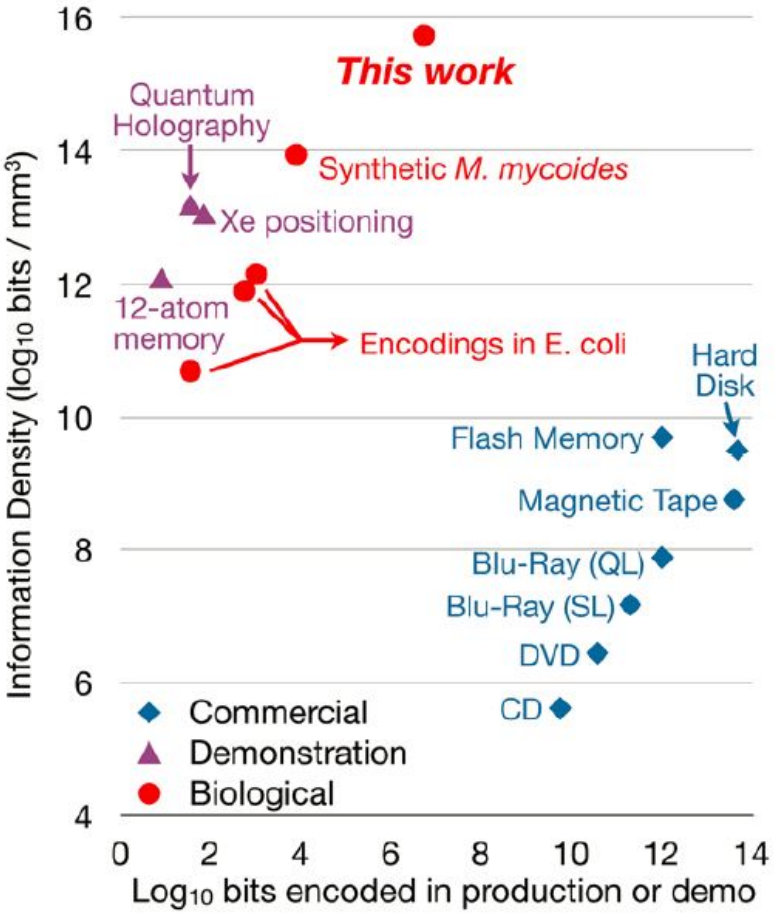
Cost per cell: $0.000001

Top and bottom: Esvelt & Wang, Mol Sys Biol 2013;
Leclercq et al, Genome Biol Evol 2010

Nucleic Acids as Memory Storage



Pray, L. Nature Education 2008



Church et al, Science 2012

Bit Density Upper Bound:

2 bit / ((3.4e-7)*π*(1e-6)^2) mm^3 = 1.87e18 bit / mm^3

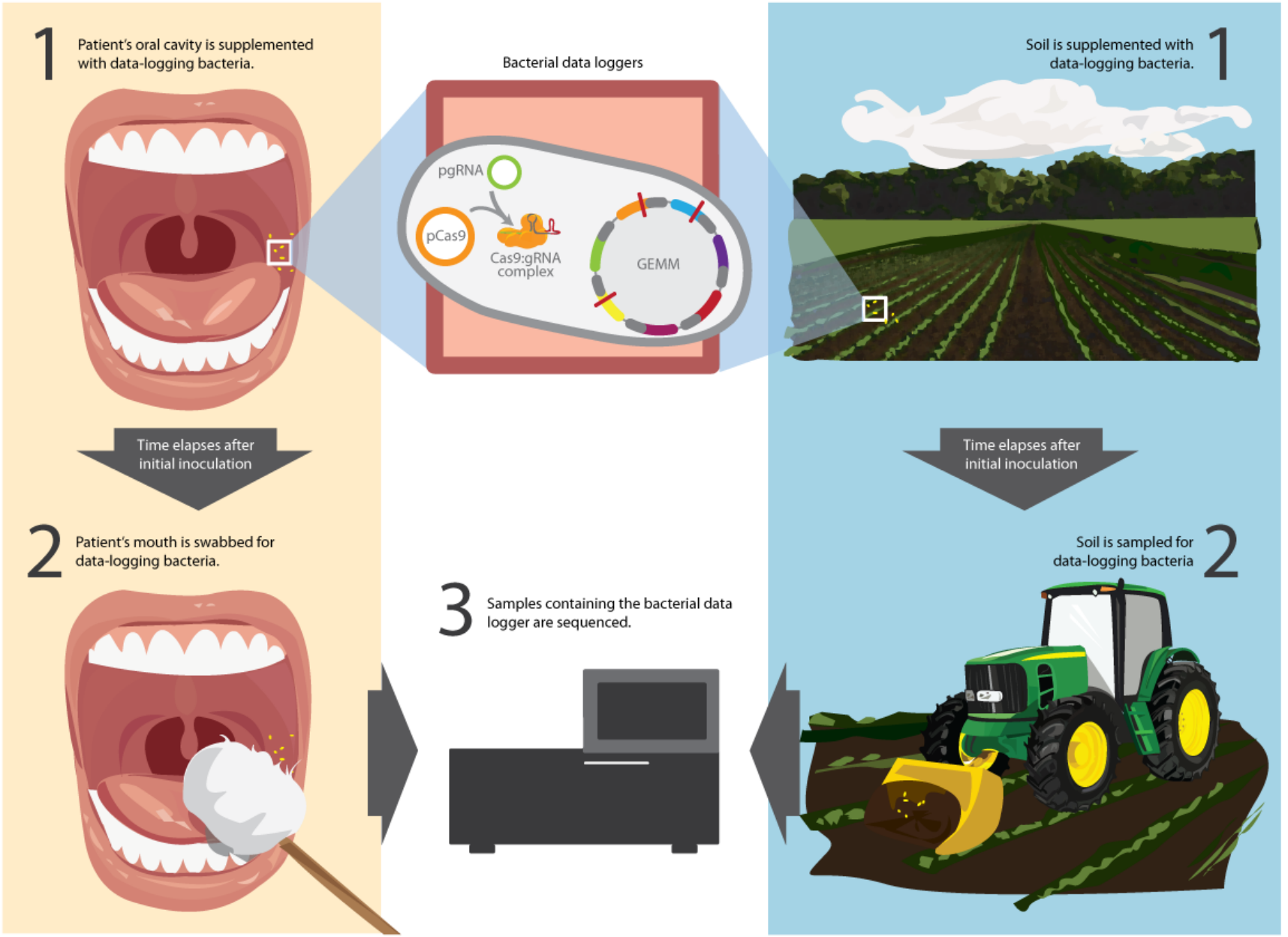
Synthesis Cost:

($0.06 / 200 bases) / (2 bit / base) = $0.00015 / bit

Sequencing Cost:

($1e-6 / base) / (2 bit / base) = $5e-7 / bit

Need for Genome Encoded Mutations



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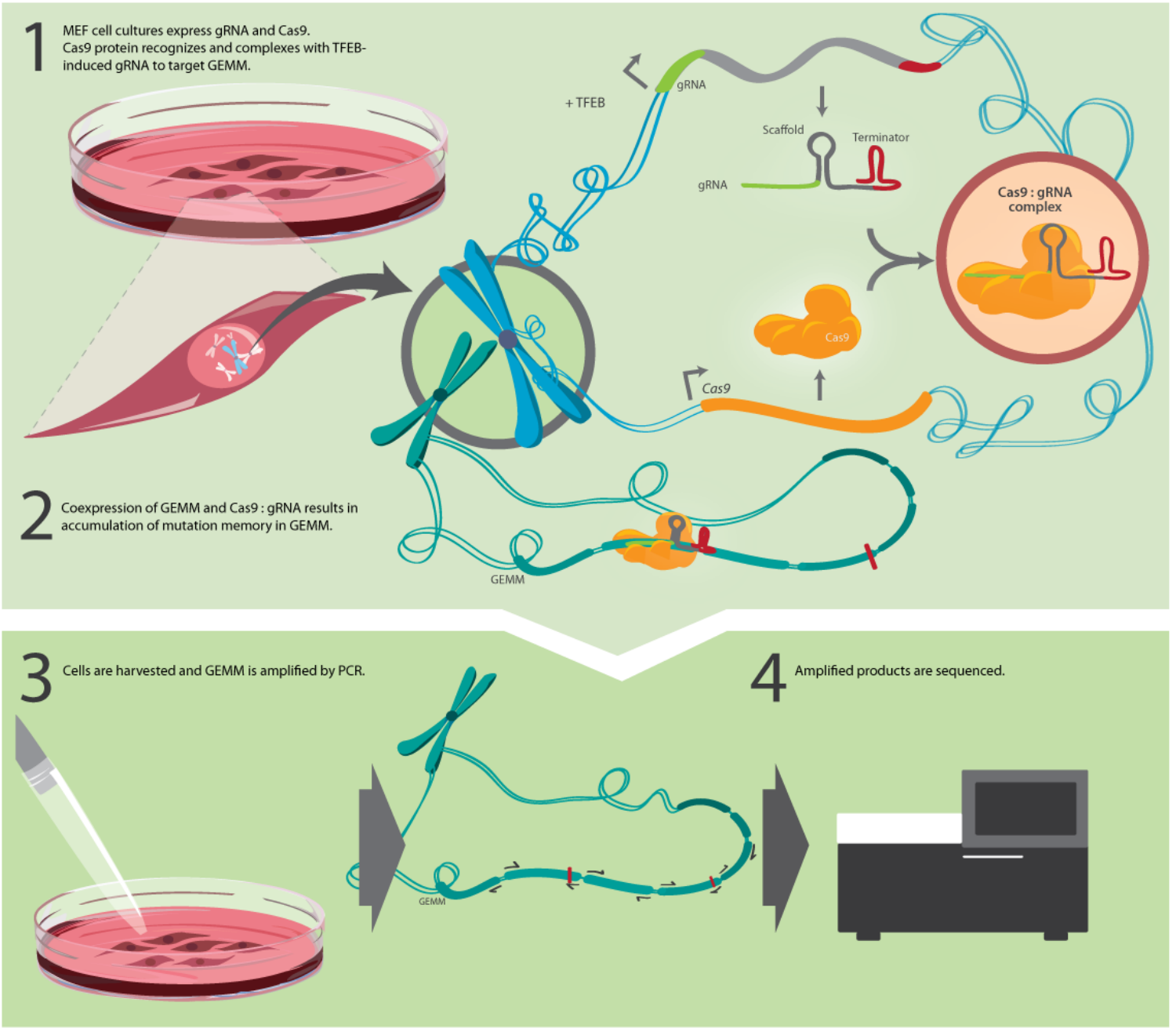
Genome Encoded Mutation Memory



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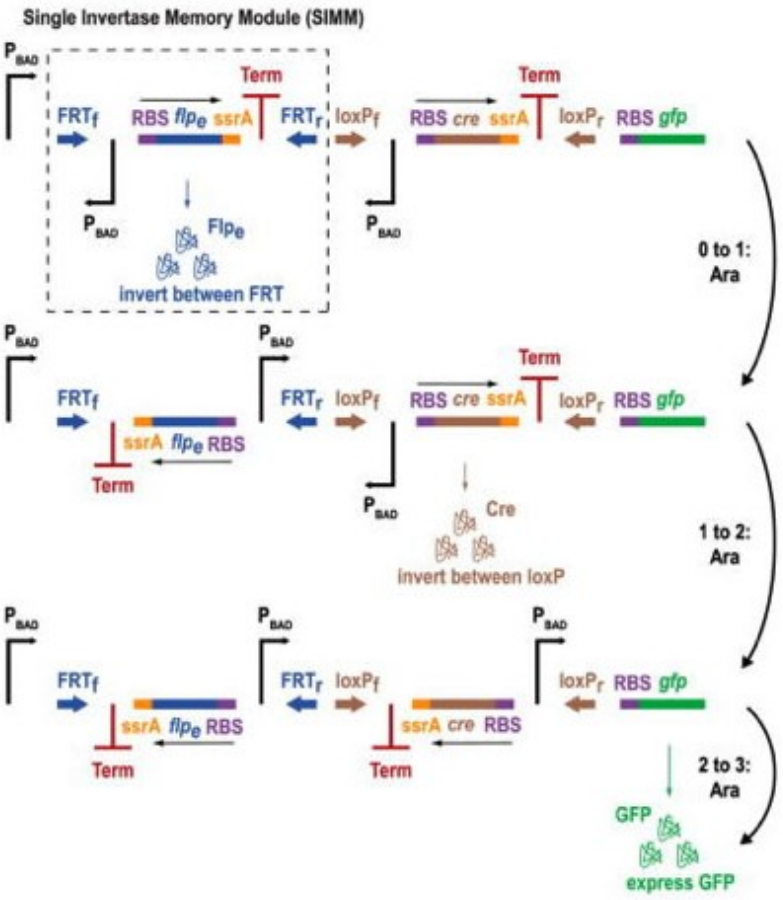
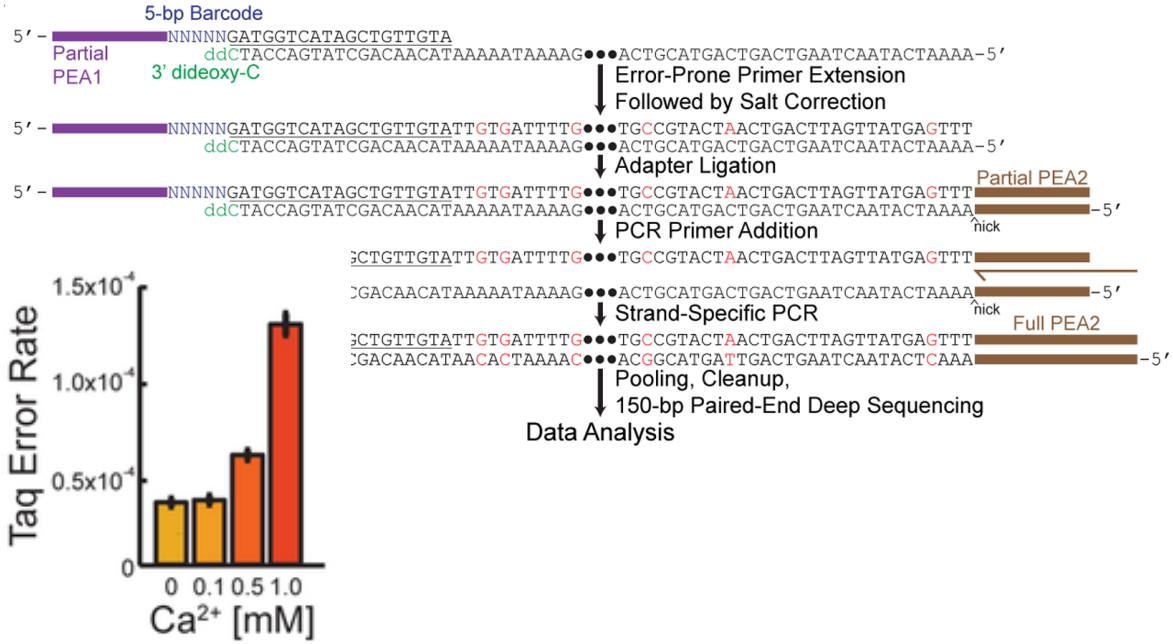
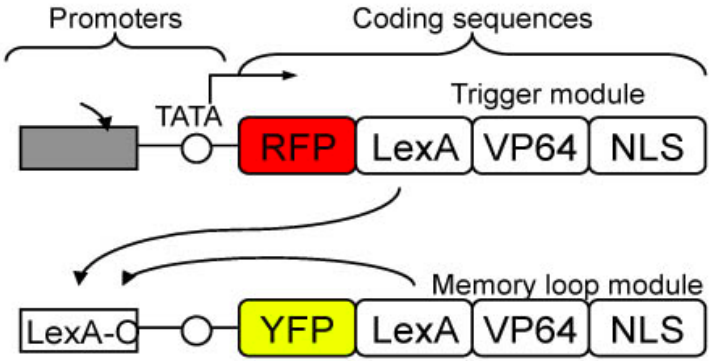
Genomic Nucleic Acid Memory

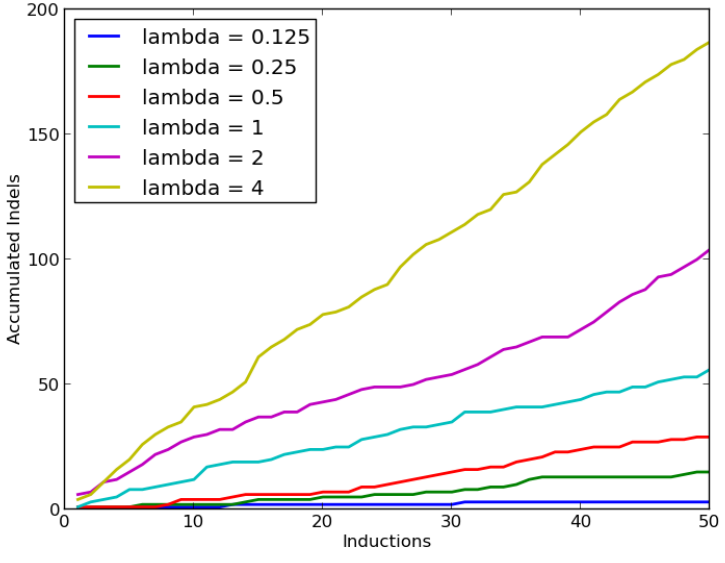






Clockwise from Top Right: Zamft et al, PLOS ONE 2012; Ajo-Franklin et al, Genes and Dev 2007; Friedland et al, Science 2009

Modeling GEM Bits



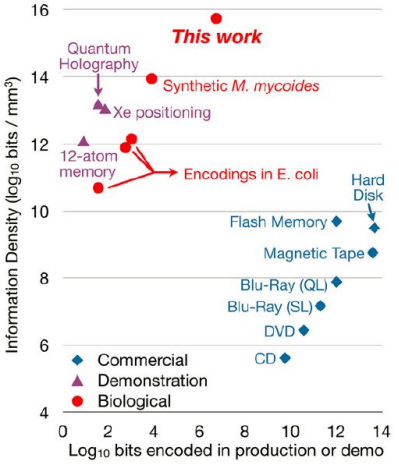
Repeat Unit Sequence = 30 bases

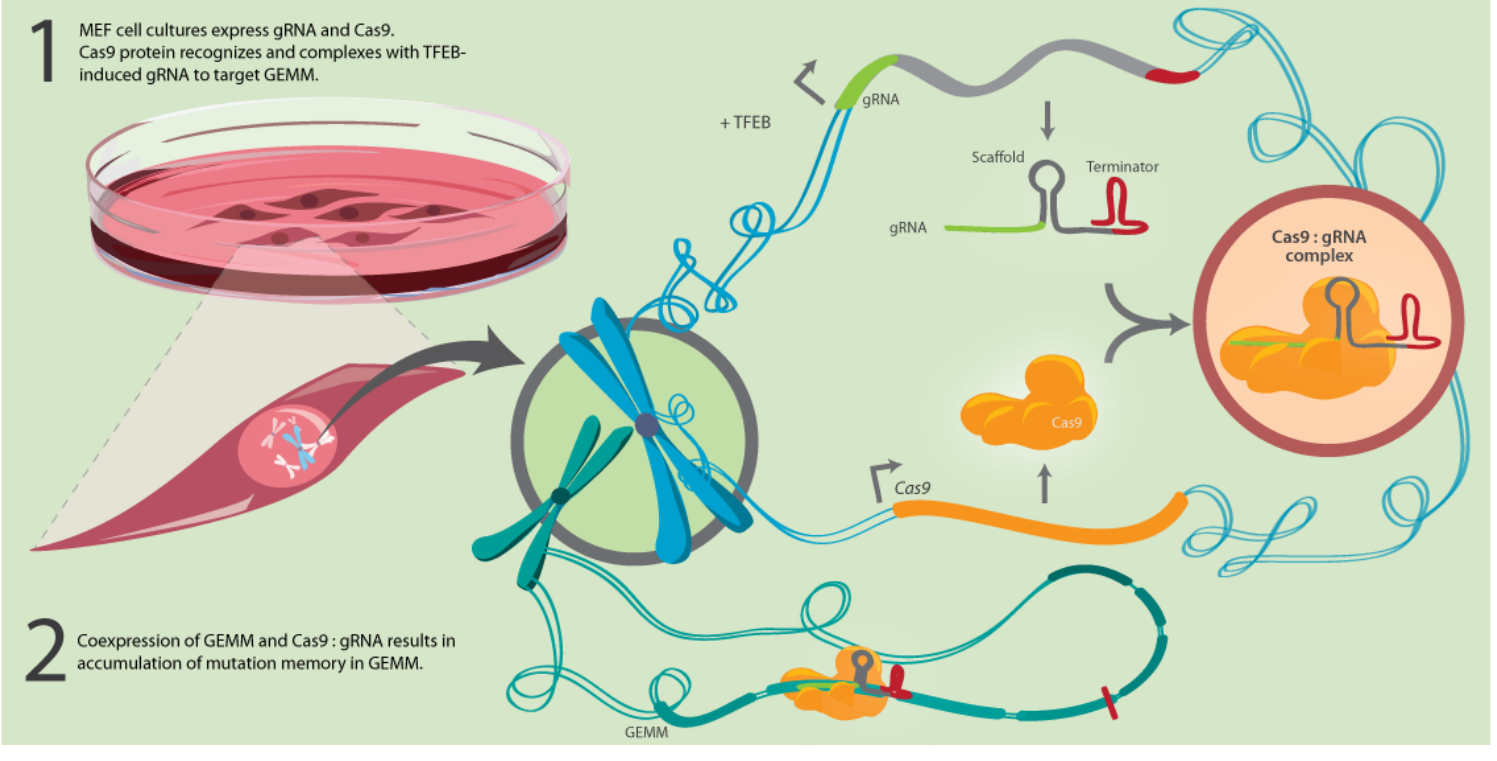
Avg # indels per induction = λ indels

indels per induction ~ Poisson(λ)

Expected bit length = Sum [(30 bases * k * e^-λ * λ^k) / k!]
= 30 bases Sum [(k * e^-λ * λ^k) / k!]
= 30 λ bases

Bit density = 1 bit /(30 λ * (3.4e-7) * π * (1e-6)^2) mm^2
= (3.12e16 / λ) bit/mm^2





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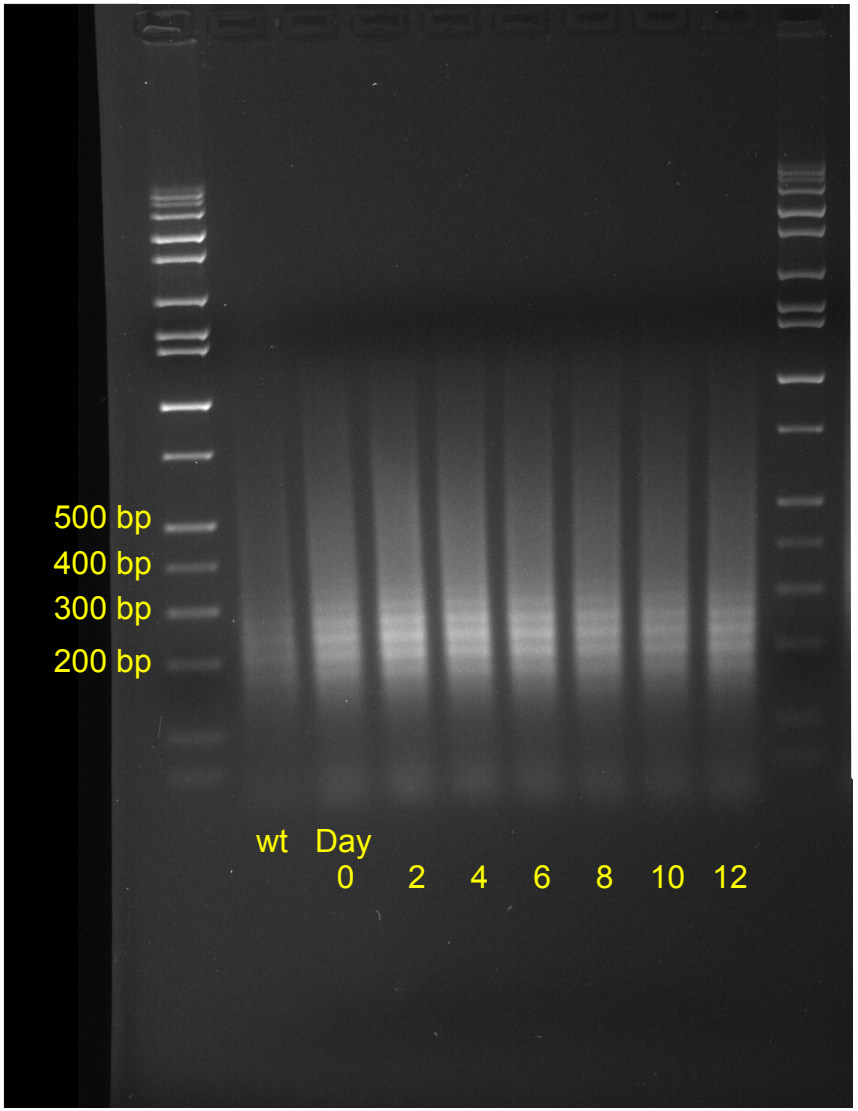
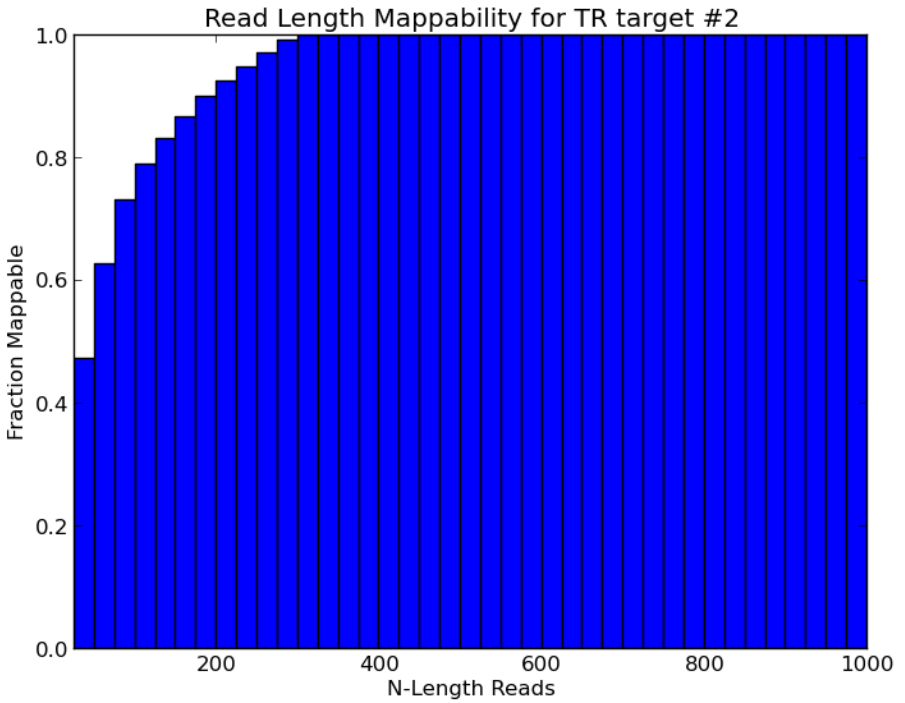
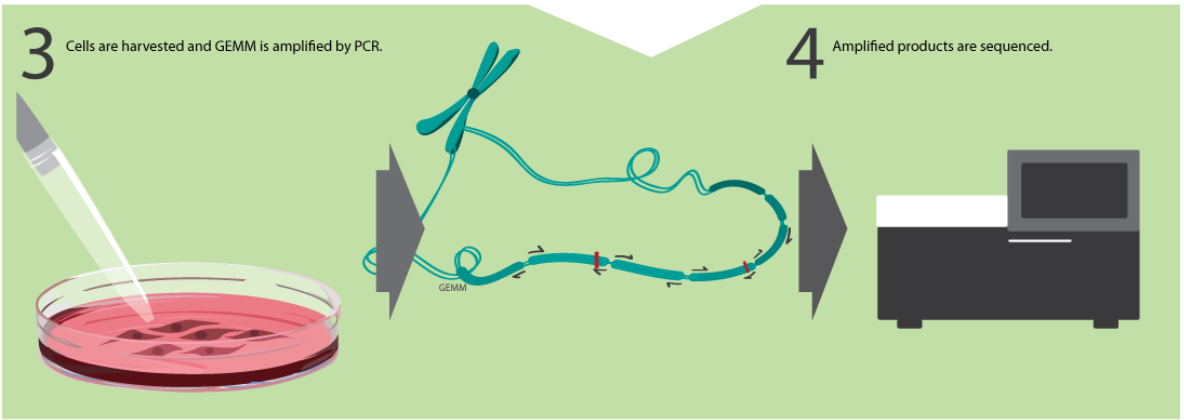
Tandem Repeat GEM Amplification







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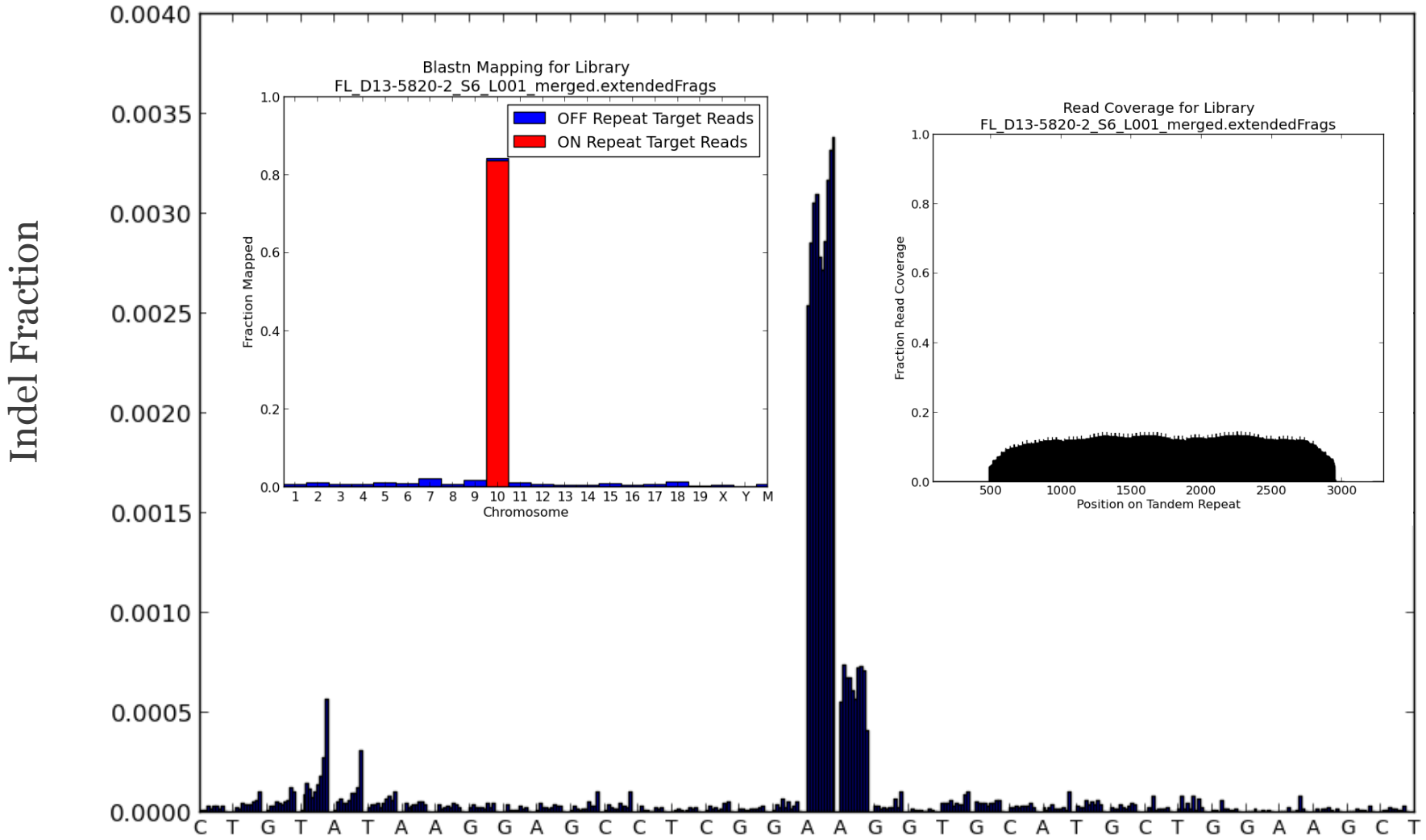
NGS Sequencing of GEM

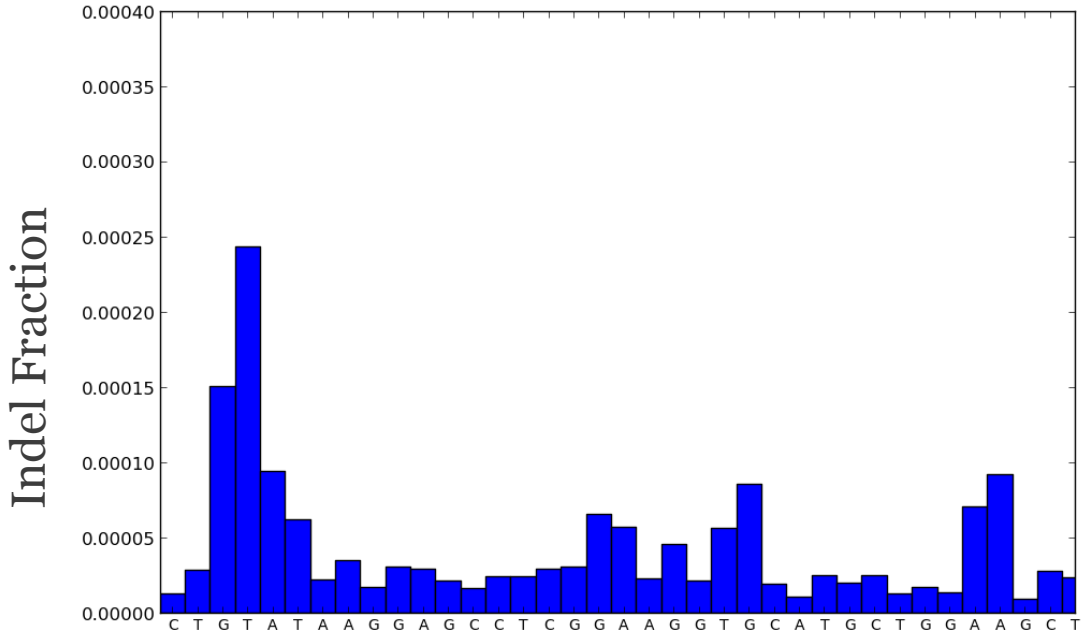
GEMM Indels from U6 Expression of gRNA



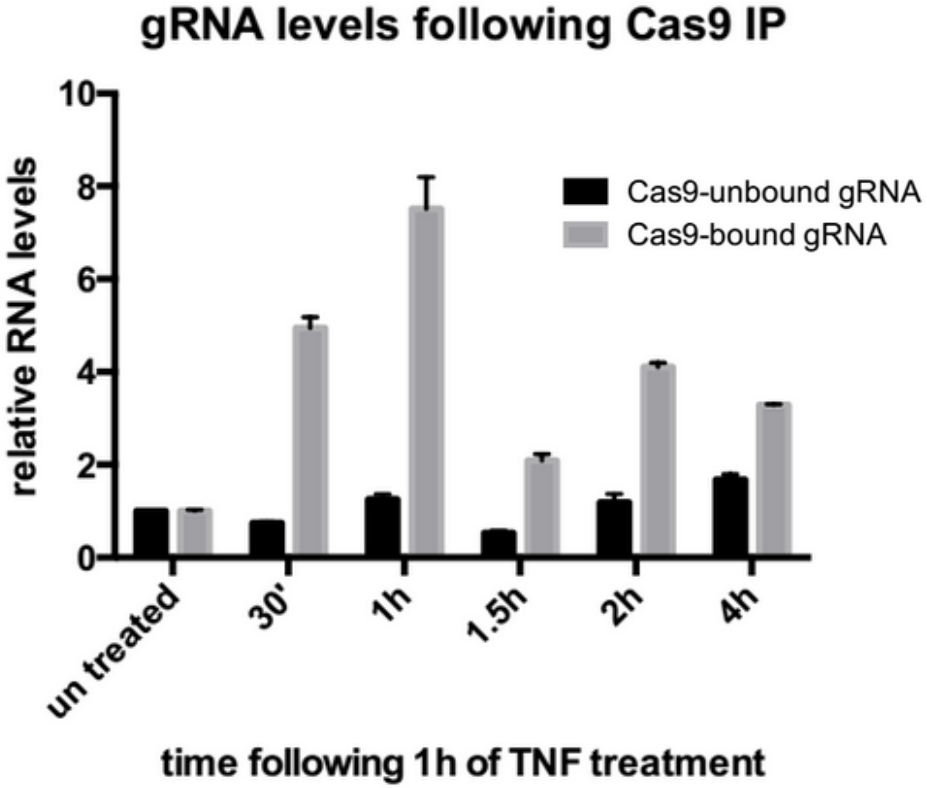
Position on Unit Sequence of Tandem Repeat
(WT, Day 0, 2, 4, 6, 8, 10, 12 at each Position)

Inducible Pol II Guide Transcription

GEM Indels from TNF Induced gRNA Expression

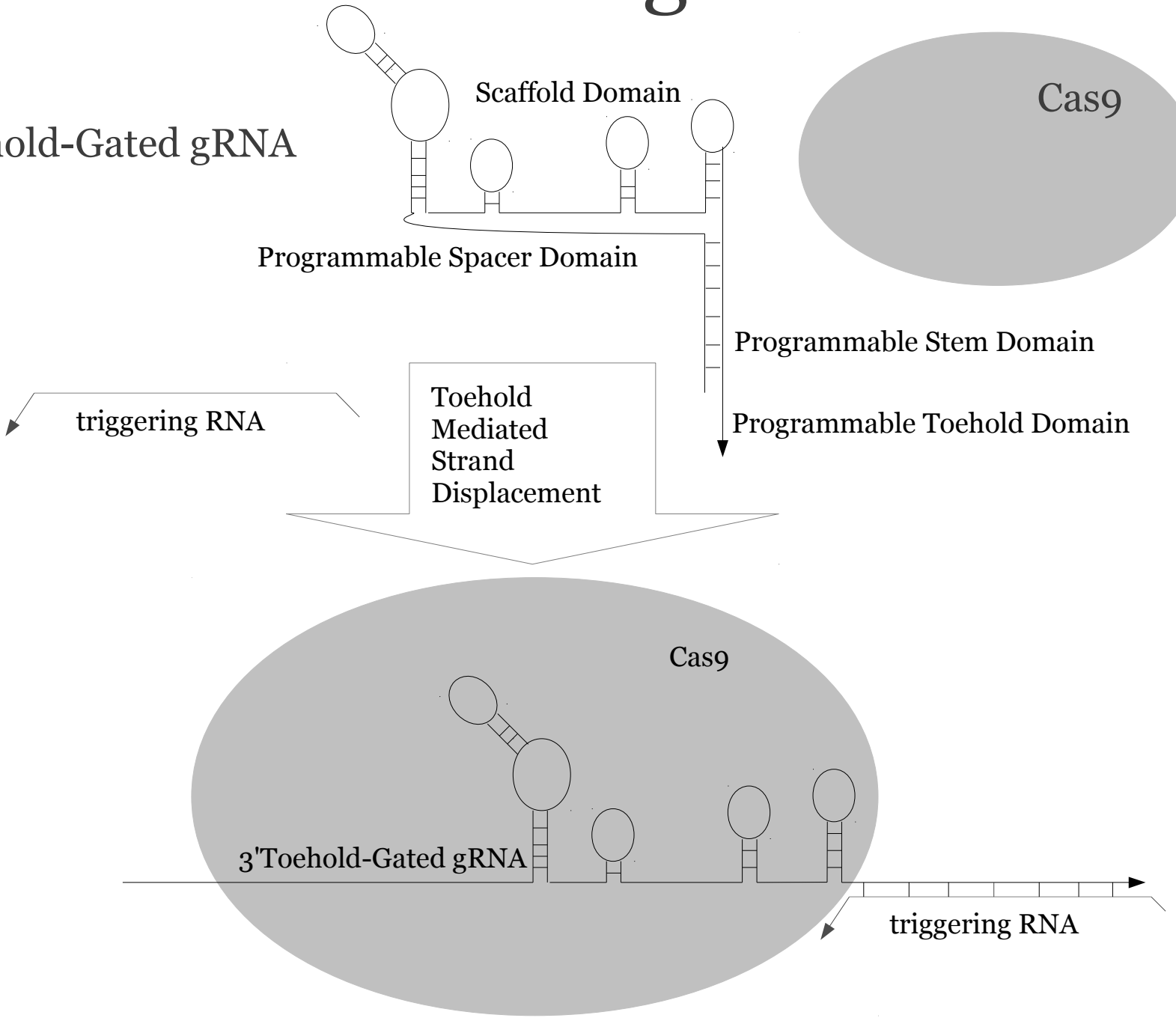


Position on Tandem Repeat Unit Sequence
(Day 6 of 1 Hour TNF Treatment)

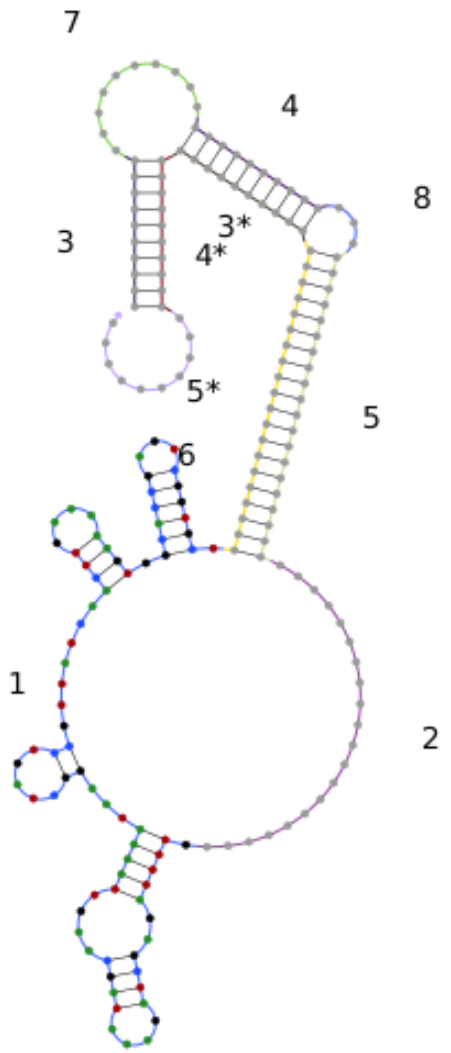


Naama Kanarek

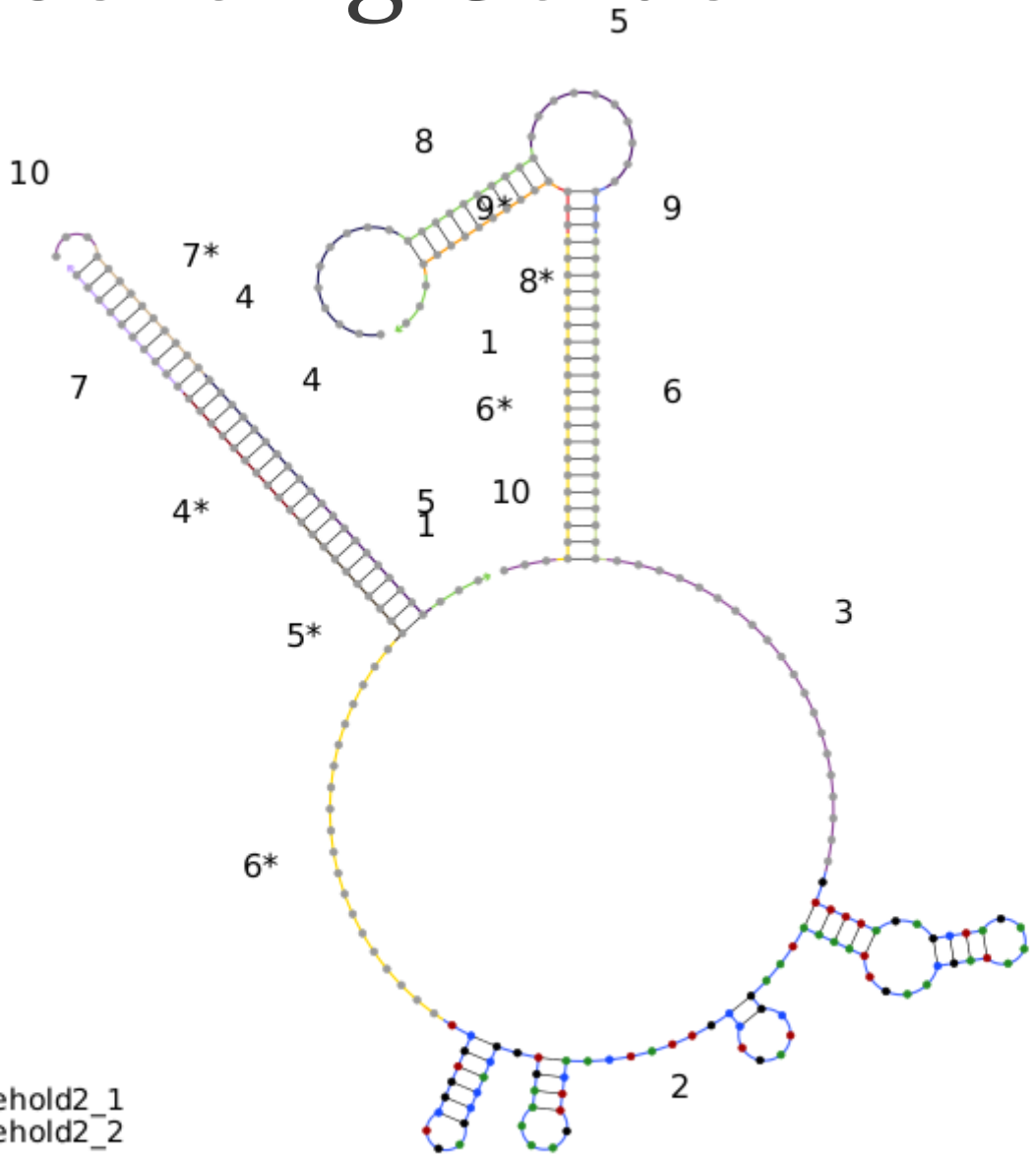
Nucleic Acid-Sensing Guide RNA



AND Logic Demonstrated in a Nucleic Acid-Sensing Guide RNA



1: Scaffold
2: Spacer
3: Stem1_1
4: Stem1_2
5: Stem2
6: Toehold1
7: Toehold2_1
8: Toehold2_2



A
C
G
U
?

1: Downstream
2: Scaffold
3: Spacer
4: Stem1_1
5: Stem1_2
6: Stem2
7: Toehold1
8: Toehold2_1
9: Toehold2_2
10: Upstream

Acknowledgements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