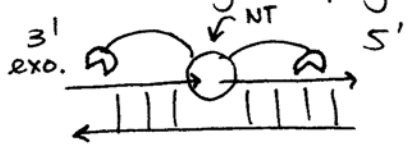
BE.440
15 September 2004
Essigmann

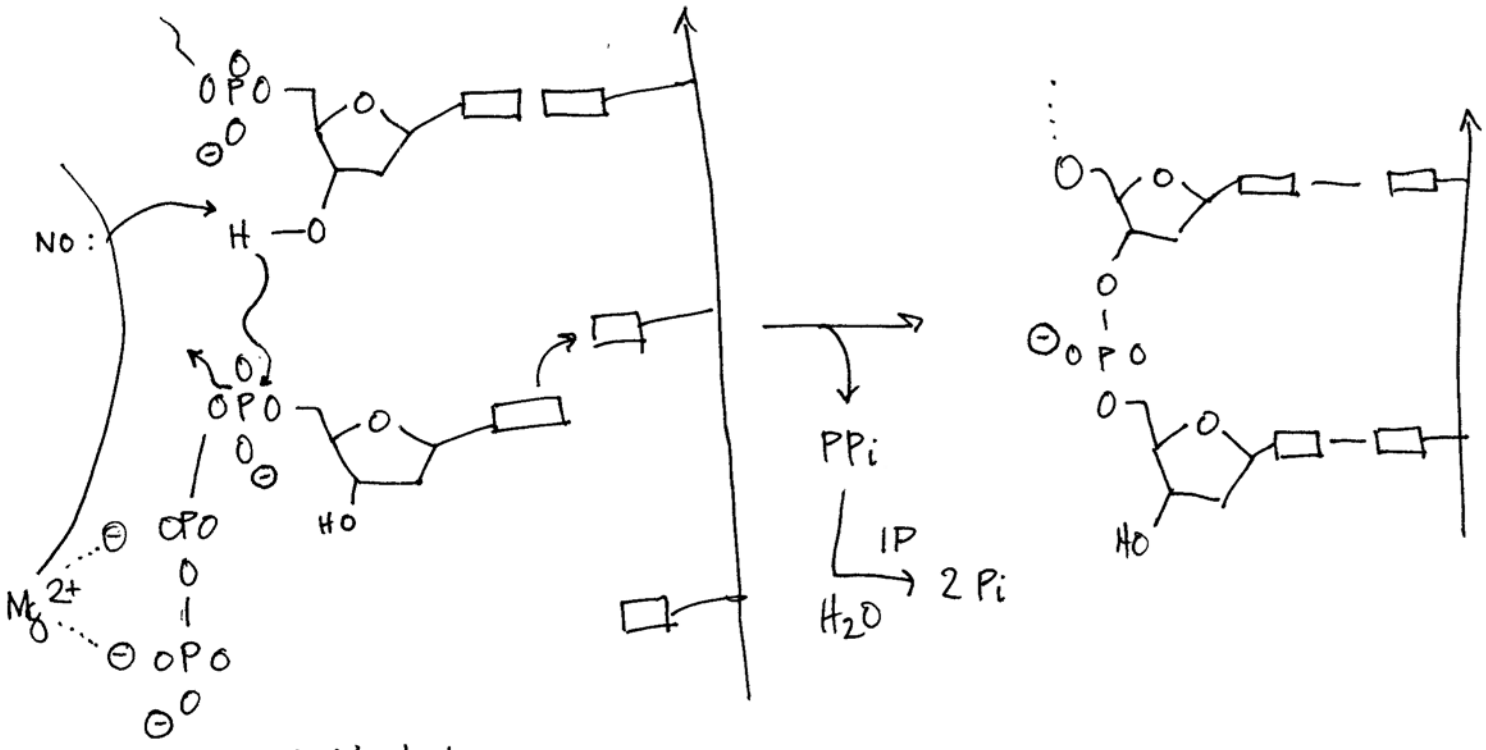
Last day: sources of genetic error for evolution... through H-bonding W/C errors

Polymerases: three activities

1. NT nucl. transferase
2. 3' → 5' exonuclease — kinetic proofreading
3. 5' → 3' exonuclease — nick transl. + Okazaki fragments

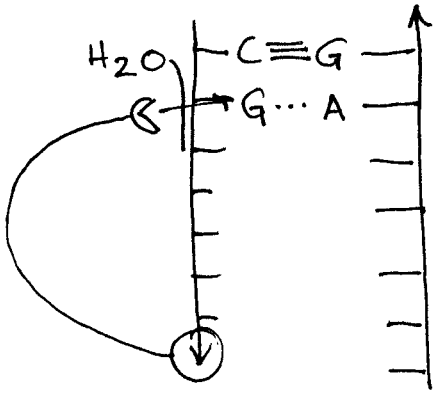


NT Activity:

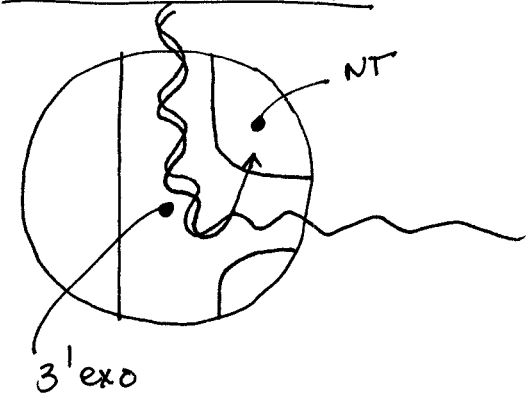


β-γ- bidentate complex

3' exo



What it looks like:



- Sites close together in 3D although $3.4 \times 7 \sim 25$ Å apart.
- Can hand off 3' exo'd chain to NT and start again.

5' exo : just mentioned Okazaki fragment maturation and DNA repair.

Back to Arkin : Replication

System protects against mutations to 10^{-11} to 10^{-12}

10^{3-4} BP specif. in NT

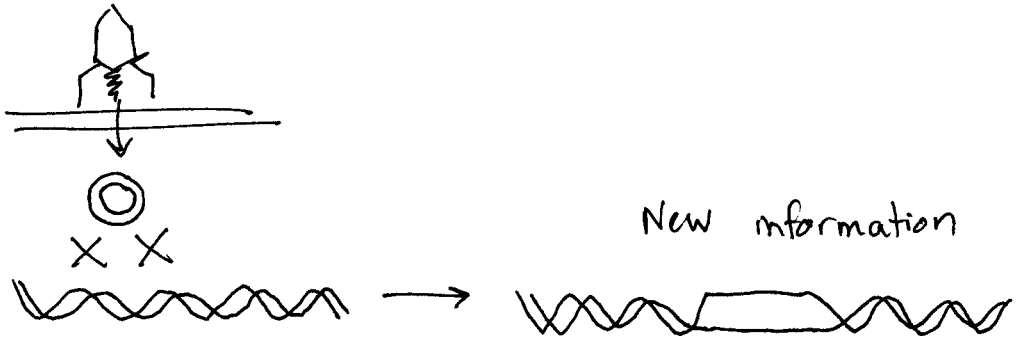
10^{3-4} 3' exo

10^{3-4} MMR

Horizontal Gene Transfer (Radman):

1. Vast pop. bact. some are MMR⊖
2. Environment changes → many die.
3. B. sub / P. aruginosa / E. coli etc. all together
4. HGT in MMR⊖ cells
   ↑ genes are a mosaic ⟹ acquired from other species
5. Pathways introduced
6. MMR⊖ tweaks to optimize for codon utilization
7. Acquire MMR gene from neighbor to re-aquire genetic stability

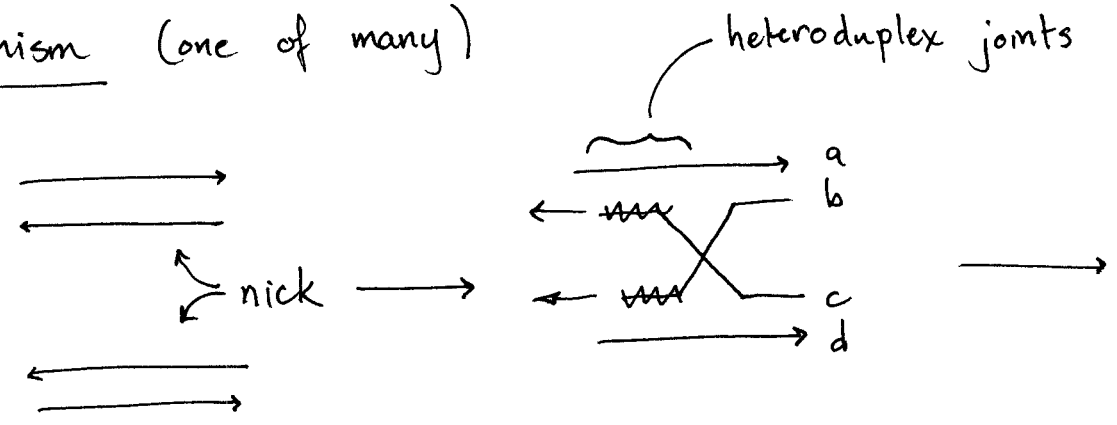
MMR prevents gene transcription from species to species:

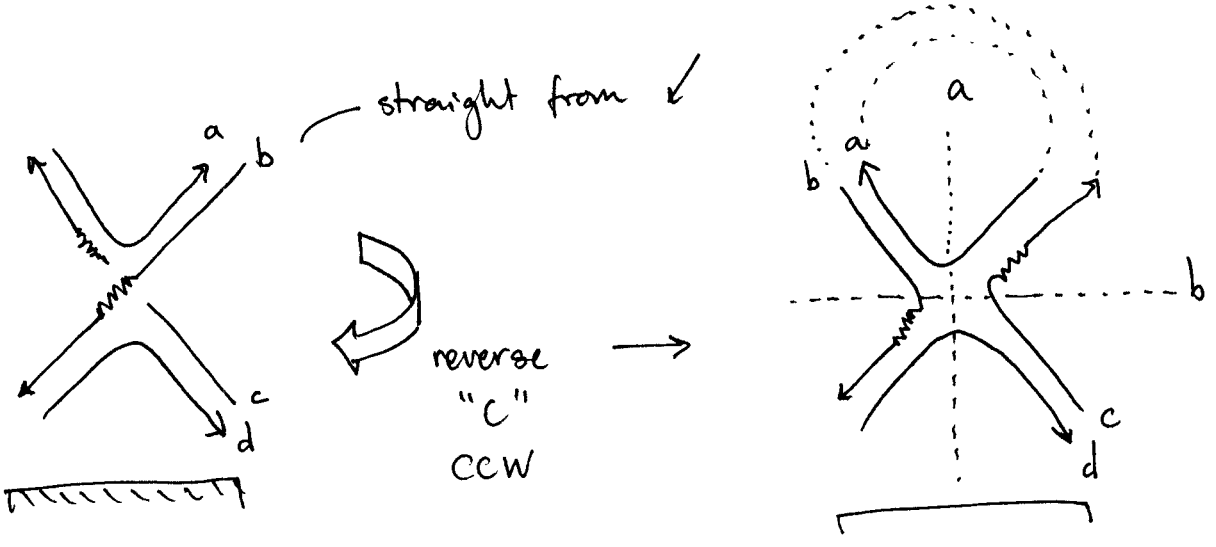


- insertion
- deletion
- inversion
- multi-point mutation

But: horizontal gene transfer gives vast opportunity for large-scale genetic change

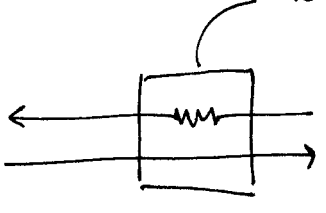
Mechanism (one of many)





a
→ insertion
plane
cleavage

b plane
cleavage



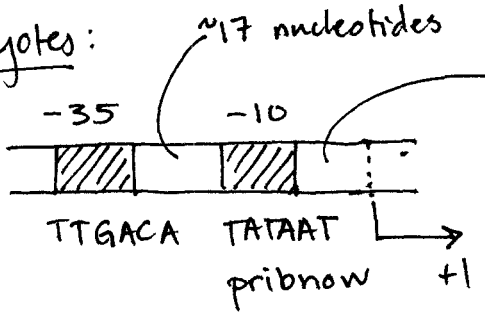
} MMR will homogenize
- could have lots MM.

Take-home point: MMR reverses above if too many MM — in absence MMR lots of mutations b/c error-prone

General Features of Promoter Architecture.

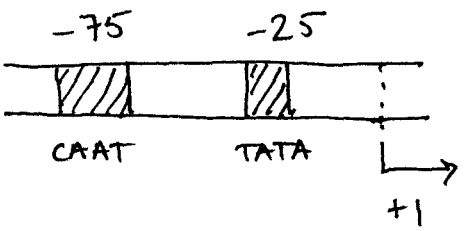
Promoter = site where polymerase binds

Prokaryotes:



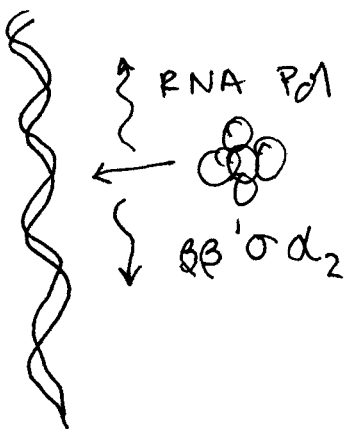
} segments here cause 10^3 x variation in promoter recognition by RNA Pol.

Eukaryotes:



NOTE: these 10^3 x variations are for constitutive genes (one way to have different expression levels)... (not really regulation)

How does pol. find promoter?



ρ-dep. and ρ-indep. termination

Close-up of Transcription: