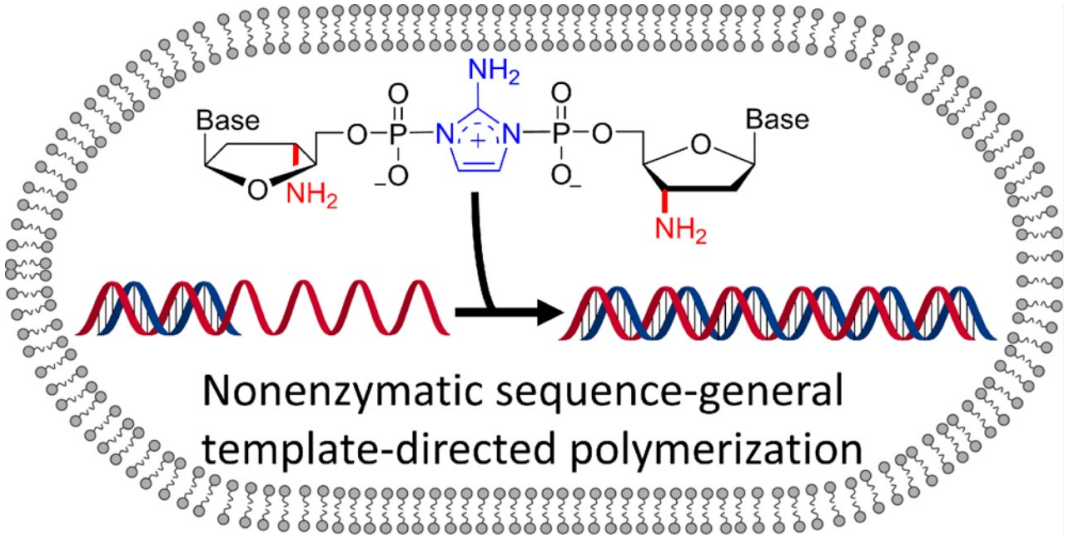
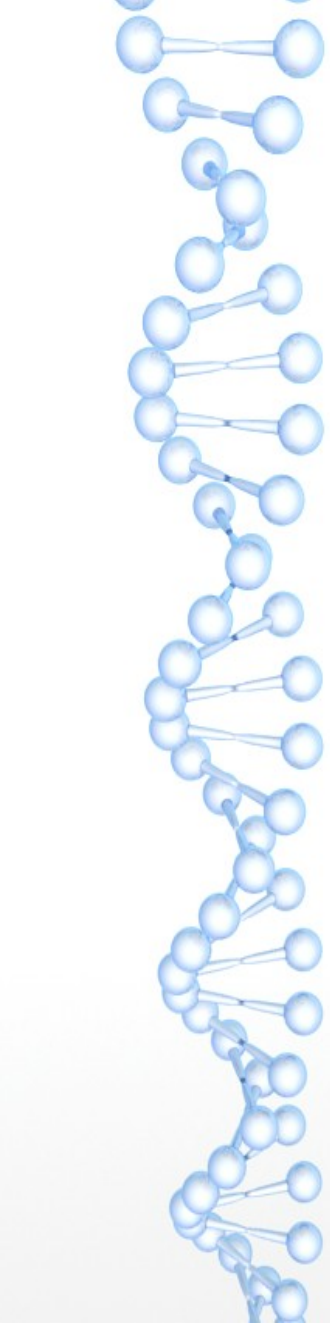
Replication Chemistry with Imidazole



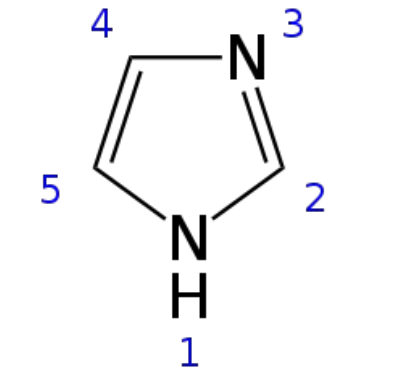
Talk in the physics seminar “Physics of early life”
with Prof. Braun, LMU, by Felix Dänekamp, 18.12.2020

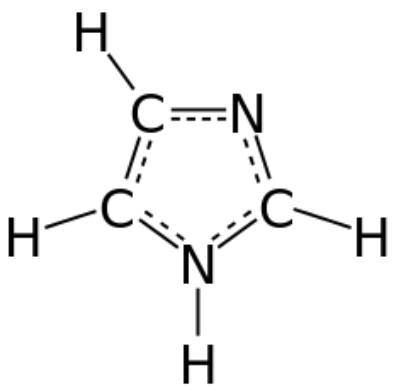


Replication without enzymes

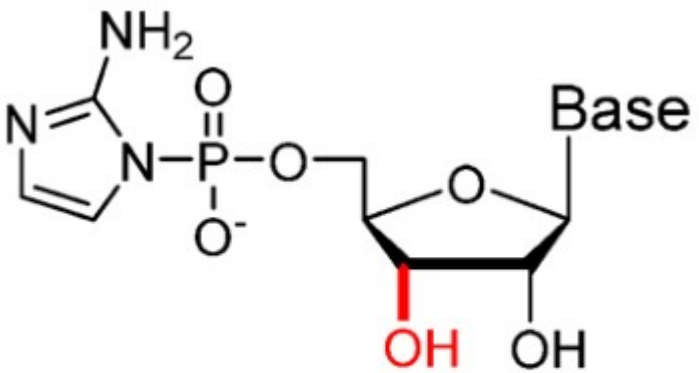
- 1. Activate the nucleotides, add ‘bridge’-molecules
- 2. Add ions to the environment
- 3. Alter the DNA structure

1. Imidazole as an activator / bridge

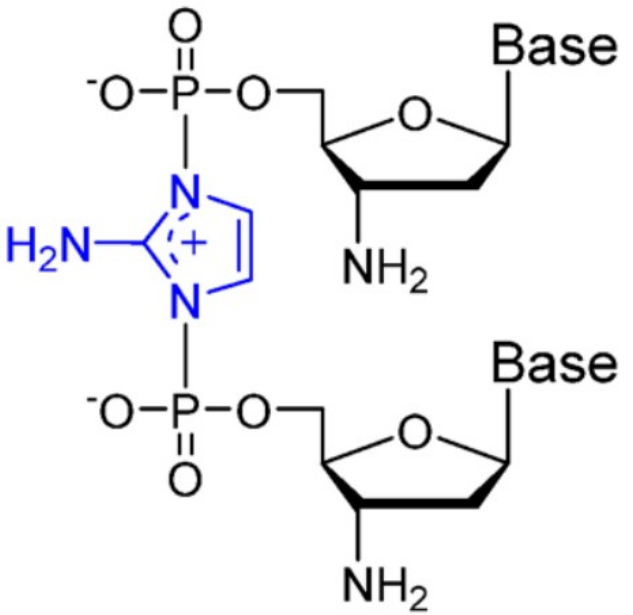




Imidazole

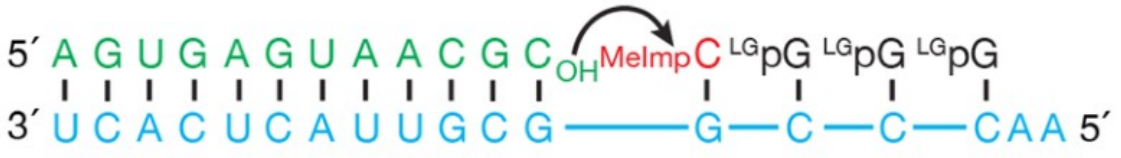


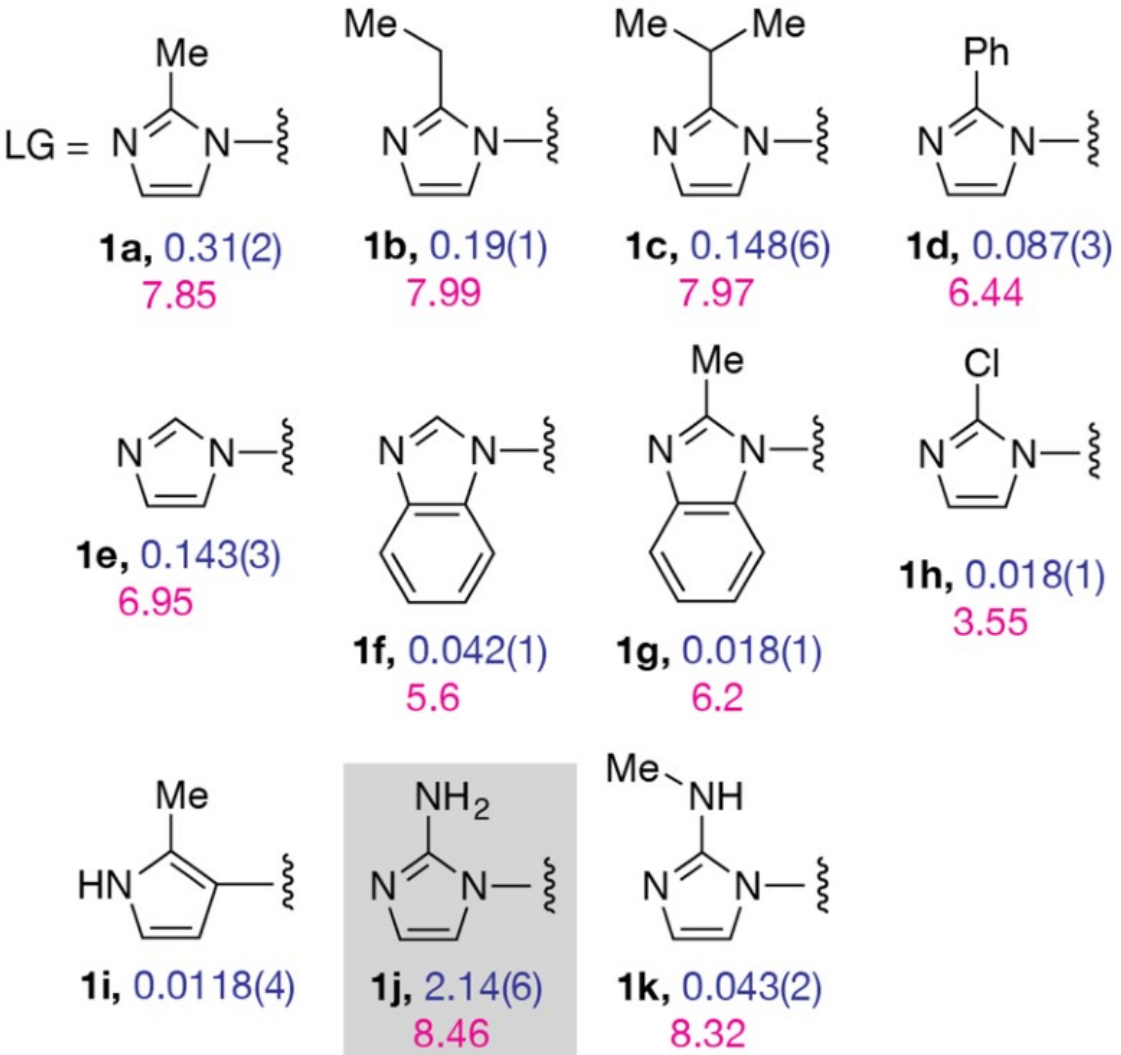
2AI-activated ribonucleotide
(RNA monomers)



2-aminoimidazolium bridged
3'-NP dinucleotide

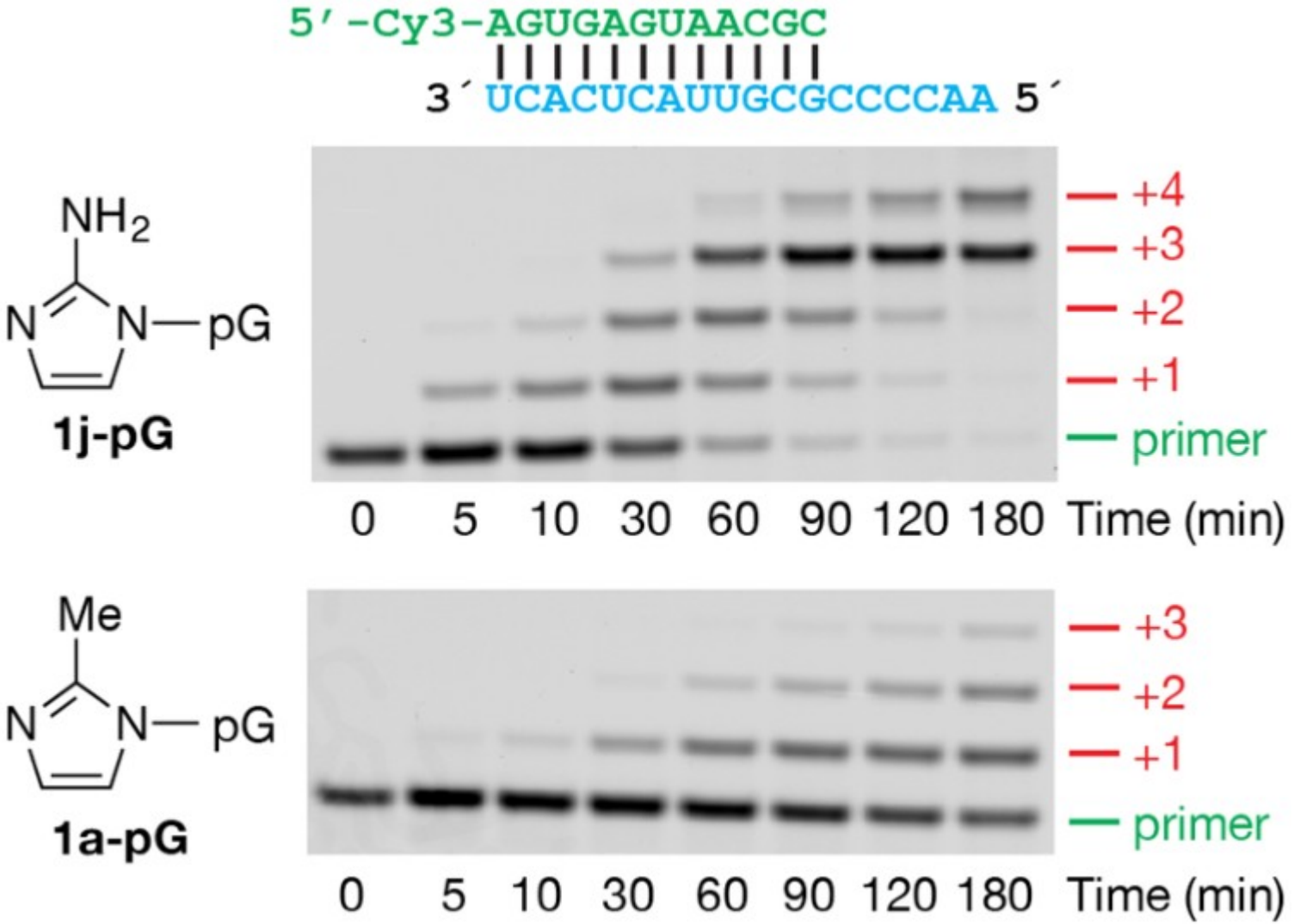
Which imidazole?



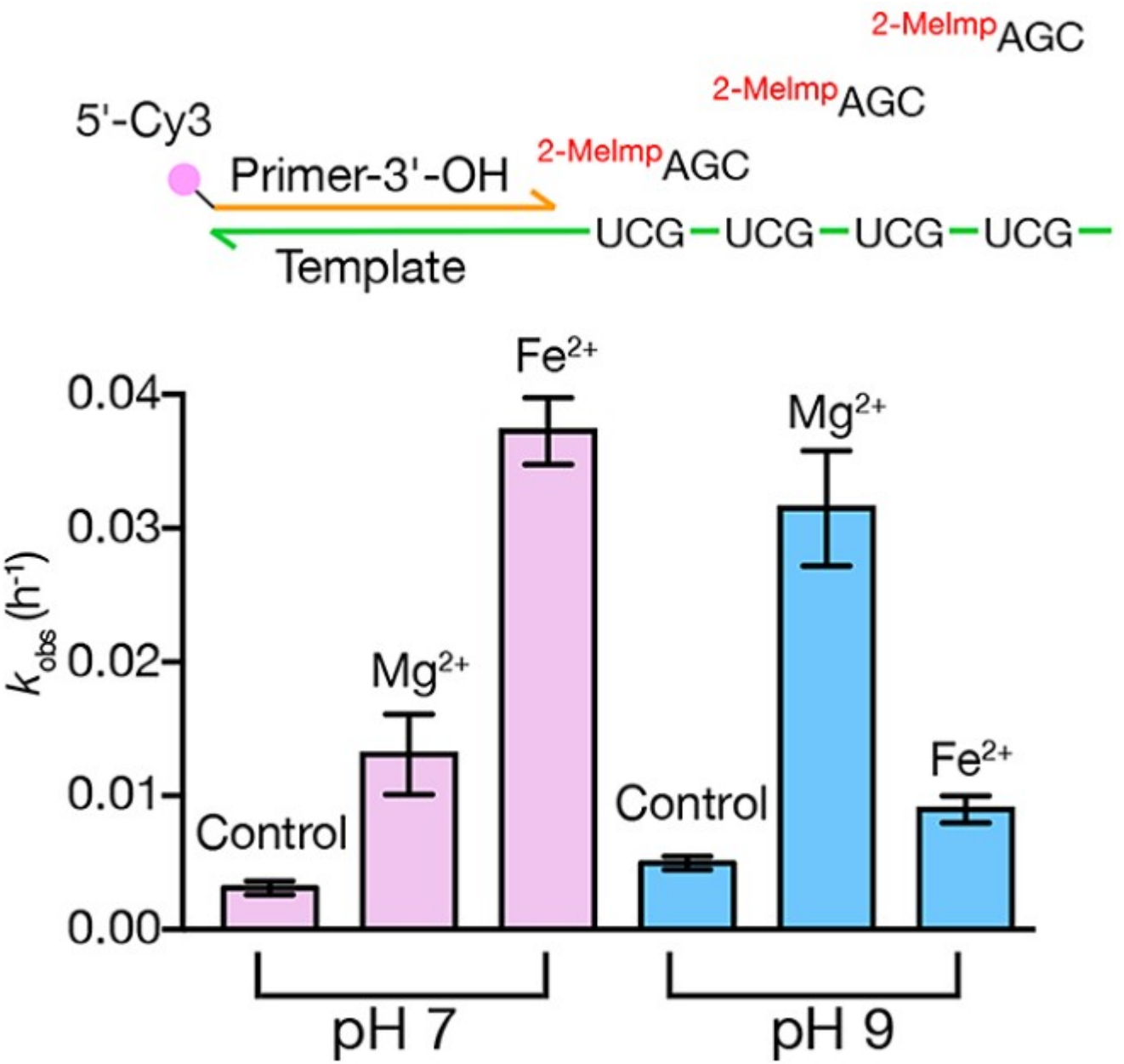


Blue: Mean rate of reaction (#/hour)

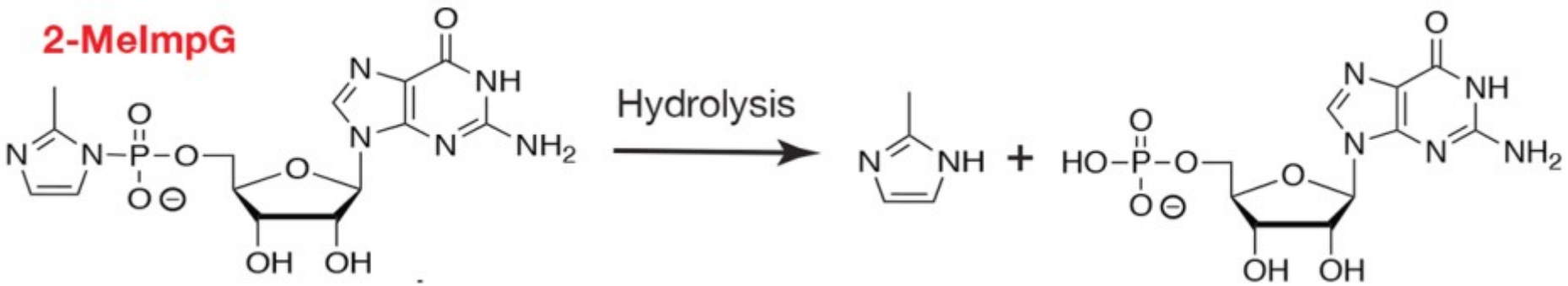
Detection by electro-phoresis

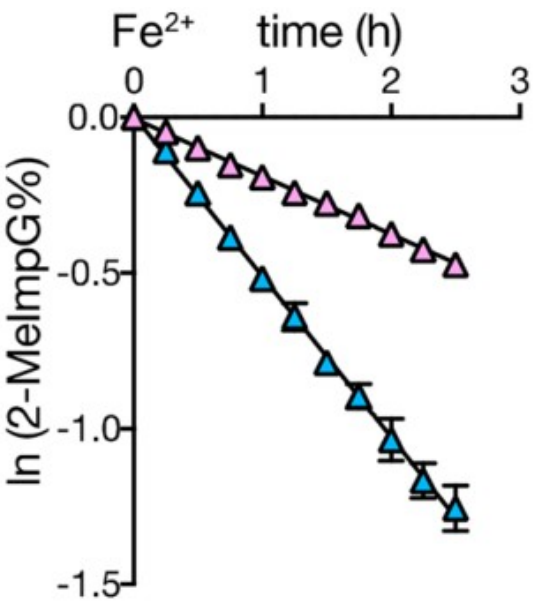


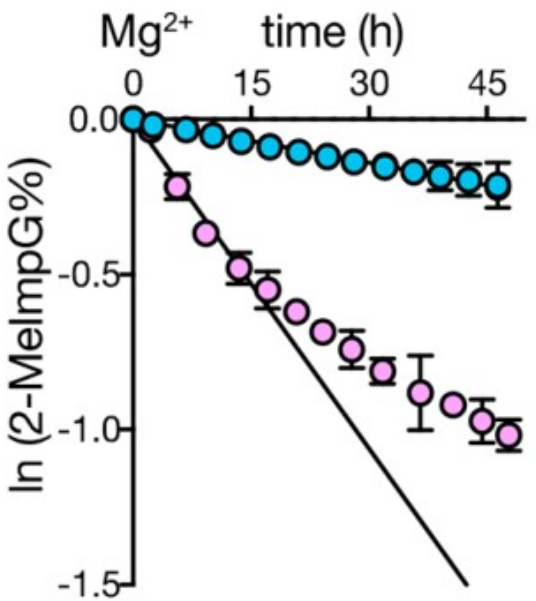
2. Ionic environment

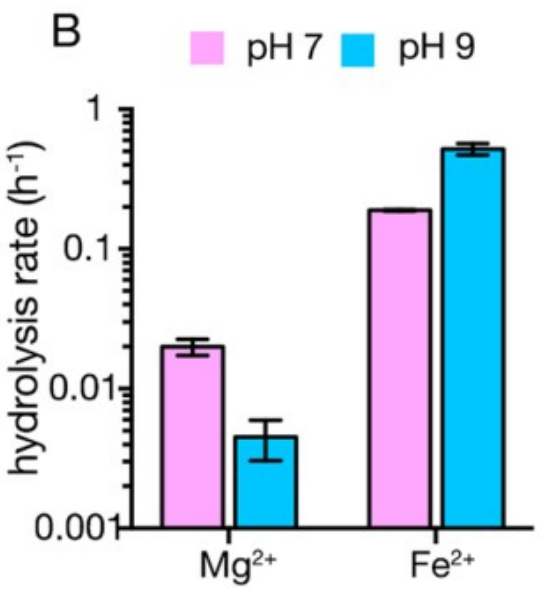


Hydrolysis

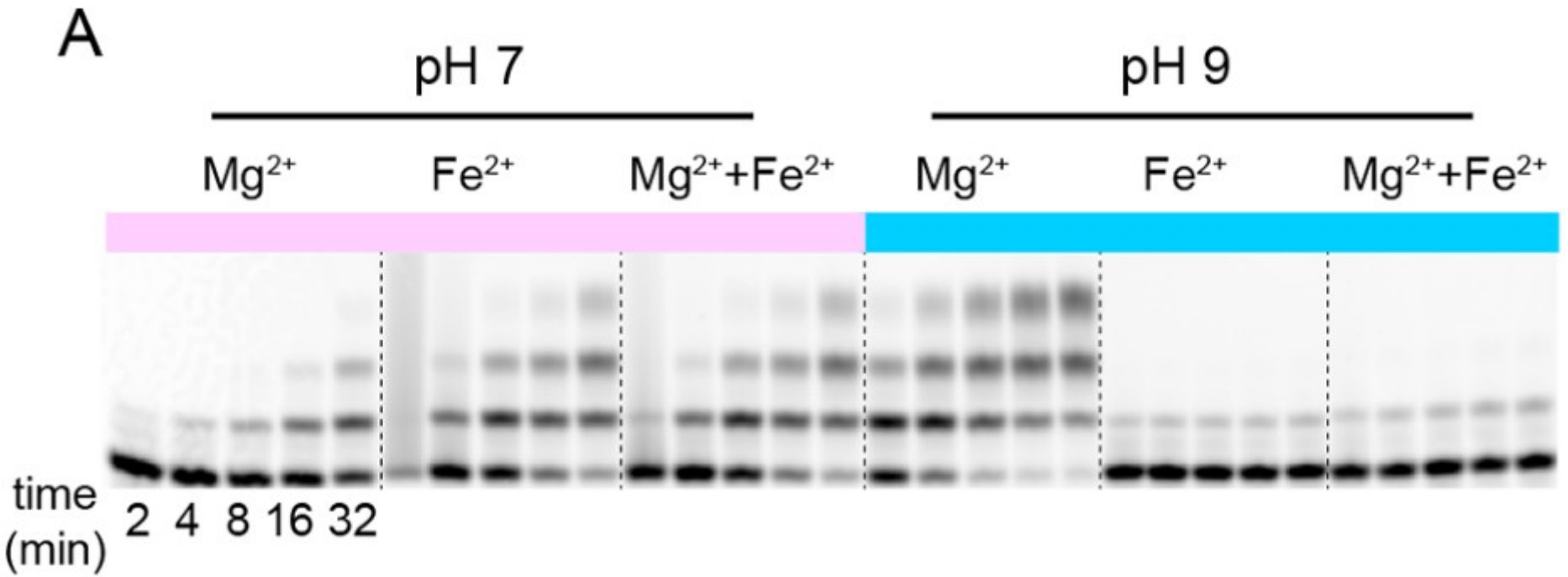

2-MeImpG
Hydrolysis
OH OH
OH OH


Fe2+ time (h)
0 1 2 3
0.0
-0.5
-1.0
-1.5
ln (2-MeImpG%)

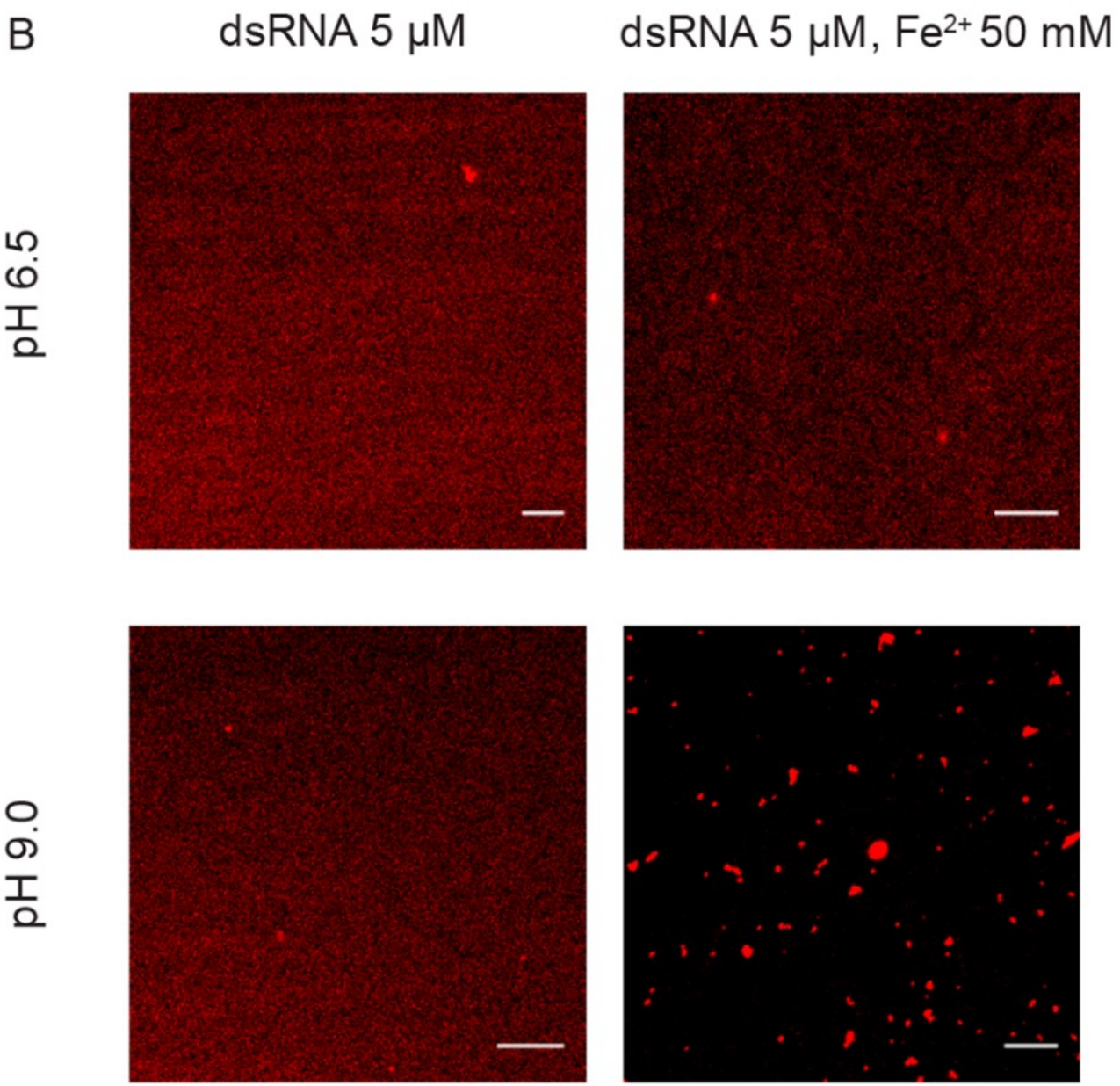

Mg2+ time (h)
0 15 30 45
0.0
-0.5
-1.0
-1.5
ln (2-MeImpG%)


B
pH 7
pH 9
1
0.1
0.01
0.001
hydrolysis rate (h-1)
Mg2+
Fe2+

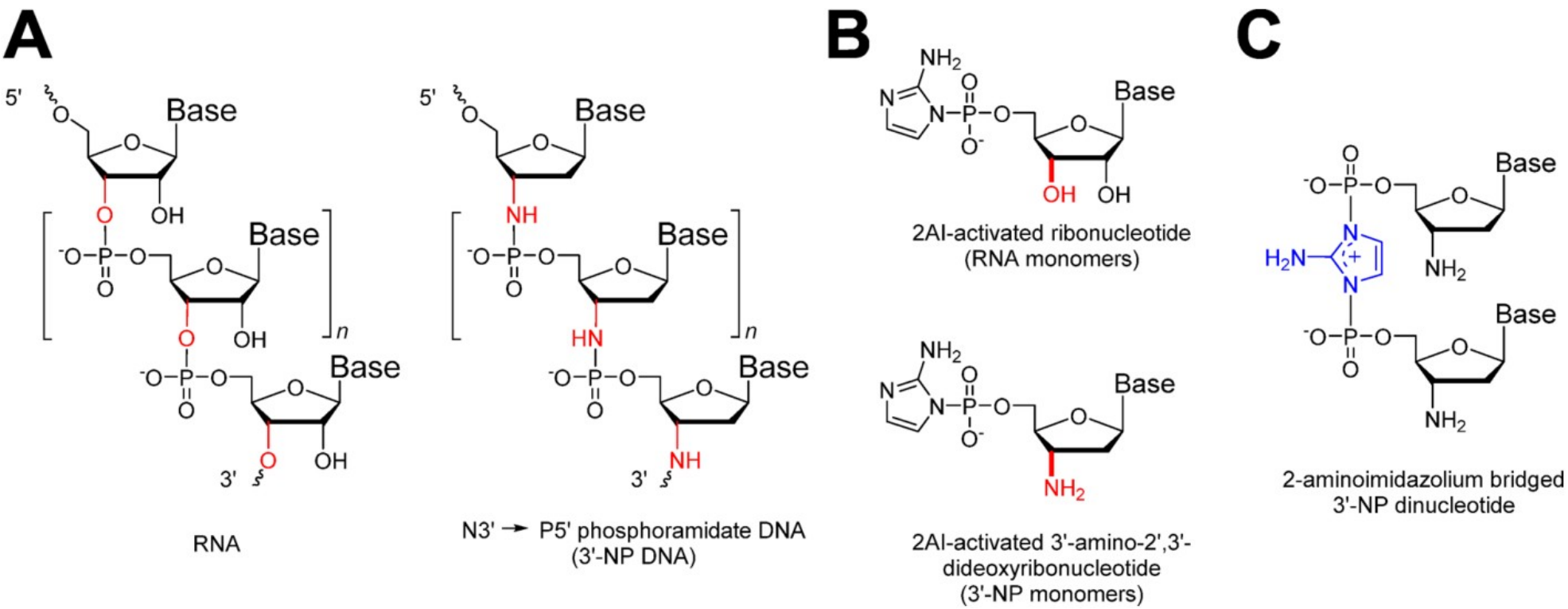
Iron as an inhibitor



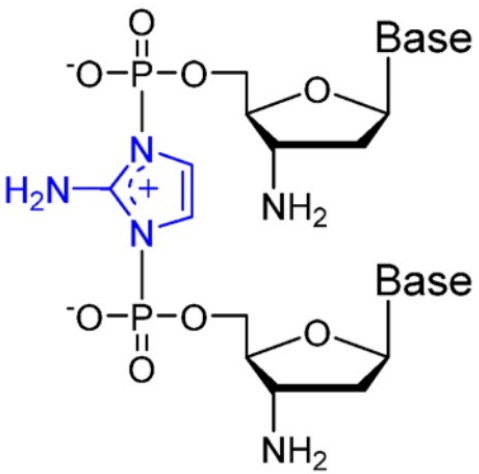
Explanation: Clumping



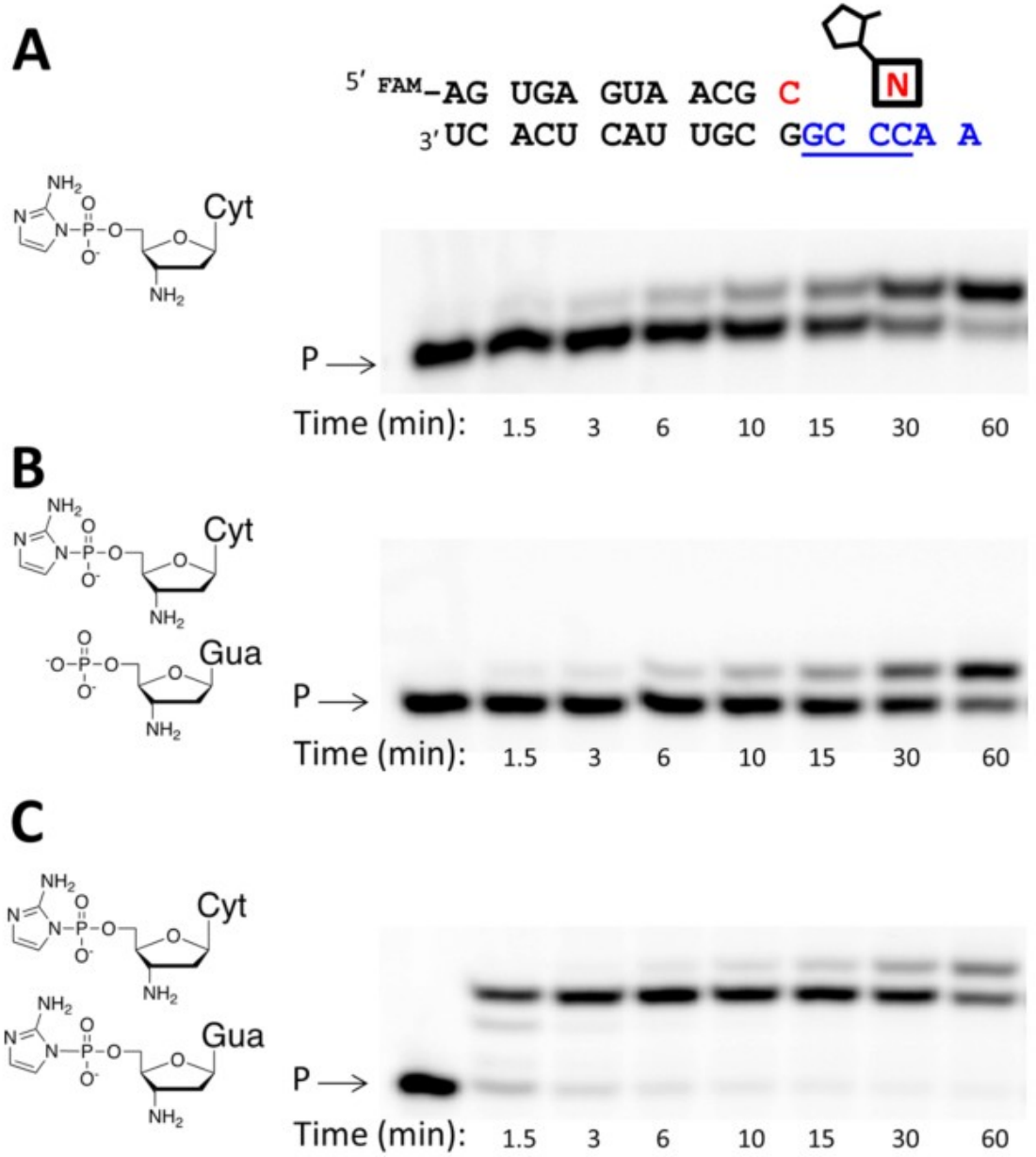
3. Alternative DNA



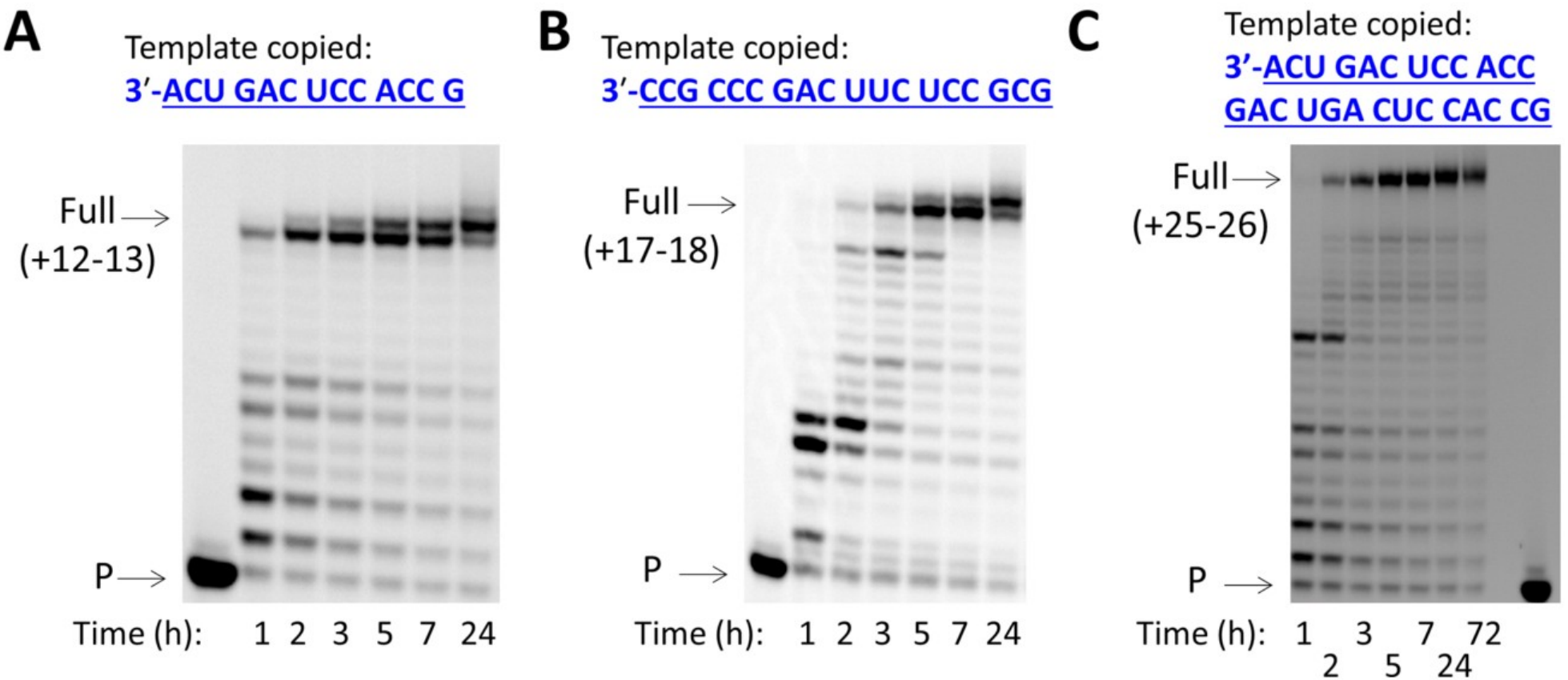
Bridging: dinucleotide intermediates



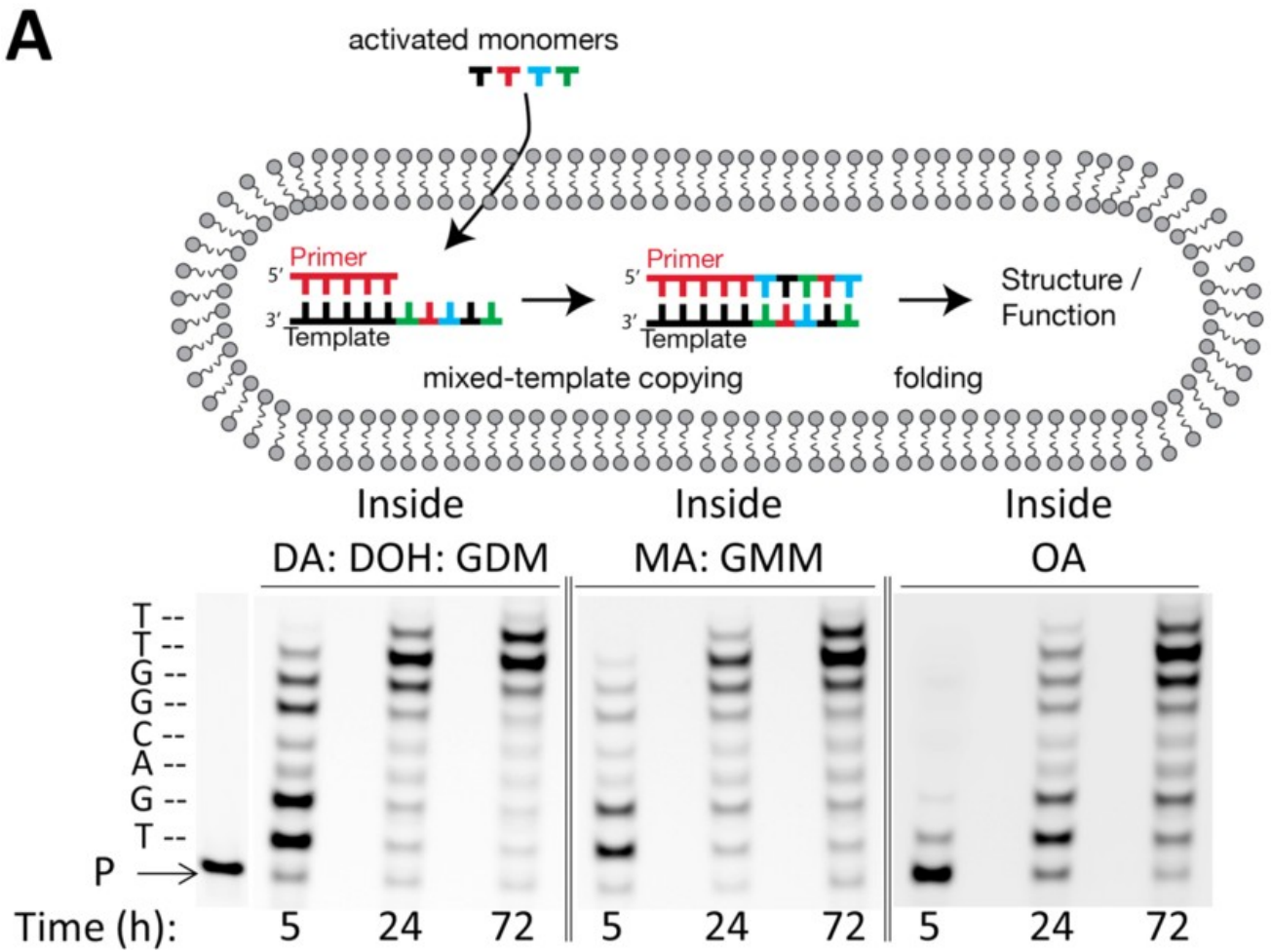
2-aminoimidazolium bridged
3'-NP dinucleotide

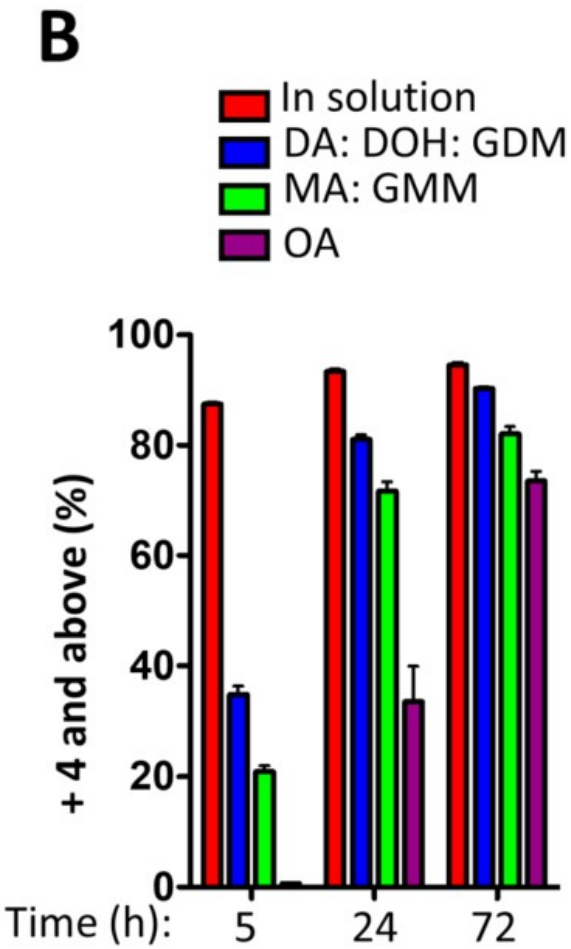


Long templates

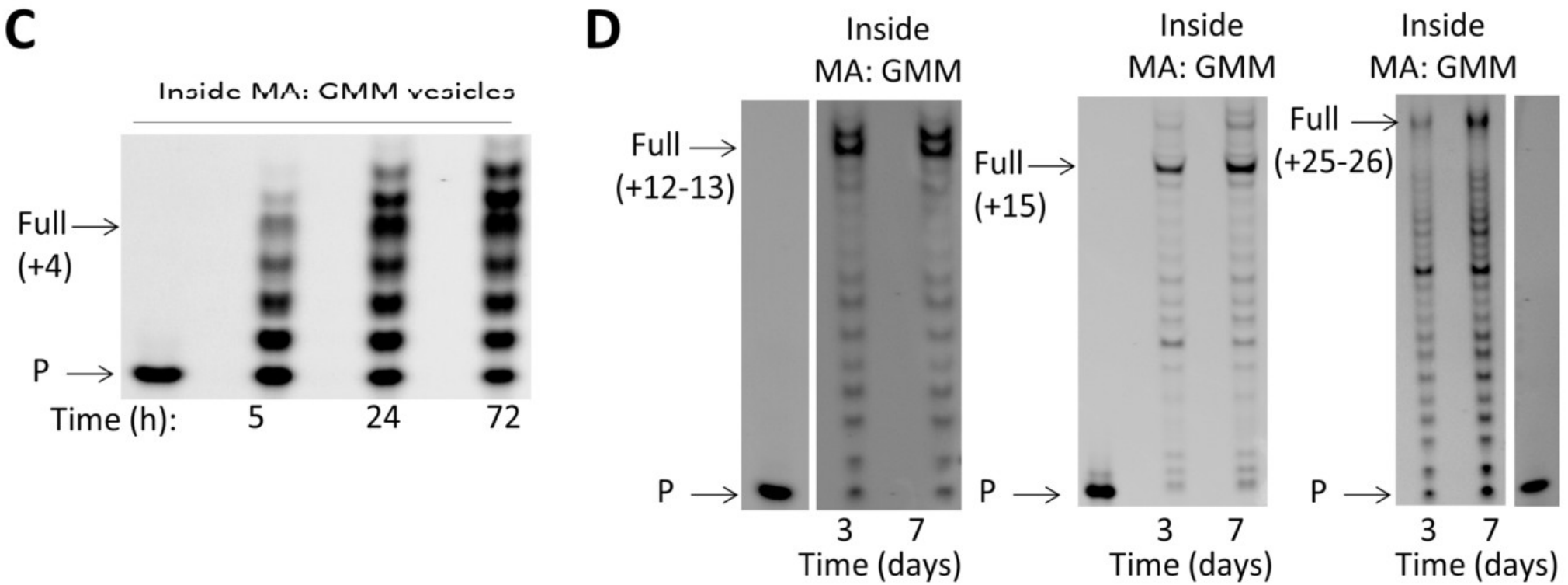


In-cell reactions



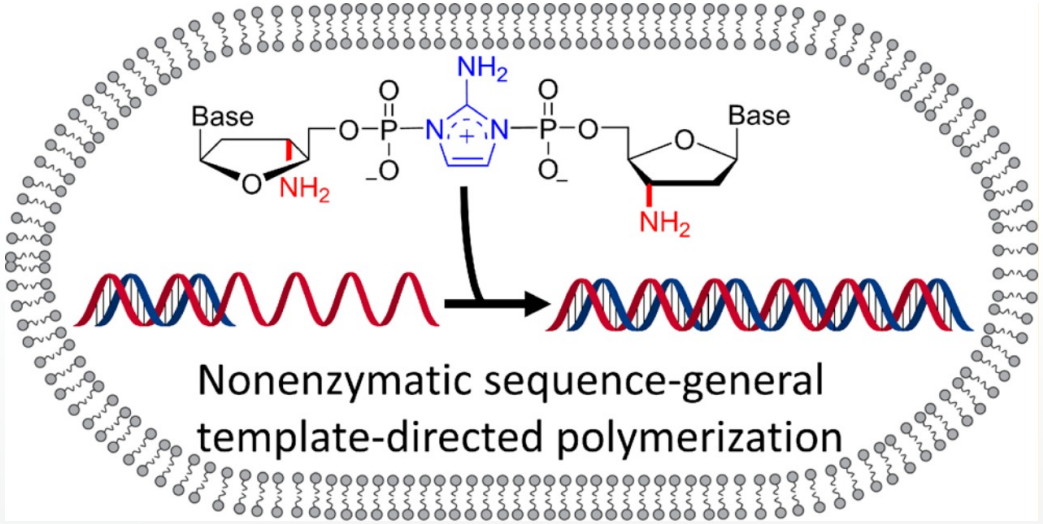


Random sequences and long in-cell templates



Conclusion / Outlook

- Promising pathways to early life
- Some sequences are harder to copy
- Need nutrient influx from the outside
- Need a mechanism to remove waste
- Secondary structure?



References

- Enhanced Nonenzymatic RNA Copying with 2-Aminoimidazole Activated Nucleotides, Li Li *et al.*, *Journal of the American Chemical Society* **2017** *139* (5), 1810-1813, DOI: 10.1021/jacs.6b13148
- Catalysis of Template-Directed Nonenzymatic RNA Copying by Iron(II), Lin Jin *et al.*, *Journal of the American Chemical Society* **2018** *140* (44), 15016-15021. DOI: 10.1021/jacs.8b09617
- Nonenzymatic Template-Directed Synthesis of Mixed-Sequence 3′-NP-DNA up to 25 Nucleotides Long Inside Model Protocells, Derek K. O'Flaherty, Lijun Zhou, and Jack W. Szostak, *Journal of the American Chemical Society* **2019** *141* (26), 10481-10488, DOI: 10.1021/jacs.9b04858

All figures are taken from those papers, with the exception of the imidazole sketches, which are available on Wikipedia for free. The papers loosely correspond to each section of the presentation (in this order).