

Using Lasers to Examine the Molecular Machinery of Life

Everett A. Lipman (#65/68; 1.47%)

Department of Physics
University of California, Santa Barbara



Using Lasers to Examine the Molecular Machinery of Life

Everett A. Lipman (#65/68; 1.47%)

Department of Physics
University of California, Santa Barbara



Using Lasers to Examine the Molecular Machinery of Life

Everett A. Lipman (#65/68; 1.47%)

Department of Physics
University of California, Santa Barbara



Johann Müller



Friedrich Leibniz (Leipzig 1622)



Jakob Thomasius (Leipzig 1643)



Otto Mencke (Leipzig 1665)



Johann Wichmannshausen (Leipzig 1685)



Christian August Hausen (Halle–Wittenberg 1713)



Abraham Gotthelf Kästner (Leipzig 1739)



Johann Christian Polykarp Erxleben (Göttingen 1767)



Christian Ehrenfried Von Weigel (Göttingen 1771)

Dissertation: *Observationes circa vermes intestinales*
“Father of helminthology”



Karl Asmund Rudolphi (Greifswald 1795)



Johannes Peter Müller (Bonn 1822)



Hermann Ludwig Ferdinand von Helmholtz (Berlin 1842)



Albert Abraham Michelson (Berlin 1882)



Henry Gordon Gale (Chicago 1899)



William Ralph Smythe (Chicago 1921)



Charles Hard Townes (Caltech 1939)



All of us!

Townes and Colleague at Mt. Wilson Observatory

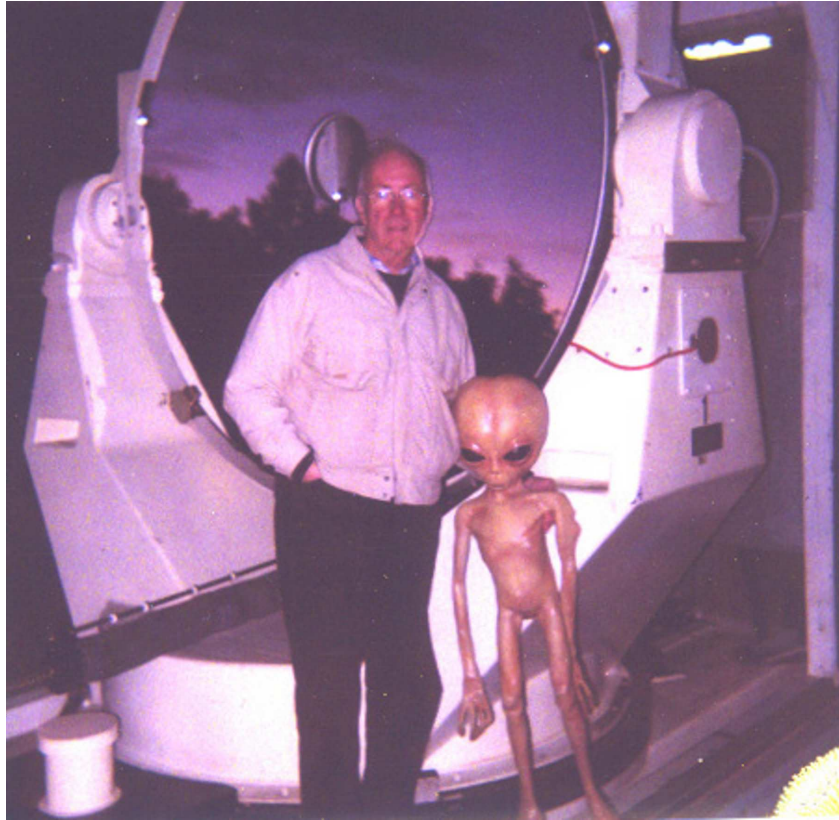
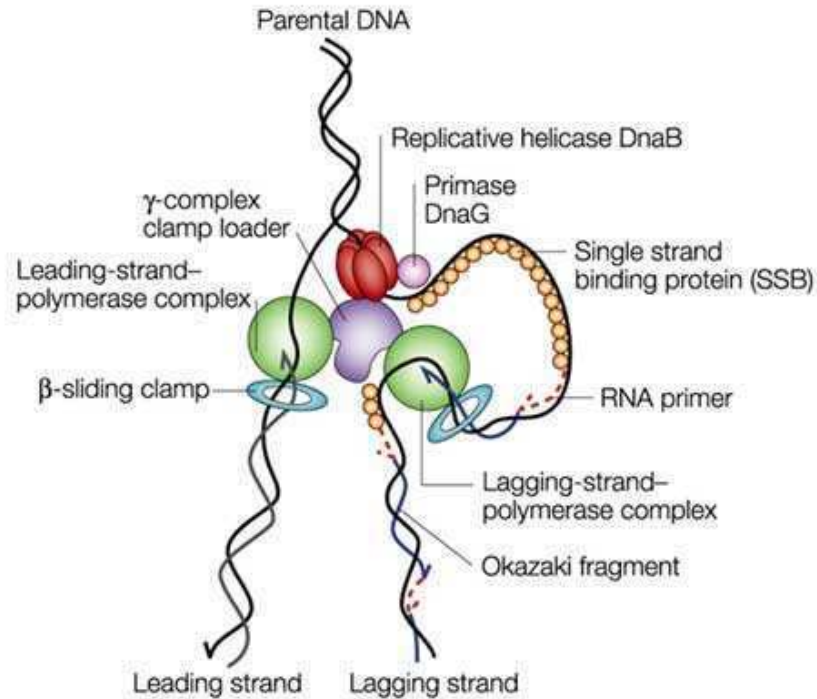


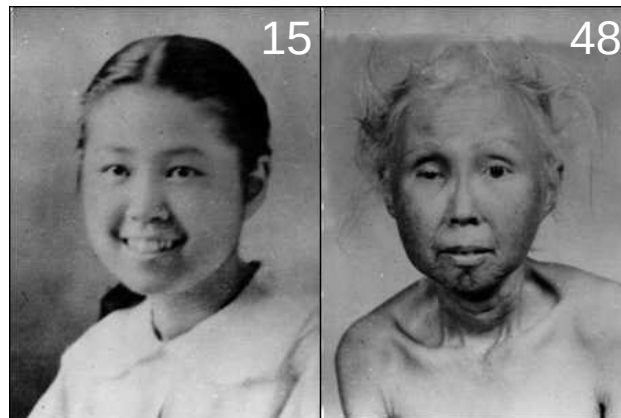
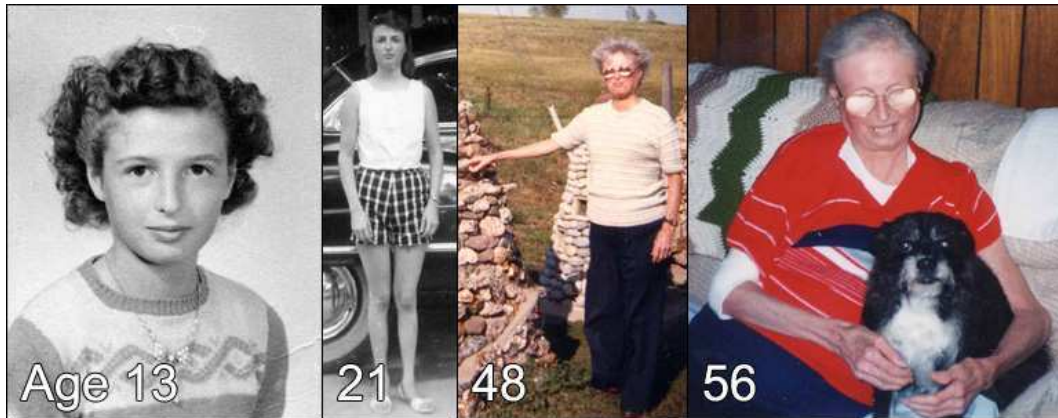
Photo by David Hale

E. coli Replisome



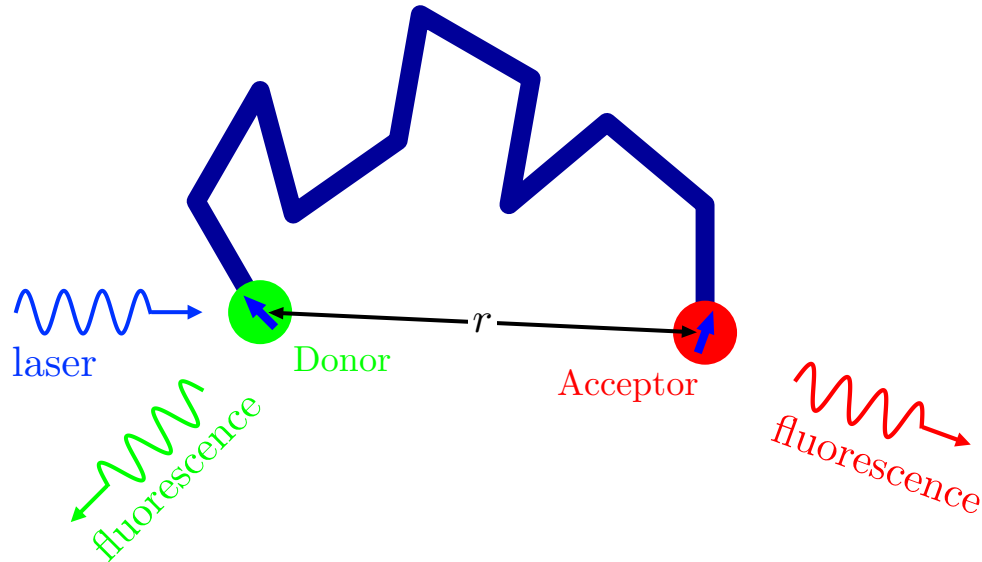
Peter McGlynn and Robert G. Lloyd
Nature Reviews Molecular Cell Biology **3**, 859 (2002)

Werner Syndrome (helicase mutation)



University of Washington Department of Pathology
C.J. Epstein, et al. Medicine 45, 177 (1966)

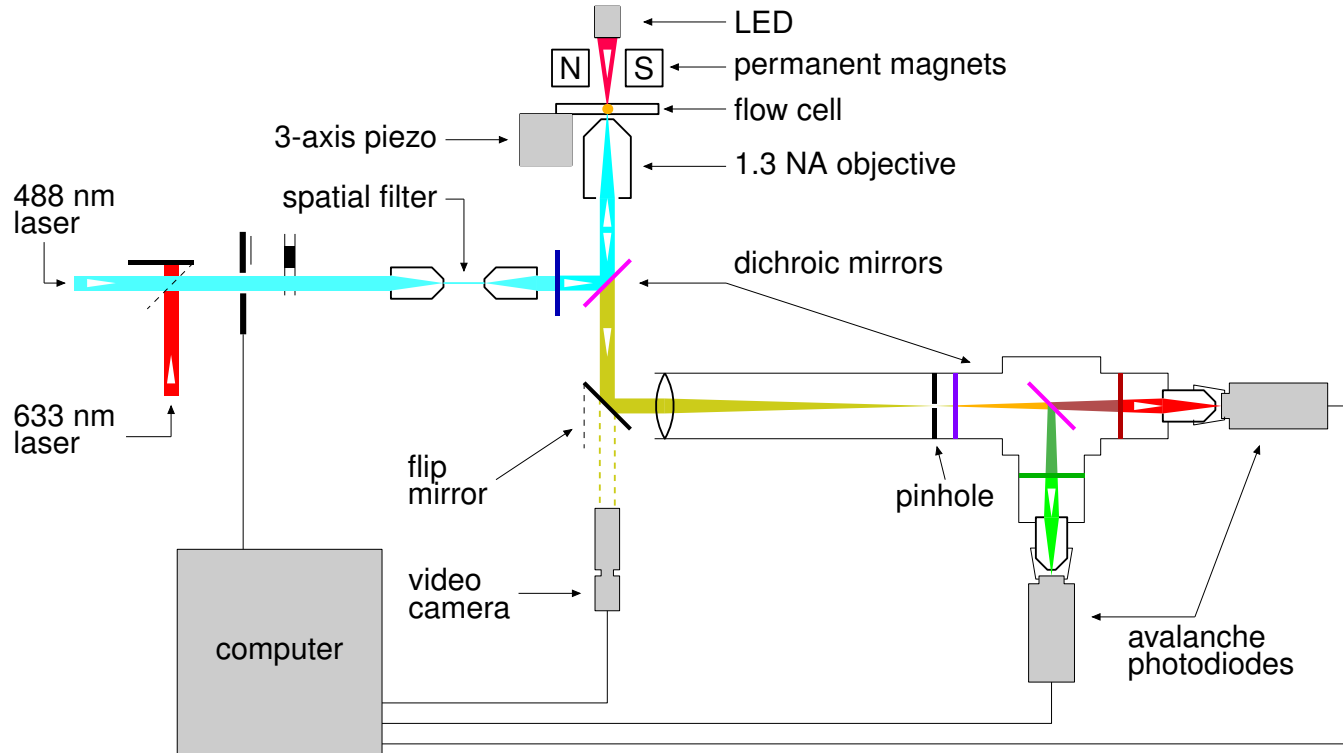
Förster Resonance Energy Transfer



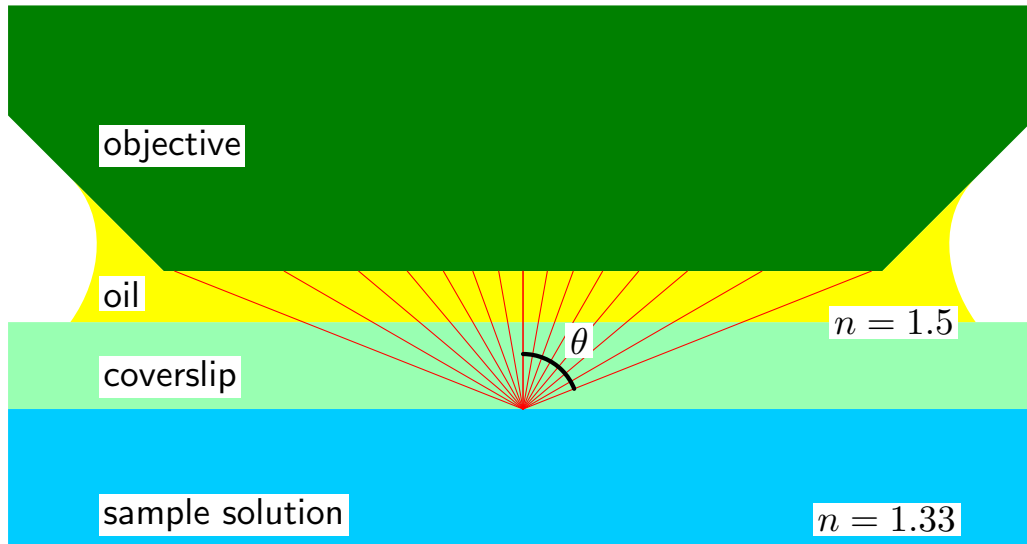
Ideally, the *energy transfer efficiency*

$$E = \frac{n_a}{n_a + n_d} \quad \begin{array}{l} n_a: \text{number of acceptor photons.} \\ n_d: \text{number of donor photons.} \end{array}$$

Single-Molecule Fluorescence Instrument



High Numerical Aperture Light Collection

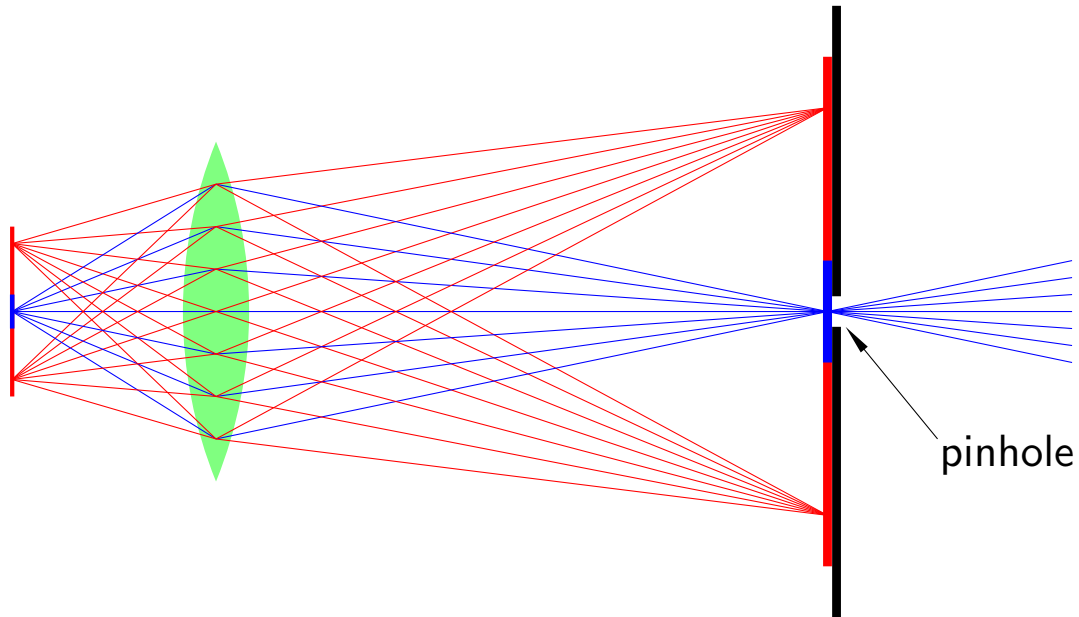


$$\theta = 69^\circ$$

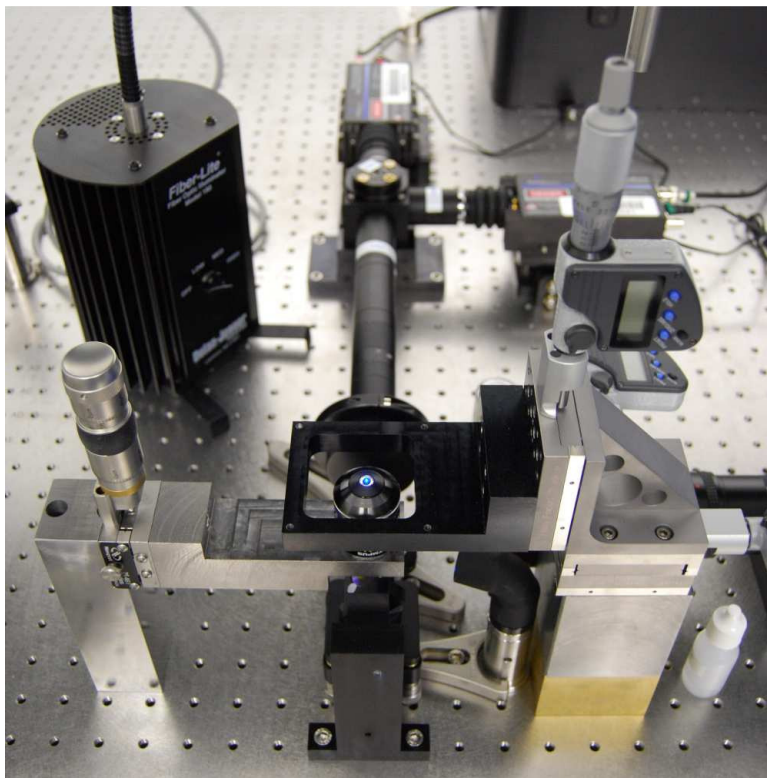
$$\text{N.A.} = n \sin \theta = 1.4$$

$$\text{Collection} \approx 32\%$$

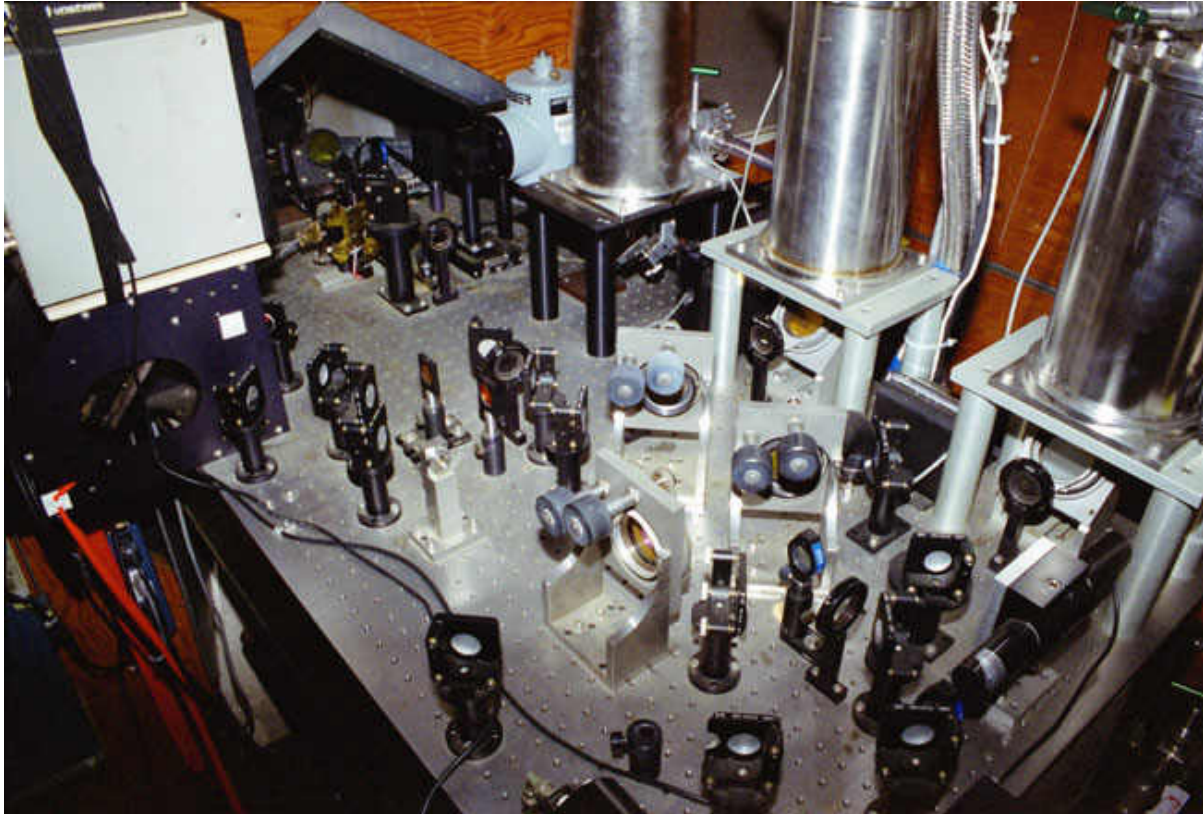
Confocal Imaging



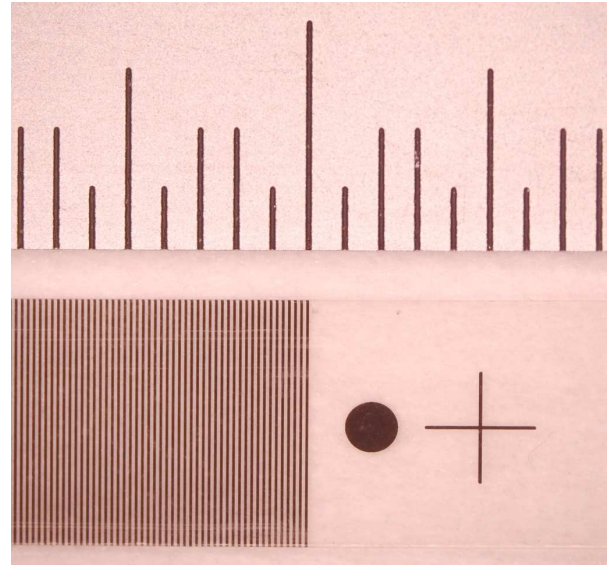
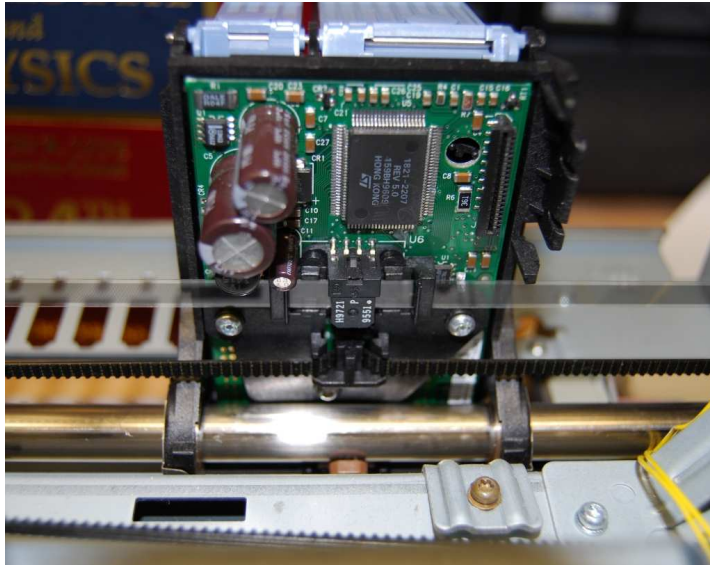
Single-Molecule Fluorescence Instrument



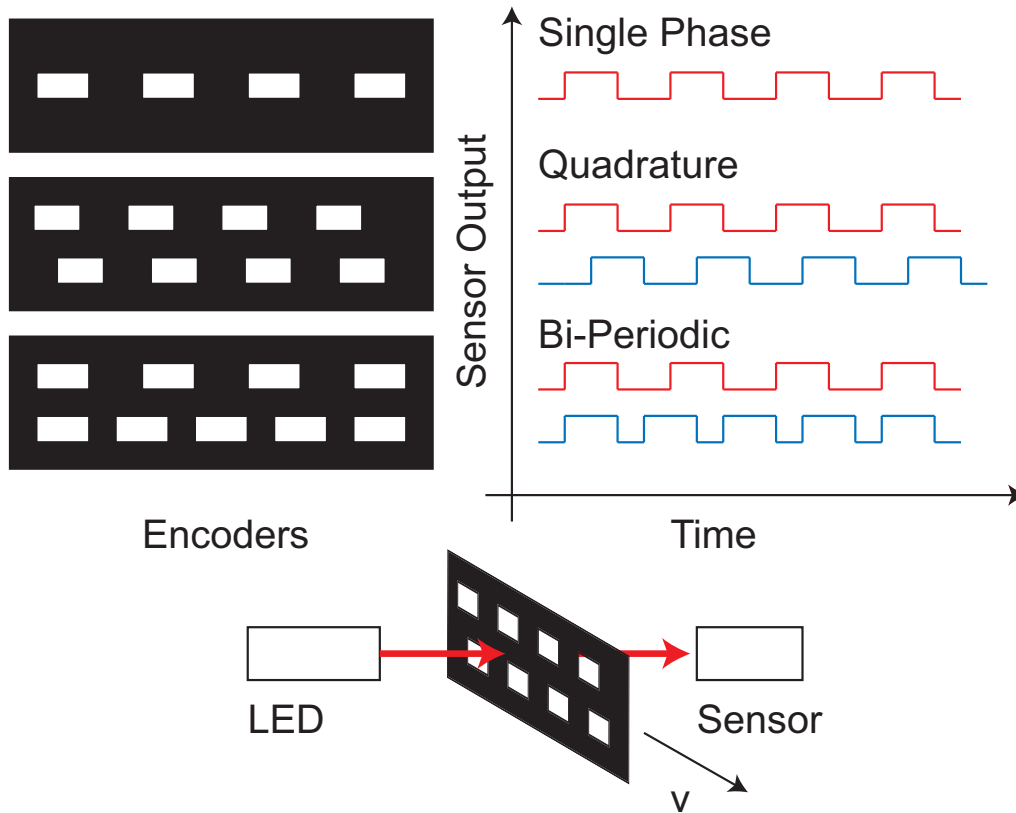
ISI Telescope Optical Table



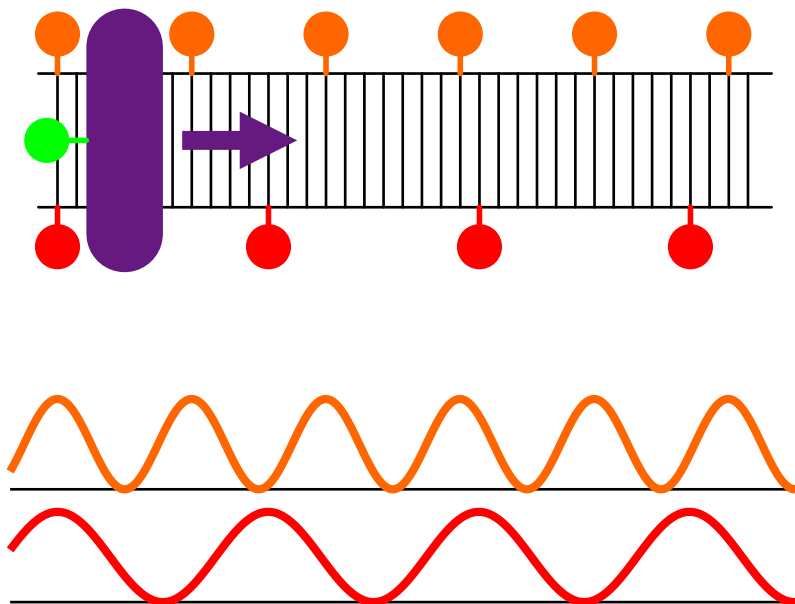
Inkjet Printer Optical Encoder



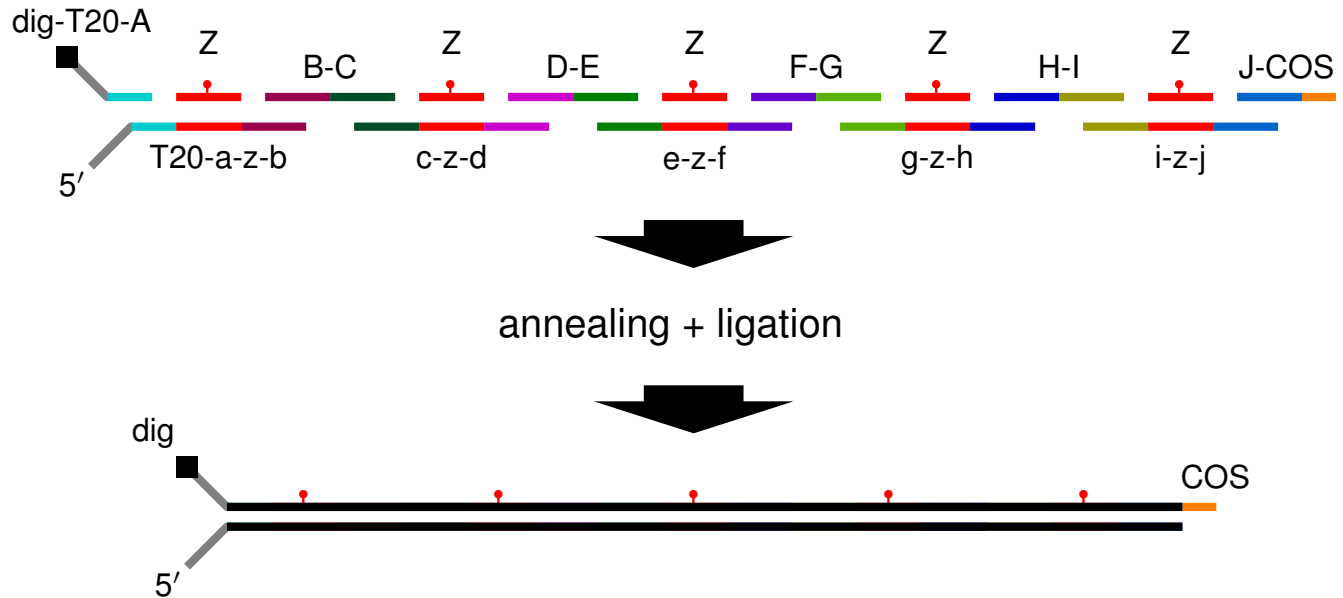
Linear Optical Encoder



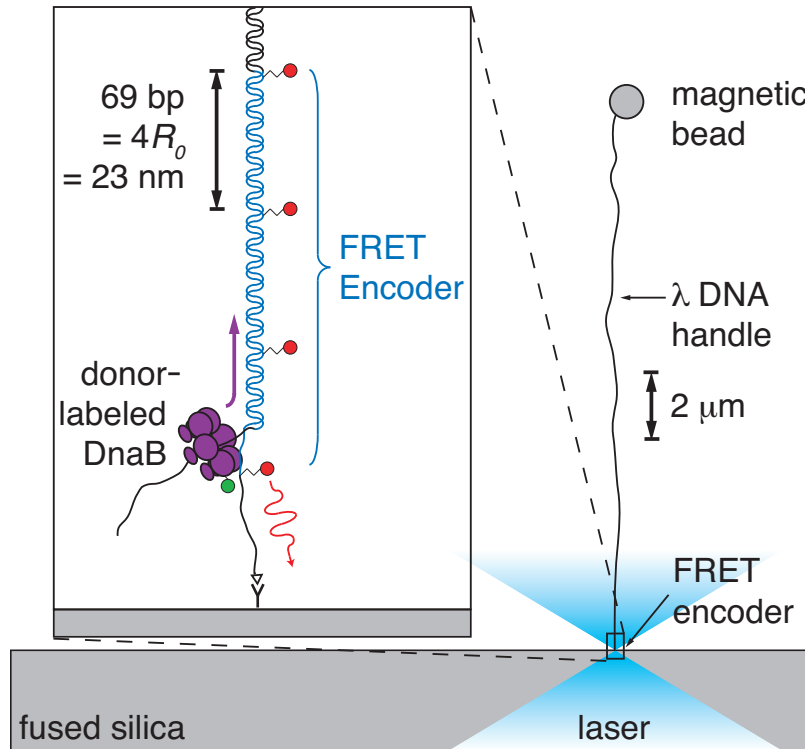
Single-Molecule Encoder Concept



Directed Self-Assembly of an Encoder

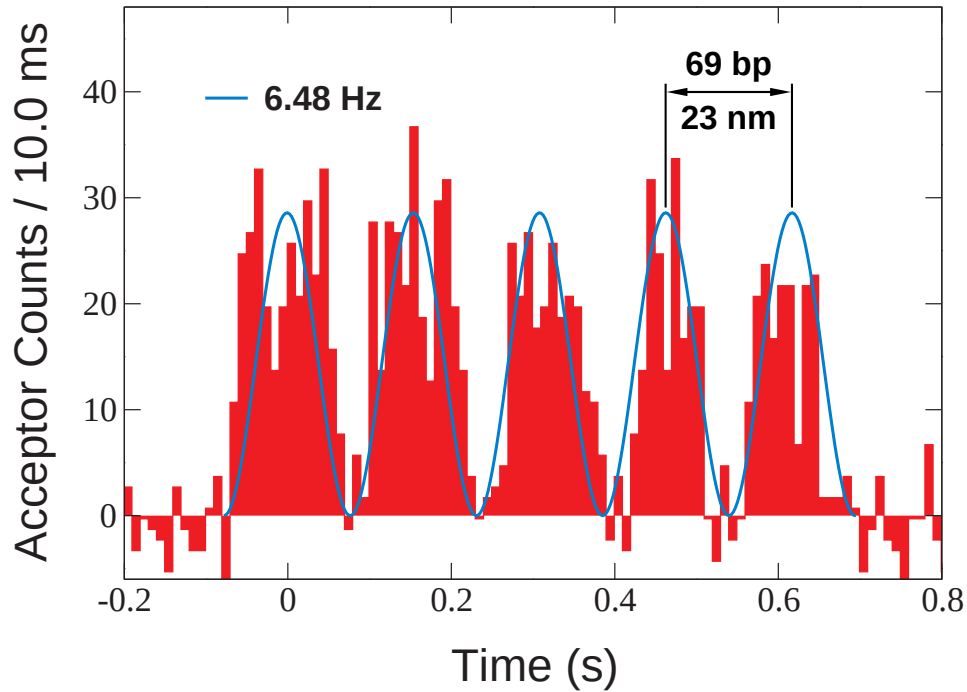


DnaB Helicase FRET Encoder Experiment



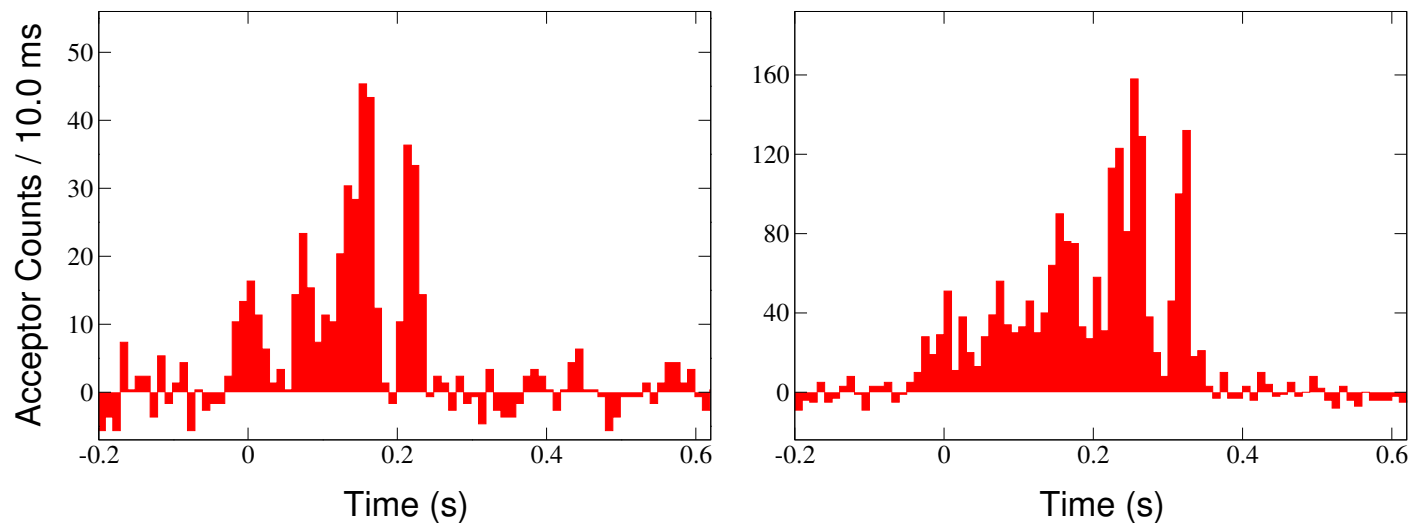
C.E. Wickersham, et al. *Nano Lett.* **10**, 1022 (2010)

DnaB Encoder Data with Least-Squares Overlay



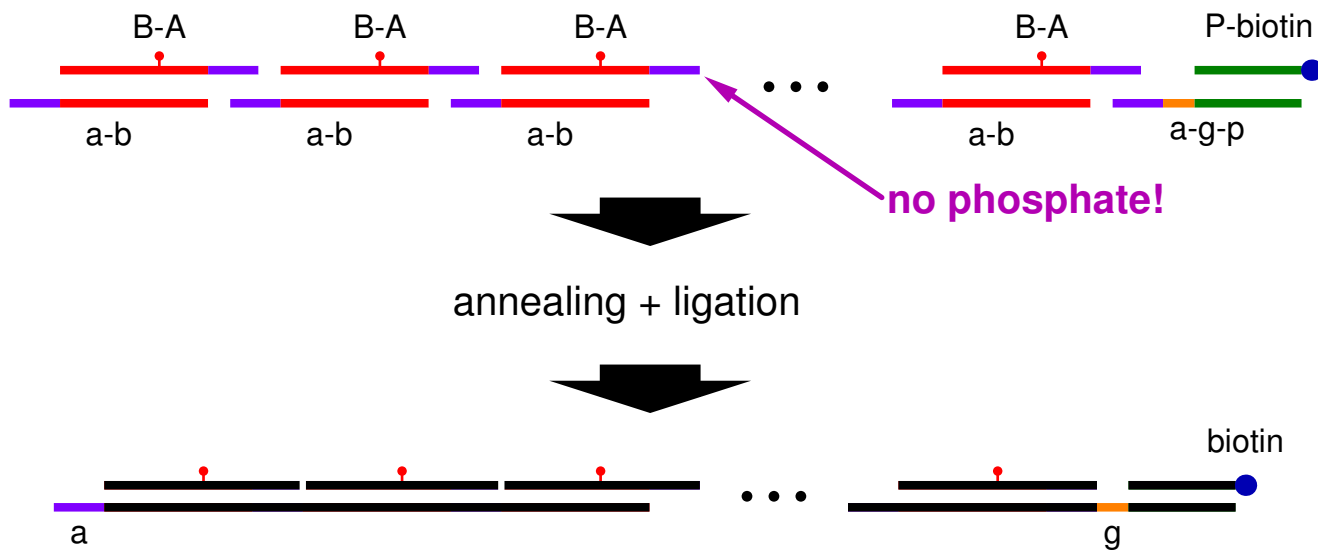
C.E. Wickersham, et al. *Nano Lett.* **10**, 1022 (2010)

FRET Encoder Data Exhibiting Modulation

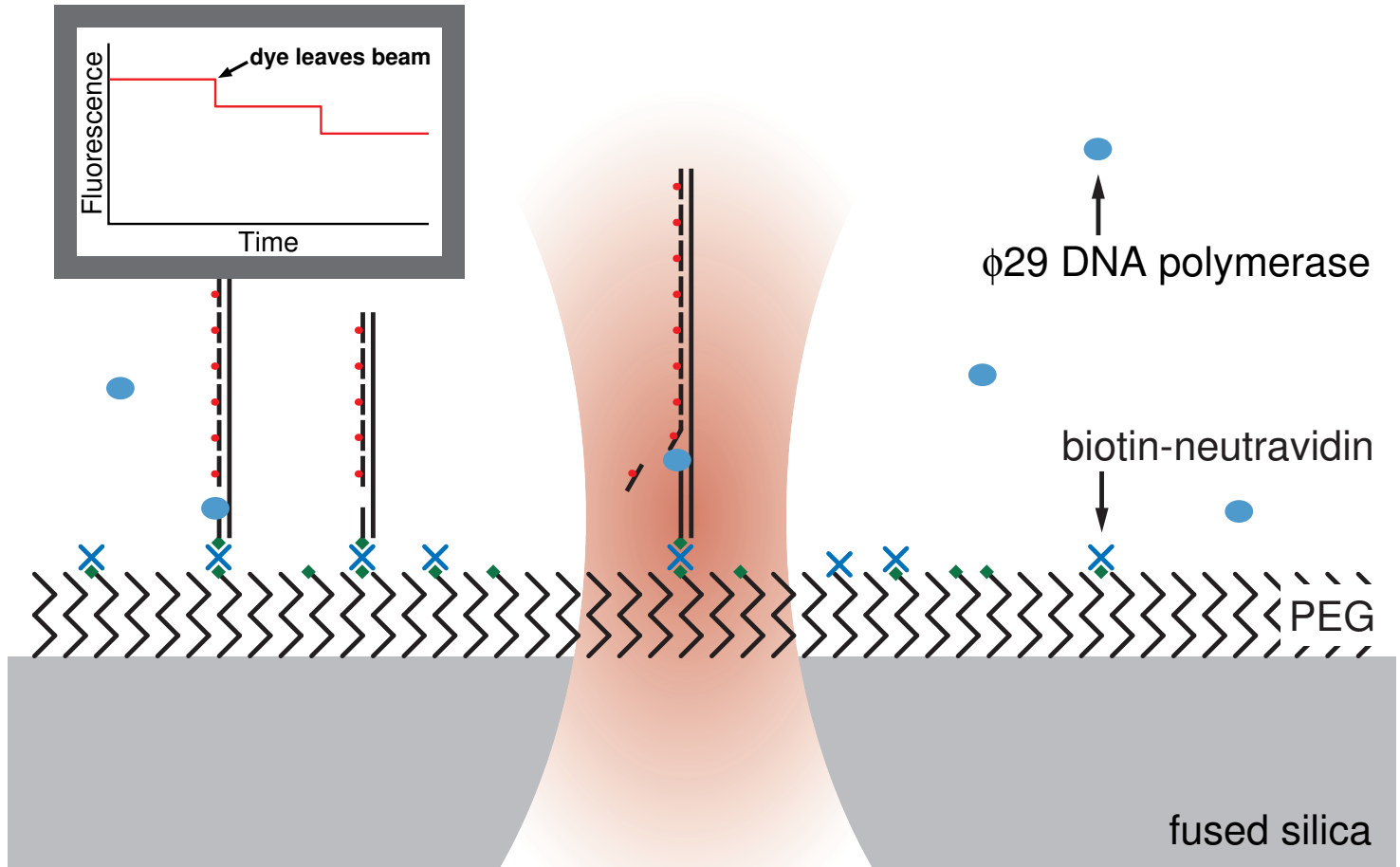


C.E. Wickersham, et al. *Nano Lett.* **10**, 1022 (2010)

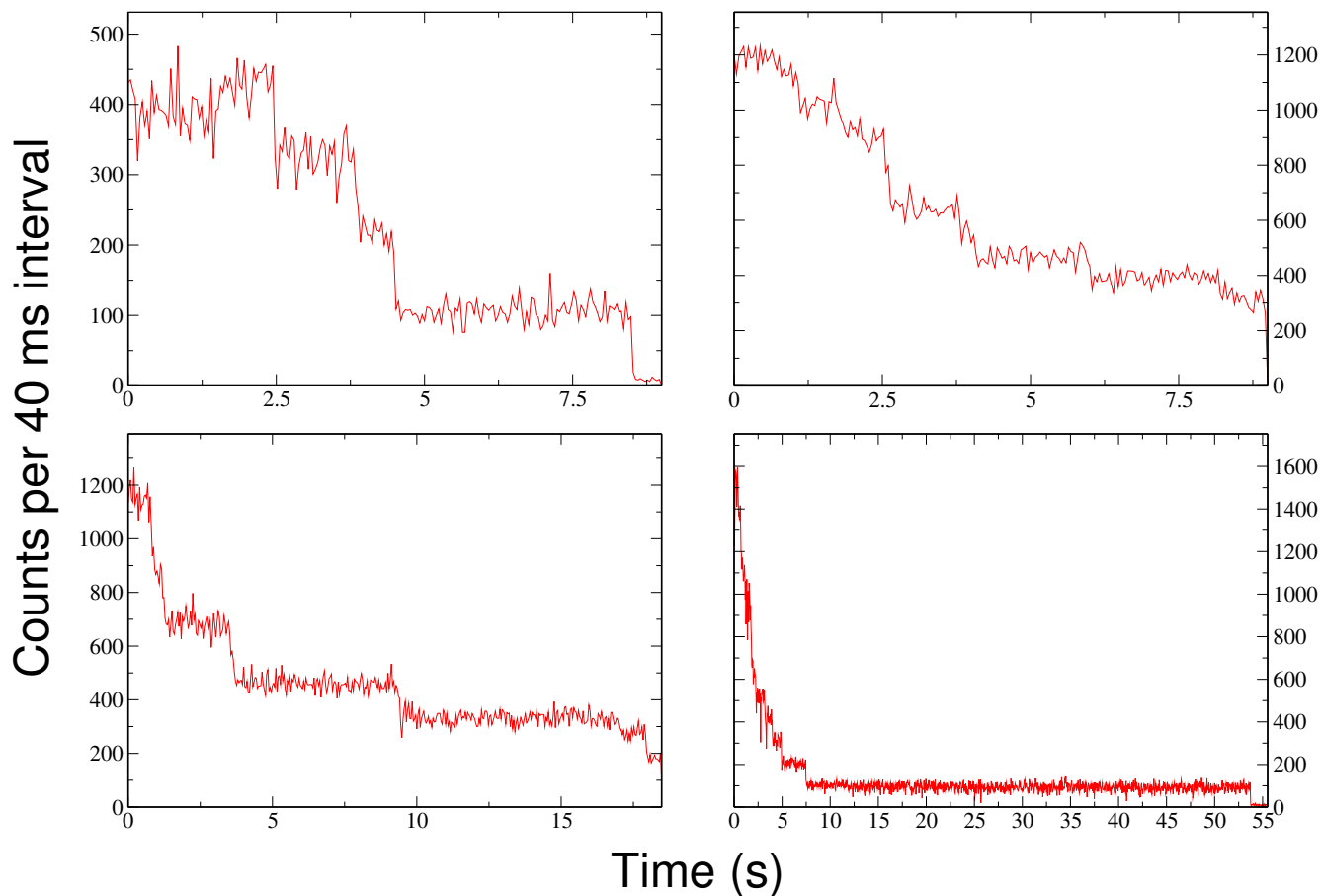
Displacement Encoder Synthesis



Displacement Encoder Experiment



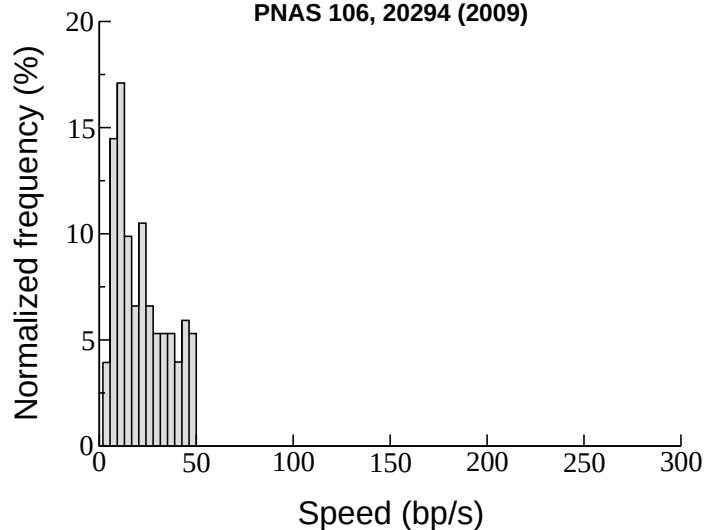
ϕ 29 DNA Polymerase Displacement Encoder Data



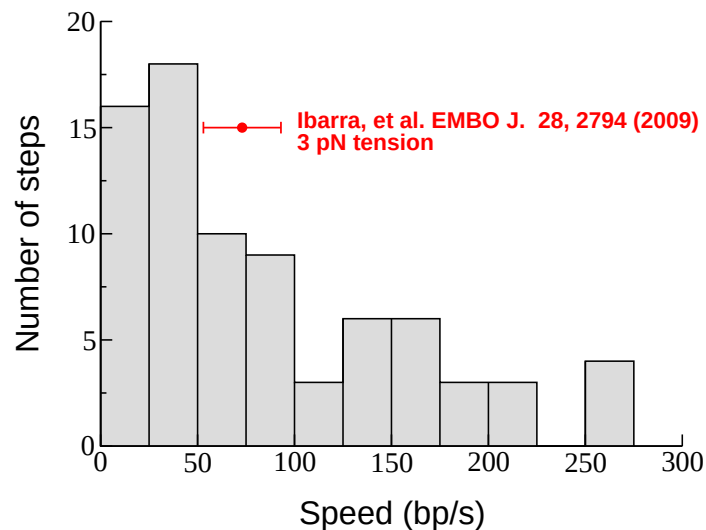
ϕ 29 DNA Polymerase Replication Rates

Schwartz and Quake

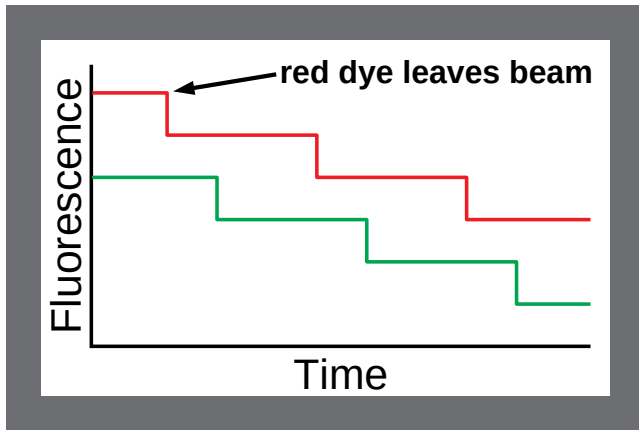
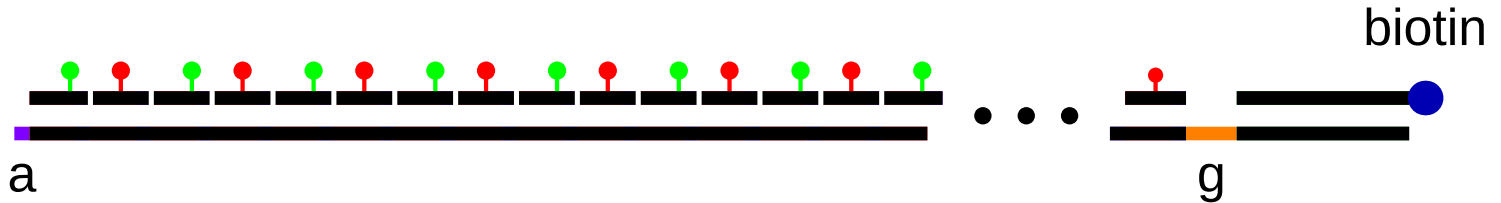
PNAS 106, 20294 (2009)



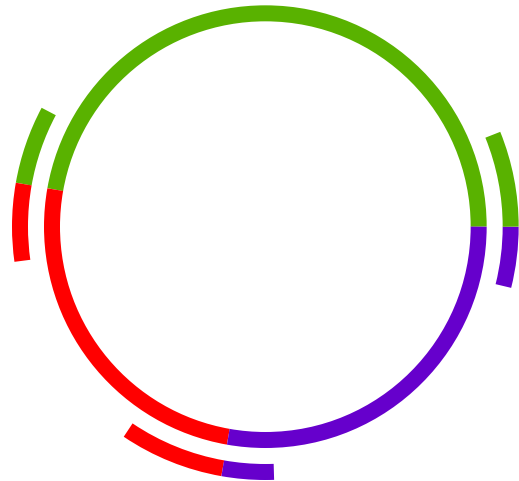
This work



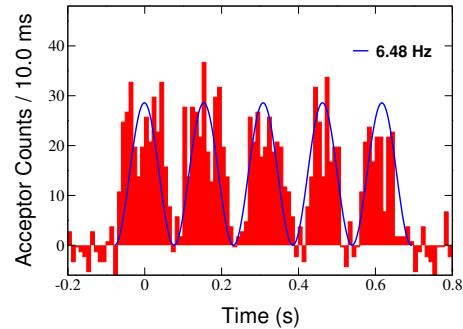
Future Displacement Encoder Experiments



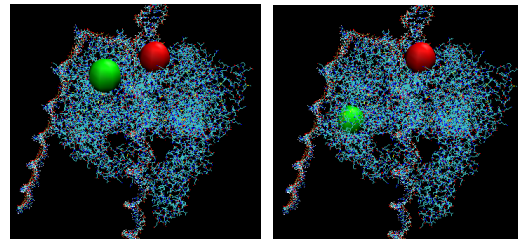
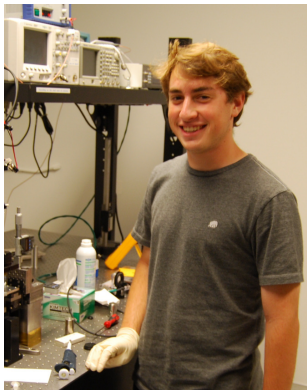
Complex rolling circle templates



Group Members



Charlie Wickersham



Daniel Kerr

Collaborators

Irina Bruck

Daniel Kaplan

Vanderbilt University

Shawn Pfeil

Kevin Cash

Kevin Plaxco

Noah Ribeck

Omar Saleh

Paul Atzberger

UC Santa Barbara

Funding

Hellman Foundation

HFSP

Sloan Foundation

CNSI

5. "Latest Technical Developments at the Infrared Spatial Interferometer," M. Bester, C.G. Degiacomi, W.C. Danchi, L.J. Greenhill, and C.H. Townes, *Proc. of IAU Symposium No. 158, Very High Angular Resolution Imaging*, J.G. Robertson and W.J. Tango (eds), 257, Kluwer (1994).

Other Significant Publications Related to Proposal

1. "158 μm [CII] Line: A Measure of Global Star Formation Activity in Galaxies," with G.J. Stacey, N. Geis, R. Genzel, J.B. Lugten, A. Poglitsch, and A. Sternberg, *Ap. J.* **373**, 423 (1991).
2. "Neutral Gas in the Central 2 Parsecs of the Galaxy," with J.M. Jackson, N. Geis, R. Genzel, A.I. Harris, S. Madden, A. Poglitsch, and G. Stacey, *Ap. J.* **402**, 123 (1993).
3. "158 μm [CII] Mapping of the Orion Molecular Cloud," with G.J. Stacey, D.T. Jaffe, N. Geis, R. Genzel, A.I. Harris, A. Poglitsch, and J. Stutzki, *Ap. J.* **404**, 219 (1993).
4. "Surprise and Sociology in Multi-disciplinary Sciences," *Very High Angular Resolution Imaging, Proc. of IAU Symposium No. 158*, J.G. Robertson and W.J. Tango (eds), 47, Kluwer (1994), and also in *Current Science Assn.* M.S. Venugopal (ed) Bangalore, India, Dec. 1993.
5. "The Nucleus of Our Galaxy," with R. Genzel and D. Hollenbach. *Rep. Prog. Phys.* **57**, 417 (1994).

Ph.D. Advisor: W.R. Smythe

Postdoctoral Advisor: none

Ph.D. Advisees: L.C. Aamodt, I.D. Abella, L.E. Alsop, J.O. Artman, S.H. Autler, A.H. Barrett, S.C. Beck, A.L. Betz, E.E. Bloemhof, R.W. Boyd, G. Burns, D. Carter, A.C. Cheung, R.Y. Chiao, M.F. Chui, H.Z. Cummins, A. Das, G.C. Dousmanis, G. Ehrenstein, N.J. Evans, P.C. Fletcher, E. Garmire, S.D. Gassster, T.R. Geballe, S. Geschwind, J.A. Giordamine, P.F. Goldsmith, J.P. Gordon, L.T. Greenberg, R. Gunther-Mohr, W.A. Hardy, A. Harris, J.Z. Holtz, A. Honig, A. Javan, F.M. Johnson, M.A. Johnson, P. Kisliuk, J.H. Lacy, H. Lashinsky, H. Lecar, B. Lopez, J.F. Lotspeich, W. Low, J. Lugten, M. Mandel, A.J. Manucci, D.N. Matsakis, S.L. Miller, F.R. Nash, J.J. Ottusch, A. Penzias, W. Rose, B. Rosenblum, T.M. Sanders, Jr., G. Serabyn, H.A. Smith, M.L. Stitch, E.C. Sutton, P. Thaddeus, T.C. Wang, D.M. Watson, R.L. White, E.R. Wollman, ⁴ E.A. Lipman #65

Postdoctoral Advisees: E. Amble, J. Askne, F. Baas, M. Bester, G.R. Bird, R.G. Brewer, J.F. Clauser, R.L. Covey, M. Crawford, W.C. Danchi, M. Danos, F. de Martini, C.G. Degiacomi, M.M. Denariez-Roberge, Palmer Dyal, N. Geis, R. Genzel, L.J. Greenhill, E. Gustafson, S.G. Hansen, O.S. Heavens, D.J. Hollenbach, T.S. Jaseja, P. Kelly, N. Knable, J.R. Lifshitz, J.H.N. Loubser, H. Mahr, J.M. Mays, R.A. McLaren, R.C. Mockler, A.H. Nethercot, Jr., A. Okaya, F. Pandarese, J.D. Poll, D.M. Rank, A.L. Schawlow, K. Shimoda, R.G. Shulman, G. Silvey, G.J. Stacey, J.W.V. Storey, J.P. Taran, M.W. Werner, J.F. Westerkamp, D.H. Whiffen, S. Yngvesson, H.J. Zeiger.

Collaborators in the Last 48 Months:

D.C. Backer, M. Bester, W.C. Danchi, C. Degiacomi, A. Eckart, T.R. Geballe, N. Geis, R. Genzel, L.J. Greenhill, E. Haller, A. Harris, F. Herrmann, D.J. Hollenbach, J.M. Jackson, D.T. Jaffe, A. Krabbe, T. Krenz, J. Lefèvre, B. Lopez, S.T. Lowe, J. Lugten, D. Lutz, S.E. Madden, P.R. McCullough, J.M. Moran, F. Najarro, A. Poglitsch, A. Sternberg, G.J. Stacey, J. Stutzski, M. Shao, E.C. Sutton, R. Treuhaft, P. Tuthill.