# Toward Synthesis of Arbitrary Optical Waveforms

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ment is mediated by the Fat-Hippo signaling pathway is possible but is not addressed in this study.) And it establishes a mechanistic link between the cellular computation of Dpp signal activity over time and cell growth. However, although the authors show that the model holds up to different experimental challenges and numerical simulations, the existence of a causal relationship is not firmly demonstrated. Direct observations, at the single-cell level, of cell division in response to an increase (by about 50%) in its Dpp activity should bolster the model.

The findings by Wartlick *et al*. point to new avenues of investigation. One question is how Dpp signaling activity is integrated over time, and the form in which this information is stored and measured in the cell (*11*). Another concerns how polarized cell divisions in some regions of the wing imaginal disc could affect homogeneity of tissue growth and consequently the temporal variations in Dpp signaling that cells experience. The authors report the intriguing observation that the degradation rate of Dpp is inversely proportional to tissue size and decreases over time, thereby potentially explaining gradient scaling. This suggests that tissue growth affects Dpp dynamics. The existence and mechanism of this feedback will be an important problem to address in the future.


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PHYSICS

# Toward Synthesis of Arbitrary Optical Waveforms

Light with different frequencies (colors) can be combined to synthesize optical waveforms such as square and sawtooth waves, as well as short pulses.

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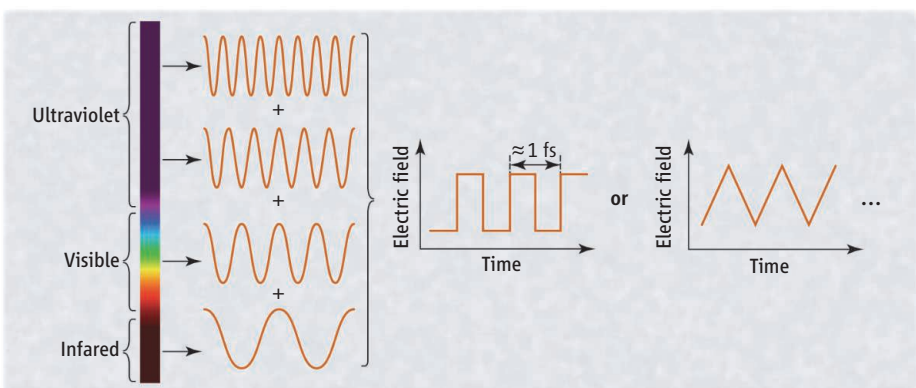
Waveform generation underlies the operation of many electronic devices, especially those used in broadcasting and signal processing. Electronic waveform generators produce a prescribed series of voltages or currents as a function of time, which may then be used as an input for a variety of circuits. The simplest versions of these devices, known as function generators, are used in undergraduate classes to produce the familiar sinusoidal, square, or sawtooth voltage waveforms seen on oscilloscopes. Arbitrary waveform generators (called synthesizers) that can create almost any pulse shape are now a common piece of equipment (and often used by graduate students to test misbehaving electronic equipment). By comparison, synthesizing optical waveforms, in which the electric and magnetic fields of light waves are not simply oscillatory but are specified functions of time, has proved to be difficult. This task has been a long-standing goal of physicists since the invention of the laser in 1960 provided a source of coherent light. On page 1165 of this issue, Chan *et al*. (*1*) demonstrate an important step toward synthesizing and characterizing arbitrary waveforms in the optical domain.

The key difference between electronic and optical synthesizers is the time scales of these devices. Electronic synthesizers are generally limited to nanosecond ($10^{-9}$ s) time scales, or frequency scales of 1 gigahertz. Optical synthesizers need to produce waveforms with time scales of 1 femtosecond (1 fs = $10^{-15}$ s), and frequency scales of 1 petahertz (PHz), so processing must be faster by six orders of magnitude. Synthesizing arbitrary optical waveforms first requires broadband coherent light. Most lasers are narrowband: for example, a laser pointer may emit only in red or green wavelengths. Thus, a large number of laser beams emitting over infrared, visible, and ultraviolet spectral regions would be needed as a source. The required range of frequencies to cover the optical spectrum (the bandwidth) approaches 1 PHz.




**Arbitrary can be good.** An ideal arbitrary optical waveform generator will produce coherent light covering visible, infrared, and ultraviolet spectral regions. Appropriate superposition of light waves at different colors can create arbitrary waveforms, for example, square and sawtooth waveforms.

A second requirement is precise control over the phase and amplitudes of the frequencies (called spectral components) to allow for temporal shaping of the output (creating pulses of longer or shorter duration). As illustrated in the figure (see the figure), each beam of a particular color is a sinusoidal wave with a certain frequency, and appropriate superpositions of these waves result in arbitrary waveforms. Different waveforms are obtained by varying the phase and amplitude of the different frequencies.

At the heart of the approach of Chan *et al*. is molecular modulation (*2*–*7*). This technique, pioneered by Harris's group at Stanford University, uses the excitation of vibra-

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tional and rotational transitions of molecules to modulate laser light at very high frequencies. Using the fundamental vibrational transition in molecular hydrogen, Chan *et al*. generated five spectral components ranging in wavelength from 2406 nm (infrared) to 481 nm (orange). The frequency difference between adjacent spectral components is 125 terahertz (THz), which is the vibrational frequency of hydrogen. By adjusting the phase and amplitude of each spectral component, they synthesized trains of square, sawtooth, and other waveform pulses (typically with a width of a few femtoseconds). Although the current experiment uses only five spectral components, future improvements on the technique may result in the generation of thousands of spectral components covering the full optical region of the spectrum.

If perfected, an arbitrary optical waveform generator has broad implications for a number of research areas. If the spectral components are all brought into phase, flashes of light that last only 0.1 fs are formed. These ultrashort pulses of light are ideal for probing processes in atoms, molecules, and solids that occur at the subfemtosecond time scale. Although 0.1-fs-long pulses are routinely produced in the soft–x-ray region through high harmonic generation (*8*–*10*), synthesizing such pulses in the more accessible optical region will expand the scope of ultrafast imaging.

Another application is in quantum control, in which light pulses are used to control the excitation of states in atoms and molecules (*11*, *12*). Efficient quantum control can be achieved only if the spectral components of the light match all possible excitations in the system. By using arbitrary optical waveforms with a broad spectrum, it should be possible to control electronic, vibrational, and rotational coordinates at the same time and induce chemical reactions.

Recently, there has been some progress in extending the molecular modulation technique from excitation with short laser pulses to excitation with continuous-wave (CW) laser light (*13*, *14*). These efforts may produce a broad spectrum in which each spectral component is a narrow-linewidth CW beam. Precision spectroscopy of atoms and molecules would be possible by choosing components of the spectrum that are close to spectral transitions of interest. Furthermore, the whole spectrum can be locked to a frequency reference so that the absolute frequency of each spectral component is known to a very high precision. With this approach, it may be possible to simultaneously produce thousands of optical clocks covering the full optical region of the spectrum (*15*, *16*).

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BIOCHEMISTRY

# Molecular Motors, Beauty in Complexity

X-ray crystallography provides some surprising insights into the dynein class of molecular motors.

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Among the most fascinating enzymes are the molecular motors, which exquisitely couple adenosine triphosphate (ATP) hydrolysis to directional mechanical motion. They power the movement of intracellular vesicles, chromosomes, and messenger RNA–protein complexes through the cytoplasm of nearly all eukaryotic cells, using actin filaments and microtubules as their tracks. A prominent theme in these motors is allostery, or communications that occur across the enzyme at several nanometer distances. Chemical events occurring in the motor's active site, for instance, are coordinated with tight binding of the motor to the track along which it moves, and then its subsequent release, and with mechanical elements that amplify small movements occurring near the active site. In the 1980s, researchers used quantitative in vitro motility assays, sensitive to single molecules, to study two of the three major classes of motor enzymes: the microtubule-based kinesin family and the actin-based myosin family. In the 1990s, investigators solved the crystal structures of kinesin 1 (*1*) and muscle myosin II (*2*). These complementary approaches ushered in a new era of understanding the mechanisms of these molecular machines. Dynein, the third important class of molecular motor, is a complex that processively moves along microtubules in the opposite direction to kinesin 1. Although single molecule assays have been applied to dynein, detailed structural information on this mammoth machine has remained elusive, until now. On page 1159 of this issue, Carter *et al*. (*3*) report a crystal structure for a 610-kD homodimer of yeast cytoplasmic dynein. The structure reveals surprises about how this massive molecular motor might work.

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Dynein was first discovered by Gibbons in 1965 (*4*) as the adenosine triphosphatase (ATPase) that drives the beating of cilia and flagella. Subsequent studies showed that dyneins play diverse motility roles in eukaryotic cells. Paschal *et al*. (*5*) identified a cytoplasmic version of dynein, which subsequent studies showed powers the movement of many cargoes. A final type of dynein (cytoplasmic dynein 2) powers the movement of protein building blocks in cilia and flagella.

Given how much we know about kinesins and myosins from structural and single-molecule studies, one might think that we could make a reasonable guess about how dynein works. However, dynein emerged from an evolutionary lineage that is separate from kinesin and myosin (which share an ancient evolutionary origin) and seems to be a completely different type of molecular machine. Phylogenetic sequence analysis (*6*) showed that dynein is a member of the AAA fam-