intriguing possibility. Mutations in the tumor suppressor gene *VHL* that are associated with qualitatively different tumor predispositions (pheochromocytoma versus clear cell renal carcinoma) appear to be associated with quantitative differences in impairment of HIF regulation (*10*–*12*). Conceivably, matching of cellular context to a relatively precise, quantitatively restricted, level of HIF activation (that is the consequence of an IDH1 Arg^{132} mutation) is necessary for glioblastoma multiforme predisposition. If true, then alteration of such a balance, through metabolic interventions that target α-KG, might offer a therapeutic or preventive strategy.

Finally, although Zhao *et al.* provide an explanation for dominant mutational inactivation of IDH1, they do not completely explain why the pathogenic effects are restricted to Arg^{132}. Other arginine residues (Arg^{100} and Arg^{109} in human IDH1) are implicated in isocitrate binding (*13*), and in recombinant porcine IDH1, mutations at all these sites are inactivating (*14*). Perhaps the proposed disruption of subunit cooperation is restricted to Arg^{132} mutations, or Arg^{132} mutations in some way favor the heterodimerization that is required for dominant inactivation. Alternatively, Arg^{132} mutations might have some quantitatively specific effect on enzyme inhibition that is necessary for oncogenic predisposition.

On the other hand, could there be a primary genetic explanation? Mutational predisposition at CG dinucleotides can explain the common Arg^{132} → His substitution but not all of the other mutations. Moreover, Yan *et al.* recently sequenced the homologous exon of the *IDH2* gene in tumors that did not contain an *IDH1* mutation, and found nine mutations at the equivalent Arg^{172}, a residue that is encoded by a codon not containing the CG dinucleotide (*3*). This mutation was shown to be inactivating, although neither dominant inactivation nor effects on HIF were tested. Further studies to test this and other (non–disease-associated) mutations in the model proposed by Zhao and colleagues should be of great interest.

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APPLIED PHYSICS

Laser Beams Take a Curve

Complex energy flows within laser beams can cause them to curve as they travel.

Jérôme Kasparian and Jean-Pierre Wolf

The properties usually associated with laser beams are illustrated by laser pointers, which are monochromatic (red or green), coherent (they create speckle patterns), and directional (the beam travels in a straight line). However, the advent of laser sources that emit ultrashort laser pulses has changed this simple picture: These sources are broadband and may maintain coherence for very short times—just for one or a few cycles of the electric field. These sources are so intense that, when traveling through a medium such as air, they can ionize atoms and create plasmas. On page 229 of this issue, Polynkin *et al.* (*1*) exploit linear optical effects of laser beams with complex profiles, as well as nonlinear effects that arise at high intensities, to create laser beams that can form plasma channels whose paths curve as they propagate.

Laser beams with complex profiles (that have multiple maxima and minima and are not a single peak) can curve in part because energy can flow between components within these beams. Polynkin *et al.* use a beam profile based on the Airy function, which has its own history in optics—it was introduced in the study of rainbows. A two-dimensional (2D) Airy beam (*2*, *3*) (see the figure, panel A) can be prepared by inserting an active element such as a matrix of liquid crystals oriented so as to tailor the distribution of phase in the plane perpendicular to the beam. This Airy profile is asymmetrical and its intensity is strongly localized in a main peak on one side of the beam profile.

As the beam propagates, interferences between the phases in different locations in the beam profile impose a curved trajectory to the main peak in the Airy profile. This interference effect is linear—it depends neither on the beam intensity nor on interactions with the propagation medium. Viewed head on, the pulse would appear to swing from the left and back to the right. However, the beam's center of mass still propagates on a straight line (the red line in panel A) because the energy fraction contained in the long trail on the other side of the beam balances the main Airy peak.

A further remarkable property of the Airy beam is that it is "self-healing": If part of the beam hits an opaque object, energy flows from the rest of the beam profile and reconstructs the original asymmetric pattern (*4*). A similar self-healing effect occurs in high-intensity laser beams that form self-guided plasma channels, also called filaments (*5*–*8*). A dynamic balance develops between the nonlinear optical Kerr effect, which changes the refractive index of its propagation medium to create a virtual converging lens, and diffraction by the self-generated plasma, which creates long plasma channels. If a laser filament impinges on a particle, the scattered light is released into the periphery of the profile, where it contributes to the optical Kerr effect, thereby reconstructing the filament shortly after the interaction (*9*). This self-healing capability may allow high-intensity laser beams to access remote locations and to be transmitted through clouds and turbulence, opening the way to atmospheric applications (*8*, *10*).

Polynkin *et al.* combined the complex profile of an Airy beam with nonlinear optical effects to create plasma channels that can turn and follow the shape (or "caustic") shown in panel A of the figure; the plasma forms only in the high-intensity region of the main peak. A key issue is whether the natural (linear) energy flow (see the figure, panel B) that displaces the transverse beam will dominate the nonlinearly induced energy flow from the optical Kerr effect, which attracts energy toward the plasma filament (see the figure, panel C) and feeds it during its propagation.

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