that specifically inhibit a range of enzymes that use chorismate or isochorismate could be developed to enhance agricultural productivity. Furthermore, kiwellins could be used to manipulate chorismate metabolism to enhance the production of a variety of commercial chorismate-derived products[17].

Kiwellins might also have the potential to be developed as antimicrobial agents for the treatment of human disease. Certain bacteria, including the bacterium that causes tuberculosis, use chorismate to make molecules that they require for infection[14]. The human genome encodes neither chorismate-using enzymes nor kiwellins; therefore, kiwellin-based inhibition of these microbial targets should be investigated. The range of metabolic proteins bound by kiwellins probably extends beyond enzymes that use chorismate, and it will be exciting to uncover the full versatility of those proteins. ■

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PLASMA PHYSICS

Statistical models boost fusion performance

Research into a technique called inertial confinement fusion aims to enhance nuclear–fusion performance in laboratory experiments. Improvements in the technique have been made using a clever statistical approach. SEE ARTICLE P.581

MARK C. HERRMANN

The pursuit of thermonuclear fusion, the power source of stars, in the laboratory is an ambitious endeavour. For a useful number of fusions to occur, fusion fuel must be heated to tens of millions of degrees so that it produces an ionized gas called a plasma. If such a plasma could be confined for long enough, the energy released by fusions, known as the yield, would greatly exceed the energy invested in the plasma — a long-elusive goal of fusion researchers. In inertial confinement fusion (ICF) experiments, the fusion plasma is generated when high-power drivers, such as lasers, are used to implode fusion fuel. On page 581, Gopalaswamy *et al.*[1] report the use of experimentally trained statistical models to triple the fusion yield and substantially improve the plasma confinement in ICF experiments.

Gopalaswamy and colleagues studied ICF implosions at the OMEGA Laser Facility at the University of Rochester in New York[2]. In these experiments, 60 high-power laser beams are directed onto a millimetre-sized capsule that contains fusion fuel (Fig. 1). The intense light produces large pressures, imploding the fuel at high velocities. When the imploding fuel stagnates, kinetic energy is rapidly converted to temperature and pressure, generating a fusion plasma that is confined by its own inertia.

The number of design choices for optimizing this fusion plasma is enormous, because all aspects of the capsule's dimensions and structure, as well as the details of the laser and the time dependence of the laser's power, can be varied. Implosion performance can also be considerably affected by 'hydrodynamic' instabilities that are seeded by inevitable imperfections in the manufactured capsule and imbalances or instabilities in the applied laser light. Unsurprisingly, the complexity of this implosion system leads to fusion performance that is extremely sensitive to design details and instabilities.

With so many design choices, and with limited experimental data, the standard approach to optimizing fusion performance has been to use theoretical insights along with sophisticated radiation–hydrodynamic simulations that follow, as well as we know how, the physics of the implosions and their degradations. This technique produced the previous record fusion yield at OMEGA[3]. However, for these implosions, the simulations significantly overestimate the experimentally observed fusion performance. The causes of this discrepancy are not fully understood. A lack of accurate physics models in the simulations or

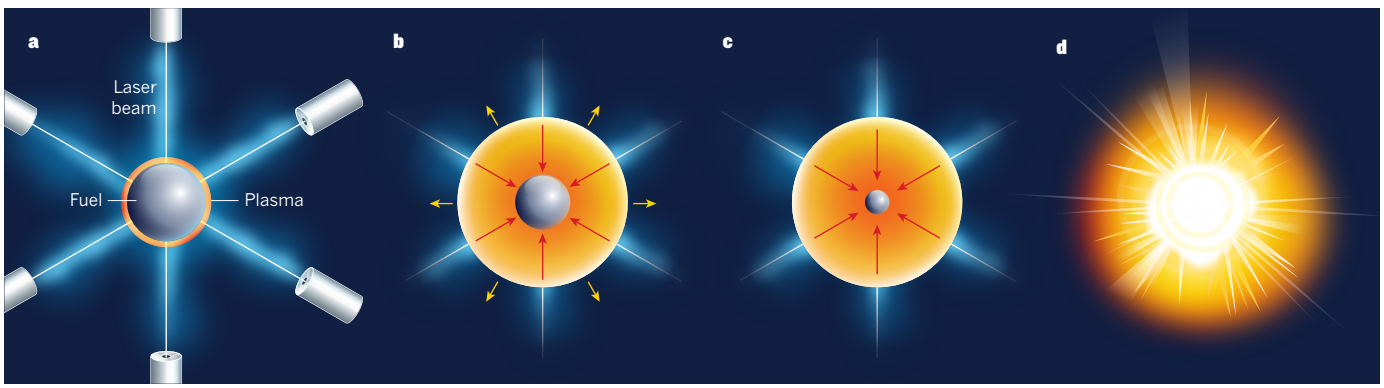

Figure 1 | Inertial confinement fusion. Gopalaswamy *et al.*[1] present a method for increasing the energy output from experiments at the OMEGA Laser Facility[2] that involve a process called inertial confinement fusion. **a**, In these experiments, laser beams rapidly heat the surface of a millimetre-sized fuel capsule, producing an envelope of highly ionized gas known as a plasma. **b**, The plasma blasts outwards (yellow arrows), generating large forces (red arrows) that compress the fuel. **c**, The compression continues until the fuel reaches extreme pressures. **d**, Finally, the fuel heats up and undergoes nuclear fusion.

incomplete knowledge of the instability seeds and their evolution, or both, could be to blame.

In light of this discrepancy, Gopalaswamy *et al.* chose a different approach to optimizing the fusion performance at OMEGA. They posited that, because both the simulations and the experiments have the same inputs (such as the geometry of the capsule and the time dependence of the laser's power), a statistical relationship might exist between simulation outputs and experimental data. The authors trained a statistical model to match an initial set of experimental data using simulation outputs. They then used this model to suggest changes to the implosion design that the model predicted would improve the fusion performance.

By consistently following this methodology to design a series of experimental campaigns, Gopalaswamy and colleagues improved the fusion yield by a remarkable factor of three compared with OMEGA's previous record[3]. Buoyed by this success, the authors expanded their approach to work on increasing the plasma confinement time by increasing the areal density (the mass per unit area) of the imploded fuel. They trained a second statistical model to suggest changes to the time dependence of the laser's power. Such changes led to a 60% increase in the areal density of the fuel, while maintaining the record fusion yield, resulting in a dramatically improved overall implosion performance.

These advances have major implications. For instance, further optimization of OMEGA fusion performance will probably be possible using further refinements of the authors' statistical models. It is also likely that this approach could be extended to other ICF techniques, such as indirect-drive laser fusion, in which laser beams irradiate a small metal cylinder containing the fuel capsule, rather than the capsule itself. Indirect-drive laser fusion has been the highest-performing ICF method so far[4,5].

Gopalaswamy *et al.* extrapolate their results to the energy scale of the National Ignition Facility (NIF) at the Lawrence Livermore National Laboratory in California[6], which has more than 60 times the energy of OMEGA. Although this extrapolation projects that record-breaking fusion yields could be achieved, it is also fraught with peril, because there are considerable uncertainties in how the physics and instabilities scale over such a large energy range. In addition, the laser beams at NIF are not configured to uniformly illuminate the fusion capsule for direct-drive laser fusion, meaning that such experiments could not be carried out without an expensive change to the facility. With an awareness of these concerns, an experimental effort is under way at OMEGA and NIF to better understand the prospects for direct-drive laser fusion as a path to thermonuclear fusion. Gopalaswamy and colleagues' results will greatly aid this effort.

Perhaps the most exciting aspect of the authors' work is the impetus it will give to further understanding the substantial disconnects between what is simulated and what is experimentally observed. It is empowering to know that such large improvements in fusion performance are realizable using trained statistical models, and that powerful insights can be obtained from taking a deeper look at the experimental data. At the same time, it is humbling for scientists dedicated to understanding such complex systems to recognize how much they don't understand. As a quote attributed to physicist Eugene Wigner states[7]: "It is nice to know that the computer understands the problem. But I would like to understand it, too". Gopalaswamy *et al.* have shown us that this statement is even more true for fusion developers than we knew. ■

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MOLECULAR BIOLOGY

Intron RNA sequences promote cell survival

Intron sequences are removed from newly synthesized RNA and usually rapidly degraded. However, it now seems that introns have a surprising role — helping yeast cells survive when nutrients are scarce. SEE ARTICLES P.606 & P.612

SAMANTHA R. EDWARDS & TRACY L. JOHNSON

RNA molecules that are newly transcribed from DNA contain intron and exon sequences. Introns are excised through a process called RNA splicing, during which the remaining exon sequences are joined together (ligated) to form mature messenger RNA, which is then translated into proteins. RNA splicing releases a lariat-shaped intron that is rapidly converted (debranched) to a linear form and degraded. Much of what we know about the molecular machinery — the spliceosome and its associated factors — and the mechanisms of splicing has come from genetic and biochemical experiments using baker's yeast (*Saccharomyces cerevisiae*). Laboratory studies have suggested that most yeast introns can be removed with little consequence for the cell[1]. Parenteau *et al.*[2] (page 612) and Morgan *et al.*[3] (page 606) now challenge this view by showing that introns help yeast cells in culture to sense a lack of essential nutrients in their growth medium and to adjust the rate of cell growth to adapt to this change in the environment.

Although the splicing machinery has been highly conserved during evolution, gene architecture is complex and varies across organisms. The yeast genome is highly streamlined in comparison with those of most other eukaryotes (the group of organisms that includes plants, animals and fungi). Approximately 5% of protein-coding genes in yeast contain introns, and only nine contain more than one. By contrast, 90% of genes in mammals contain introns, with an average of eight introns per gene. In yeast, as in other organisms, introns have been viewed as the dispensable by-product of exon ligation because of their rapid degradation after splicing.

Parenteau *et al.* and Morgan *et al.* shine new light on the role of introns. Each group assessed the roles of introns as yeast cells in culture enter the stationary phase, a period defined by a plateau in growth caused by decreased expression of genes involved in respiration and proliferation in response to limited nutrient availability. For example, expression of components of the ribosome, the cellular machinery that synthesizes proteins when nutrients are abundant, is downregulated during the stationary phase[4]. Both Parenteau *et al.* and Morgan *et al.* find that certain introns accumulate during the stationary phase, and that they have a role in the cells' response to nutrient deprivation (Fig. 1). However, the two groups report different intron forms, each of which might mediate the response to nutrients in distinct ways. Parenteau *et al.* identify a role for unspliced transcripts, whereas Morgan *et al.* identify introns that accumulate after being excised and debranched.

Parenteau *et al.* generated a library of 295 yeast strains, each of which had a single, different intron deleted from its genome, and 9 additional strains whose genes originally contained two introns, both of which had been