

of nucleosomes, which can present barriers to active processes such as gene expression⁵. This reduction in mobility might be achieved in many ways, including the deacetylation and methylation of histones, interactions with non-histone chromatin proteins, the use of variant histones, higher-order folding of chromatin, or a combination of these. Regardless of the precise mechanism, silencing must be maintained throughout many rounds of cell division during development — and it seems that RbAp48 is essential for this process. So, if RbAp48 levels are reduced, as in Hennig and colleagues' mutant plants, there is not enough protein to help keep every silent gene silent; some genes will become randomly activated, and will remain so during successive cell divisions. The progressive nature of the defects suggests that more and more genes become 'unsilenced' as development proceeds.

In other words, then, RbAp48 is part of a mechanism by which cells inherit 'epigenetic' changes — changes to chromatin that do not affect the DNA sequence. Just as DNA must be replicated during cell division, so too must patterns of methylation and acetylation when new nucleosomes are assembled. But how exactly does RbAp48 contribute? It is known that CAF-1 assembles nucleosomes onto newly synthesized DNA, and that the RbAp48 subunit acts as an 'adaptor' that attaches to tetramers of histones H3 and H4, making them available for the DNA to wrap around¹⁰. Specifically, RbAp48 attaches to a portion of H4 that becomes inaccessible once the nucleosome is assembled, suggesting that it can only act as an adaptor before this happens.

It is possible that RbAp48 has the same role in other chromatin-modifying complexes. CAF-1 is not essential in plants, animals and fungi¹¹, suggesting that other complexes can also assemble nucleosomes during DNA replication. Perhaps these other complexes have an RbAp48-like adaptor for holding onto the histone tetramer and presenting it for assembly (reviewed in ref. 12). And perhaps the other complexes that include RbAp48 and its relatives, such as histone-acetylation complexes, perform their tasks during replication-coupled nucleosome assembly — in which case, they might use RbAp48 to hold out exposed histones for modification. In this way, the diverse processes of histone modification and chromatin remodelling could contribute to epigenetic inheritance at the moment that histones are deposited onto newly synthesized DNA. Hennig and colleagues' finding¹ that RbAp48 is necessary for epigenetic inheritance lends weight to this idea.

If so, then this WD-40 protein might indeed resemble its namesake oil, acting in essentially the same way to perform a variety of tasks. ■

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Cosmology

Beyond the inflationary border

Steven Gratton and Paul Steinhardt

Observational data now offer strong support for inflation — a period of exponentially fast expansion in the early history of the Universe. But is the theory complete?

Cosmologists are exhilarated by recent cosmological observations¹ that have confirmed some of the long-standing predictions of the standard cosmological model, a picture based on a combination of Big Bang theory and inflationary cosmology. At the same time, some may worry that cosmology has “become a victim of its own success”² — that the basic outline of cosmic history is understood and all that remains is the unglamorous task of determining the precise quantitative details. But rest assured, there is much fundamental work still to be done, as a paper by Borde, Guth and Vilenkin³ in *Physical Review Letters* reminds us. The standard model is less a solid edifice than a scaffolding with many gaps, resting on uncertain foundations.

According to the standard picture, the Universe sprang into being about 14 billion years ago, as a space filled with matter and radiation of nearly infinite temperature and density. At birth, the space was likely to have been inhomogeneous, curved and warped, unlike the large-scale Universe we see today. After about 10^{-35} seconds, there began a brief period of exponentially fast expansion, known as inflation, that ironed out any curves or warps in space. Inflation also smoothed out the distribution of matter and radiation, leaving behind tiny wrinkles that match the observed spatial variations in the cosmic microwave background radiation and provide the seeds for galaxy formation.

The story has become familiar, but consider its foundations. Is there really a beginning to the Universe? What events led to the onset of inflation? And does the Universe even contain the ingredients necessary for inflation (in particular, the ‘inflaton field’ that purportedly drives inflation and then decays into hot matter and radiation)? Without answers to these questions, the model is incomplete. Most cosmologists have set these questions aside, assuming that advances in fundamental

physics (such as string theory) will address them. They have focused instead on the post-inflationary Universe and on comparing predictions with observations. Now that the comparison is proving to be a success, though, theorists will be giving increasing attention to the foundational issues.

A conceivable resolution is that the Universe was inflating for all time until 14 billion years ago, when the inflaton field decayed and produced a hot, expanding volume filled with matter and radiation that cooled to become our present Universe. There would be no beginning and no need for any special dynamics to kick-start inflation.

Not possible, say Borde, Guth and Vilenkin³. Given fairly mild assumptions, they track a flow of particles in a generic inflating universe and show that an extrapolation backwards in space and time must arrive at a border (a surface in space and time) beyond which there can be no inflation. So the question of what happened before inflation seems hard to avoid. (It's not impossible, though: an example has been constructed⁴ in which the original inflating region can be joined to a second one, but this is made possible only by imposing the conditions that time flows in opposite directions away from the border and that no particles or other information can pass through.)

One might think that the pre-inflationary phase is unimportant because inflation wipes out all of the details. But the border is only a finite distance away in proper time, so it is quite possible to imagine disturbances in the pre-inflationary phase that would survive to the present. In fact, only a subset of pre-inflationary conditions leads to a sufficiently homogeneous universe after inflation. So, to have a complete understanding of the present post-inflationary phase, we must understand what is on the other side of that border.

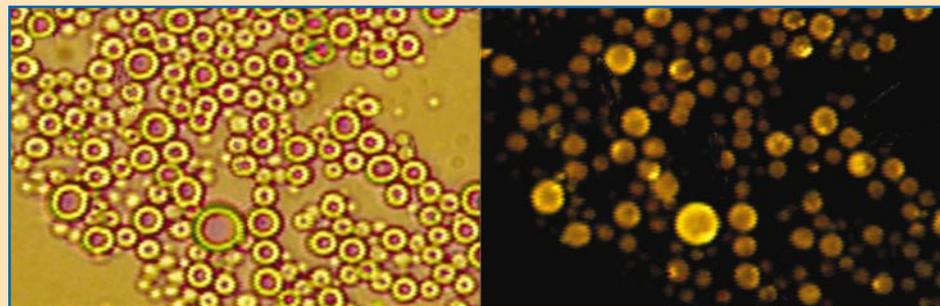
One possibility is a pre-inflationary phase that contracts for a semi-infinite period of

Materials science

Rings of excitement

Jennifer N. Cha and colleagues have taken a natural approach to create a new material for lasing applications. Emulating composite materials such as shell and bone, whose properties result from the cooperative organization of organic and inorganic components, Cha *et al.* have used specifically tailored polypeptides to organize inorganic quantum dots into microscopic laser cavities (*Nano Lett.* doi:10.1021/nl034206k; 2003).

The structures are created by mixing a solution of a positively charged diblock copolypeptide with a solution of negatively charged quantum dots — nanoscopic particles of a semiconducting material (in this case, cadmium selenide). Hollow, micrometre-size spheres form, which Cha *et al.* attribute to charge matching between the components of the mixture. The addition of silica nanoparticles to the mixture stabilizes the spheres, giving the double-layer structure of an inner wall of quantum dots and an outer



wall of silica nanoparticles that can be seen in optical-microscope images (such as the one shown here, left).

If the microspheres are excited by a laser pulse, the quantum dots emit light spontaneously; the spherical cavity acts as a resonator, modifying the resultant photoluminescence spectra. Although the microspheres are in contact with one another at their outer silica layers, the photoluminescence is confined to well-separated rings (right-hand

image): the light emitted by the quantum dots does not spread out, but is confined to the quantum-dot layer within the silica wall of each microsphere. If the intensity of the laser pulse is increased above a certain threshold value, a sharp peak appears in the photoluminescence spectra of each microsphere, and this increases rapidly with the energy of the laser pulse — a distinctive signature of lasing action in the microspheres.

Microspheres make room-

temperature microcavity lasing possible, without the need for mirrors or gratings. And, as the fabrication method is quite straightforward, it should be possible to tune the properties of both the quantum dots and the microcavity for particular lasing applications. The microspheres could also be assembled into arrays or more complex three-dimensional structures, their silica coating ensuring that individual spheres retain their functionality. **Magdalena Helmer**

time and then bounces at the border into an inflationary phase. Another is a universe, expanding at a sub-inflationary pace, that joins onto an inflating phase. But because the inflaton field is unstable during inflation (it has to eventually decay into hot matter and radiation), it must also be unstable before inflation. It turns out that the probability of decay is exponentially greater in a contracting or slowly expanding phase than in an inflating one, so how could a sufficient region of the unstable inflaton field survive through the pre-inflationary phase?

Another option is to assume that quantum mechanics takes over before the border region is reached. The Hartle–Hawking ‘no boundary proposal’⁵ deals with the transition from quantum to classical cosmology, and many have hoped that this would naturally lead directly to a description of inflation on the classical side. Unfortunately, instead it leads typically to an almost empty universe in which little or no inflation occurred⁶.

The work of Borde *et al.*³, combined with these other attempts, forces us to realize that the inflationary story is still incomplete. And this is not the only unresolved issue. The model predicts the total energy density in the Universe correctly, but the nature of 96% of that energy is unknown⁷. Furthermore, despite two decades of studies, the fields

responsible for driving inflation have not been identified, and there is no accepted explanation for the finely tuned interactions that the fields must possess for inflation to end smoothly. So, there are good reasons to cheer the recent breakthroughs, but there are also many fundamental issues that remain to be explored. And there is perhaps even room for radical alternatives. ■

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Cell cycle

Degradation ensures integrity

Anatoliy Li and J. Julian Blow

Protein degradation terminates a range of biochemical activities in living cells. New work shows that a component of the ‘licensing’ system for DNA replication must be degraded to prevent re-replication during cell division.

How would you ensure that a biochemical reaction is irreversible? This is a key problem in living organisms, because many of their control systems must progress unidirectionally through a series of different states. During the cell-division cycle, for instance, chromosomal DNA must first be duplicated (in the so-called S phase), and then the two copies must be segregated to daughter cells (during mitosis). Organisms

usually solve the problem of irreversibility by inactivating the proteins that catalyse each biochemical reaction after they have carried out their task. There are several ways of achieving this, but the most direct is simply to destroy the proteins. For example, it is known that the exit from mitosis is rendered irreversible by the degradation of mitotic proteins. Elsewhere in this issue (page 885), Zhong and colleagues¹ show that the ability