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correction

Role of HIF-1α in hypoxia-mediated apoptosis, cell proliferation and tumour angiogenesis

Peter Carmeliet, Yuval Dor, Jean-Marc Herbert, Dai Fukumura, Koen Brusselmans, Mieke Dewerchin, Michal Neeman, Françoise Bono, Rinat Abramovitch, Patrick Maxwell, Cameron J. Koch, Peter Ratcliffe, Lieve Moons, Rakesh K. Jain, Désiré Collen & Eli Keshert

Nature **394,** 485–490 (1998)

The last author's name was misspelled but is now corrected above.

Also, in the penultimate sentence of the introductory bold paragraph, growth was accelerated in HIF-1$\alpha^{-/-}$ tumours (not in HIF-1α tumours, as published). □

Tests of quantum gravity from observations of γ-ray bursts

G. Amelino-Camelia, John Ellis, N. E. Mavromatos, D. V. Nanopoulos & Subir Sarkar

Nature **393,** 763–765 (1998)

In ref. 22 of this Letter, the first author's name was incorrectly cited as C. L. Bhat instead of P. N. Bhat. □

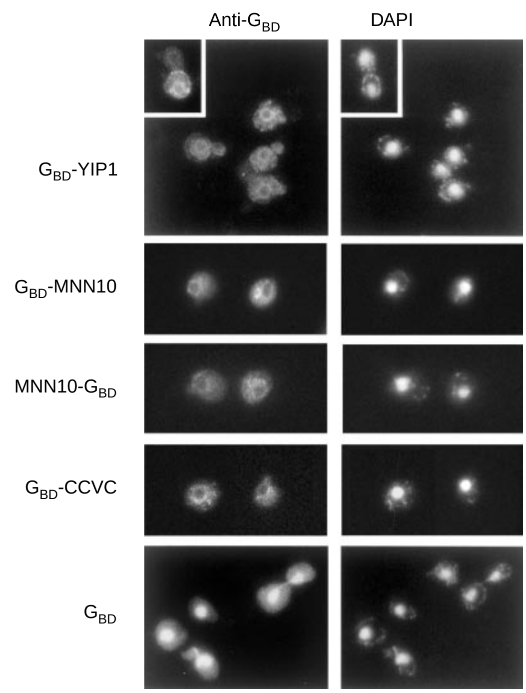
erratum

Perinuclear localization of chromatin facilitates transcriptional silencing

Erik D. Andrulis, Aaron M. Neiman, David C. Zappulla & Rolf Sternglanz

Nature **394,** 592–595 (1998)

Owing to an error in the production process, the six bottom panels of Fig. 1 reproduced poorly. The figure is shown again here. □



Tests of quantum gravity from observations of γ-ray bursts

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The recent confirmation that at least some γ-ray bursts originate at cosmological distances[1–4] suggests that the radiation from them could be used to probe some of the fundamental laws of physics. Here we show that γ-ray bursts will be sensitive to an energy dispersion predicted by some approaches to quantum gravity. Many of the bursts have structure on relatively rapid timescales[5], which means that in principle it is possible to look for energy-dependent dispersion of the radiation, manifested in the arrival times of the photons, if several different energy bands are observed simultaneously. A simple estimate indicates that, because of their high energies and distant origin, observations of these bursts should be sensitive to a dispersion scale that is comparable to the Planck energy scale ($\sim 10^{19}$ GeV), which is sufficient to test theories of quantum gravity. Such observations are already possible using existing γ-ray burst detectors.

Our interest is in the search for possible *in vacuo* dispersion, $\delta v \approx E/E_{QG}$, of electromagnetic radiation from γ-ray bursts (GRBs), which could be sensitive to a type of candidate quantum-gravity effect that has been recently considered in the particle-physics literature. (Here E is the photon energy and E_{QG} is an effective quantum-gravity energy scale). This candidate quantum-gravity effect would be induced by a deformed dispersion relation for photons of the form $c^2\mathbf{p}^2 = E^2[1 + f(E/E_{QG})]$, where f is a model-dependent function of the dimensionless ratio E/E_{QG}, $\mathbf{p}$ is the photon momentum and c is the velocity of light. In quantum-gravity models in which the hamiltonian equation of motion $\dot{x}_1 = \partial H/\partial p_i$ is still valid at least approximately, as in the frameworks discussed later, such a deformed dispersion relation would lead to energy-dependent velocities $c + \gamma v$ for massless particles, with implications for all the electromagnetic signals that we receive from astrophysical objects at large distances. At small energies $E \ll E_{QG}$, we expect that a series expansion of the dispersion relation should be applicable: $c^2\mathbf{p}^2 = E^2[1 + \xi E/E_{QG} + O(E^2/E_{QG}^2)]$, where $\xi = \pm 1$ is a sign ambiguity that would be fixed in a given dynamical framework. Such a series expansion would correspond to energy-dependent velocities:

$$v = \frac{\partial E}{\partial p} \approx c\left(1 - \xi \frac{E}{E_{QG}}\right) \quad (1)$$

This type of velocity dispersion results from a picture of the vacuum as a quantum-gravitational 'medium', which responds differently to the propagation of particles of different energies and hence velocities. This is analogous to propagation through a conventional medium such as an electromagnetic plasma[6]. The gravitational 'medium' is generally believed to contain microscopic quantum fluctuations, which may occur on scale sizes of order the Planck length $L_P \approx 10^{-33}$ cm on timescales of the order of $t_P \approx 1/E_P$, where $E_P \approx 10^{19}$ GeV. These may[7,8] be analogous to the thermal fluctuations in a plasma, that occur on timescales of the order of $t \approx 1/T$, where T is the temperature. As it is a much 'harder' phenomenon associated with new physics at an energy scale far beyond typical photon energies, any analogous quantum-gravity effect could be distinguished by its different energy dependence: the quantum-gravity effect would increase with energy, whereas conventional medium effects decrease with energy in the range of interest[6].

Equation (1) encodes a minute modification for most practical purposes, as E_{QG} is believed to be a very high scale, presumably of the order of the Planck scale $E_P \approx 10^{19}$ GeV. Even so, such a deformation could be rather significant for even moderate-energy signals, if they travel over very long distances. According to equation (1), a signal of energy E that travels a distance L acquires a 'time delay', measured with respect to the ordinary case of an energy-independent speed c for massless particles:

$$\Delta t \approx \xi \frac{E}{E_{QG}} \frac{L}{c} \quad (2)$$

This is most likely to be observable when E and L are large while the interval δt, over which the signal exhibits time structure, is small. This is the case for GRBs, which is why they offer particularly good prospects for such measurements, as we discuss later.

We first review briefly how modified laws for the propagation of particles have emerged independently in different quantum-gravity approaches. The suggestion that quantum-gravitational fluctuations might modify particle propagation in an observable way can already be found in refs 7 and 9. A phenomenological parametrization of the way this could affect the neutral kaon system[9–11] has been already tested in laboratory experiments, which have set lower limits on parameters analogous to the E_{QG} introduced above at levels comparable to E_P (ref. 12). In the case of massless particles such as the photon, which interests us here, the first example of a quantum-gravitational medium effect with which we are familiar occurred in a string formulation of an expanding Robertson–Walker–Friedman cosmology[13], in which photon propagation appears tachyonic. Deformed dispersion relations that are consistent with the specific formula in equation (1) arose in approaches based on quantum deformations of Poincaré symmetries[14] with a dimensional parameter. Within this general class of deformations, one finds[14,15] an effect consistent with equation (1) if the deformation is rotationally invariant: the dispersion relation for massless particles $c^2\mathbf{p}^2 = E_{QG}^2[1 - \exp(E/E_{QG})]^2$, and therefore $\xi = 1$. We noted that a deformed dispersion relation has also been found in studies of the quantization of point particles in a discrete space time[16].

A specific and general dynamical framework for the emergence of the velocity law (equation (1)) has emerged[17] within the Liouville string approach[7] to quantum gravity, according to which the vacuum is viewed as a non-trivial medium containing 'foamy' quantum-gravity fluctuations. The nature of this foamy vacuum may be visualized by imagining processes that include the pair creation of virtual black holes. Within this approach, it is possible to verify that massless particles of different energies excite vacuum fluctuations differently as they propagate through the quantum-gravity medium, giving rise to a non-trivial dispersion relation of Lorentz 'non-covariant' form, just as in a thermal medium. The form of the dispersion relation is not known exactly, but its structure has been studied[17] via a perturbative expansion, and it was shown in ref. 17 that the leading $1/E_{QG}$ correction is in agreement with equation (1).

It has been recently suggested[8] the vacuum might have analogous 'thermal' properties in a large class of quantum-gravity approaches, namely all approaches in which a minimum length L_{min}—such as the Planck length $L_P \approx 10^{-33}$ cm—characterizes short-distance physics. These should in general lead to deformed photon dispersion relations with $E_{QG} \approx 1/L_{min}$, though the specific form of equation (1) may not hold in all models, and hence may be used to discriminate between them. In support of equation (1), though, we recall[15,17] that this type of non-trivial dispersion in the quantum-gravity vacuum has implications for the measurability of distances in quantum gravity that fit well with the intuition emerging from recent heuristic analyses[18] based on a combination of arguments from ordinary quantum mechanics and general relativity.

We now explain how GRBs provide an excellent way of testing such ideas, now that the cosmological origin of at least some of them has been established. We recall that typical photon energies in GRB emissions are[5] in the range 0.1–100 MeV, and it is possible that the spectrum might in fact extend up to TeV energies[19]. Moreover, time structure down to the millisecond scale has been observed in the light curves[5], as is predicted in the most popular theoretical models[20] involving merging neutron stars or black holes, where the last stages occur on the timescales associated with grazing orbits. Similar timescales could also occur in models that identify GRBs with other cataclysmic stellar events, such as failed supernovae of type Ib, young ultra-magnetized pulsars or the sudden deaths of massive stars[21]. We see from equations (1) and (2) that a signal with millisecond time structure in photons of energy ~20 MeV coming from a distance of the order of 10^{10} light yr, which is well within the range of GRB observations and models, would be sensitive to E_{QG} of the order of 10^{19} GeV $\approx 1/L_P$.

Significant sensitivities may already be attainable with the present GRB data. Submillisecond time-structure has been seen[22] in GRB 910711, and a recent time-series analysis[23] of the light curve of GRB 920229 using the bayesian block technique has identified a narrow microburst with a rise and decay timescale of the order of 100 μs. This is seen simultaneously in three (of the available four) energy channels of the BATSE detector on board the Compton Gamma Ray Observatory, covering the energy regions 20–50 keV, 50–100 keV and 100–300 keV, respectively. From the time structure of this microburst we think it should be possible to extract an upper limit of $\Delta t \lesssim 10^{-2}$ s on the difference in the arrival times of the burst at energies separated by $\Delta E \approx 200$ keV. If a burst such as this were to be demonstrated in the future to lie at a redshift $z \approx 1$, as seems quite plausible, the implied sensitivity would be to $E_{QG} \approx 10^{16}$ GeV, and it would be possible to improve this to $\sim 10^{17}$ GeV if the time difference could be brought down to the rise time reported in ref. 23. We note in passing that the simultaneous arrival of photons of different energies from such a large distance also imposes an upper limit of the order of 10^{-6} eV on a possible photon mass, but this is much less stringent than other astrophysical and laboratory limits[24].

These levels of sensitivity are even more interesting in light of the fact that recent theoretical work on quantum gravity, particularly within string theory, appears to favour values of the effective scale characterizing the onset of significant quantum-gravity effects that are somewhat below the Planck scale, typically in the range 10^{16}–10^{18} GeV (ref. 25). If our scale E_{QG} were indeed to be given by such an effective quantum-gravity scale, parts of the GRB spectrum with energies around 0.1 MeV and millisecond time structure (or energies of the order of 100 MeV and 1-s time structure, or energies around 1 TeV and 1-h time structure) might be sensitive to the type of candidate quantum-gravity phenomenon discussed here.

To provide some quantitative comparison of the GRB sensitivity to this phenomenon with that of other astrophysical phenomena, we can compare values of the 'sensitivity factor' $\eta \equiv |\Delta t^*|/\delta t$, where δt represents the time structure of the signal, and Δt^* is the time delay acquired by the signal if $E_{QG} \approx E_P$, namely $\Delta t^* \approx \pm EL/(cE_P)$. As already discussed, GRB emission with millisecond time structure and energy around 20 MeV that travels a distance of the order of 10^{10} light yr has $\eta \approx 1$. Another interesting possibility is that we may observe lensing of a GRB by a foreground galaxy[26,27]. The burst would then reach us by two or more different paths whose light travel times would differ typically by weeks to years. As conventional gravitational lensing is achromatic, any energy-dependence in the time delay would be a direct probe of the new physics of interest, and would be independent of the actual emission mechanism of γ-ray bursts. We note that the HEGRA[28] and Whipple[29] air Čerenkov telescopes have already searched for TeV emission from the direction of GRBs, motivated by the EGRET telescope's detection[30] of emission up to 18 GeV from GRB940217. If such searches were to prove successful and moreover, identified a lensed GRB, one would be able to infer via equation (2) a sensitivity factor down to $\eta \approx 10^{-6}$.

As observed in ref. 17, which did not consider GRBs as the cosmological distances of these phenomena were not then established, pulsars and supernovae are among the other astrophysical phenomena that might at first sight appear well suited for probing the physics we are interested in here, because of the short time structures they display. However, although pulsar signals have very well-defined time structure, they are at relatively low energies and are observable over distances of at most 10^4 light yr. If one takes an energy of the order of 1 eV and postulates a sensitivity to time delays as small as 1 μs, one estimates a sensitivity down to $\eta \approx 10^{-10}$. With new experiments such as AXAF it may be possible to detect X-ray pulsars out to 10^6 light years, allowing us to probe down to $\eta \approx 10^{-8}$.

We note that neutrinos from type-II supernovae like SN1987a—which should have energies up to ~100 MeV with a time structure that could extend down to milliseconds—are likely to be detectable at distances of up to $\sim 10^5$ light yr, providing sensitivity down to $\eta \approx 10^{-4}$. We have also considered the cosmic microwave background. Although the distance travelled by these photons is the largest available, the only possible signature is a small distortion of the Planck spectrum due to the frequency-dependence of c, which we estimate to be of the order of $\Delta I(\nu)/I(\nu) \approx \nu/E_P \approx 10^{-32}$, where $I(\nu)$ is the frequency spectrum, which is negligible.

In principle, GRBs allow us to gain many orders of magnitude in the sensitivity factor η. Moreover, and most importantly, this high sensitivity should be sufficient to probe values of the effective scale characterizing the onset of quantum-gravity effects extending all the way up to the Planck scale, as illustrated by the estimates we have provided. Ideally, one would like to understand well the short-time structure of GRB signals in terms of conventional physics, so that the phenomena discussed here may be disentangled unambiguously. However, even in the absence of a complete theoretical understanding, sensitive tests can be performed as indicated above, through the serendipitous detection of short-scale time structure[23] at different energies in GRBs which are established to be at cosmological distances. Detailed features of burst time series should enable the emission times in different energy ranges to be put into correspondence. As any time shift due to quantum-gravity effects of the type discussed here would increase with the photon energy, this characteristic dependence should be separable from more conventional in-medium physics effects, which decrease with energy. To distinguish any quantum-gravity shift from effects due to the source, we recall that the medium effect would be linear in the source distance and in the photon energy, which would not in general be the case for time shifts at the source. To disentangle any such effects, it is clear that the most desirable features in an observational programme would be fine time resolution at high photon energies. □

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Global warming on Triton

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Triton, Neptune's largest moon, has been predicted to undergo significant seasonal changes that would reveal themselves as changes in its mean frost temperature[1–3]. But whether this temperature should at the present time be increasing, decreasing or constant depends on a number of parameters (such as the thermal properties of the surface, and frost migration patterns) that are unknown. Here we report observations of a recent stellar occultation by Triton which, when combined with earlier results, show that Triton has undergone a period of global warming since 1989. Our most conservative estimates of the rate of temperature and surface-pressure increase during this period imply that the atmosphere is doubling in bulk every 10 years—significantly faster than predicted by any published frost model for Triton[2,3]. Our result suggests that permanent polar caps on Triton play a dominant role in regulating seasonal atmospheric changes. Similar processes should also be active on Pluto.

The 4 November 1997 occultation of the star Tr180 (also known as Tycho 651672 and GSC6321–01030) was successfully observed with the Hubble Space Telescope (HST) in daylight over the northwest Pacific Ocean; Astrometer 3 of the Fine Guidance Sensors (FGS) was used to record the event[5]. Details of the HST data are given in Table 1 along with information about other observing stations; the immersion and emersion data (disappearance and reappearance of the star) are shown in Fig. 1. A central flash (the focusing of light rays by Triton's atmosphere[6,7]) was recorded, but will be presented and analysed elsewhere.

We modelled the HST light curve with a standard small-planet model that allows for a power-law temperature gradient[8] (Table 2). The background from dark counts and Triton (determined by the FGS in September and adjusted for Triton's different distance) was subtracted, and the remainder was divided by the flux from the star (also determined by the FGS in September) so that the full range of stellar flux corresponded to values between 0.0 and 1.0. In the light-curve model fits, the zero level was fixed, but the full-scale signal from the star was a free parameter. The difference of the fitted values from 1.0 shows that our calibration error is only a few tenths of one per cent.

From fitting the entire light curve, the closest-approach distance between the centre of Triton's shadow and the HST was determined to be 224 ± 4 km (first column of results in Table 2). This value places the shadow somewhat further north than predicted, but it is consistent with no detectable occultation at our Oahu station (Table 1). Using the closest-approach distance determined from the entire light curve, we fitted the main immersion and emersion sections of the light curve both separately and together (next three columns of results in Table 2). As a test of the self-consistency of our light-curve models, we fixed the atmospheric model parameters ("half-light radius", "lambda at half-light," and the "thermal-gradient exponent"; see ref. 8) at their values determined from

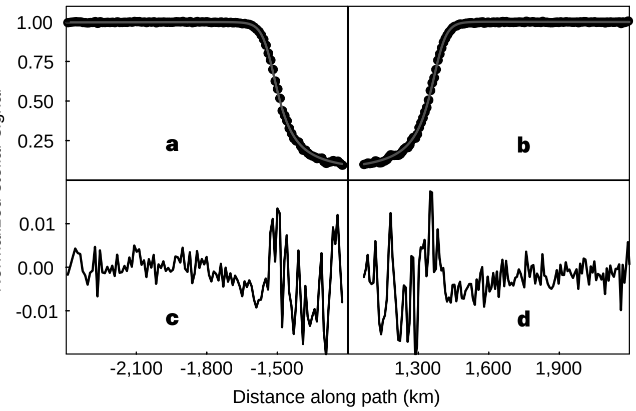

Figure 1 Triton occultation light curves from the HST. Data before and after the occultation were used to establish the modulation of the signal due to the astrometer scan, which was then removed from the entire data set. The zero and full-scale stellar flux levels were established with photometric data from an earlier FGS visit to these objects on 11 September 1997. At that time, Triton's magnitude as observed by the FGS was 13.4 and the magnitude of Tr180 was 10.6. The FGS data have been averaged at 1.0 s; **a**, immersion data (filled circles) and light-curve model fit (line); **b**, emersion data (filled circles) and light-curve model fit (line; see fits in Table 2). The zero point of the abscissa is arbitrary. The light-curve model[8] used a power-law thermal gradient; residuals from the fit in **a** are shown in **c**, and the residuals from the fit in **b** are shown in **d**. The r.m.s. residual along the full signal is ~0.0022 for a 1-s average, and is the result of photon noise. The remaining residuals that occur when the star is partially occulted are the result of unmodelled structure in Triton's atmosphere and rarely exceed 0.01. The effect of these on our determination of the 1,400-km pressure can be estimated by differences among the fits in Table 1. The omitted central portion of the light curve (see text) corresponds to radii <1,400 km (altitudes <48 km); the atmosphere below that does not affect the 1,400-km pressure.