of development on a subset of the tumour cells. The Hes1^{+} population formed slow-growing tumours, suggestive of a tumour-suppressive role for Notch signalling in that context. However, the authors also found a tumour-promoting role for Notch, because non-neuroendocrine tumour cells produce the protein midkine, a ligand for Notch2, which promotes the growth of neuroendocrine tumour cells in culture, thus maintaining the tumour.

Lim and colleagues' work was mainly carried out *in vitro*, and used either isolated human cancer cells or neuroendocrine cell lines. It therefore remains to be determined whether interactions between neuroendocrine and non-neuroendocrine cells *in vivo* might also be influenced by contact between cells and by the Notch-mediated phenomenon of lateral inhibition (in which the interaction between two adjacent cells results in the formation of two different cell types). Additional experiments, such as lineage tracing of the two cell types, will help to determine whether the proposed relationships between the cells exist *in vivo*.

Many questions remain. It has been proposed[11] that, during homeostasis, neuroendocrine cells signal to their neighbours through Notch, possibly creating a specific stem-cell niche, but this remains a contentious point that should be reassessed in light of the latest results. Do populations of Wnt-responsive cells behave as stem cells in normal lung homeostasis? One could speculate that, in homeostasis, stem cells in the lung also generate their own niches (producing Wnt and/or Notch ligands) and, similar to the situation in tumours, these could also coexist in a dynamic equilibrium.

Another question is whether the roles of Wnt and Notch are specific to lung adenocarcinomas and small-cell lung cancer, respectively, or whether these signalling molecules have roles in other tumour types. If the latter, it would be interesting to discover whether the same type of niche cell produces both factors, or whether each is produced by specialized cell types. Perhaps the two pathways are intimately connected in lung-tumour formation, similarly to how Notch works with Wnt to control cell-fate transitions during development and in adult homeostasis[6].

The observations by Tammela *et al.* and Lim *et al.* that lung tumour cells can produce their own niche has a parallel in homeostasis in the lung airways, in which stem cells signal to their immediate descendants in a Notch-dependent manner to mediate cell-fate decisions[12]. This potentially implicates the rewiring of normal homeostatic stem-cell mechanisms in tumour growth. The stage is now set to investigate such previously unsuspected aspects of lung-cancer biology. ■

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ATOMIC PHYSICS

Quantum theory verified by experiment

Systems of quantum objects can be characterized by the correlations between the objects. A technique that precisely measures even the most delicate of these correlations allows models of quantum systems to be tested. SEE LETTER P.323

IAN B. SPIELMAN

The laws of nature are inferred through the observation of correlations, which distil information about the properties of physical systems. Such correlations can be determined by studying systems in their natural state, or by performing controlled experiments in which certain quantities are deliberately manipulated. Observing correlations in quantum systems is challenging because quantum objects are fundamentally altered by the process of taking measurements, and available measurement tools do not probe the quantities of interest. But on page 323, Schweigler *et al.*[1] report a method that overcomes these problems and allows correlations to be measured for a quantum system comprising thousands of rubidium atoms at ultracold (nanokelvin-scale) temperatures. The authors show that this system is accurately described by a mathematical framework called the sine-Gordon quantum field theory[2], confirming a previous proposal[3]. Crucially, their technique could be applied to many types of quantum system — including those that have strong interactions, in which the underlying physics is not well established[4].

In quantum systems, matter behaves like a wave and has an associated phase — defining the position of the crest of the wave. The type and degree of correlation between the phases of two quantum objects can be expressed using a set of statistical parameters called correlation functions (CFs). For example, the first-order CF is simply the average relative phase between the objects at a particular position along the length of the waves. Conversely, the

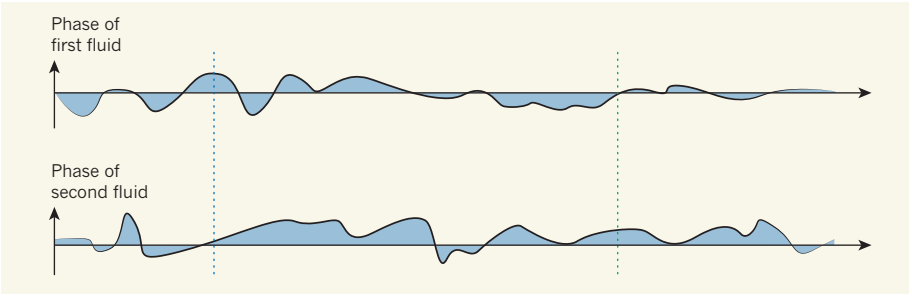

Figure 1 | Observing correlations in a quantum system. Schweigler *et al.*[1] report a method to probe the underlying physics of quantum systems. Their experiment consists of a pair of weakly interacting one-dimensional quantum fluids — thousands of rubidium-87 atoms at ultracold (nanokelvin-scale) temperatures. Each fluid acts like a wave whose shape can be described by a fluctuating phase (defining the position of the crest of the wave). The authors use a measurement technique called matter–wave interferometry[5] to determine the relative phase between the fluids at various positions (dotted lines) along the length of the waves. They then use these measured correlations to test theoretical models of such systems.

second-order CF expresses the similarity of the relative phases at two different positions: if the relative phases have the same sign, the CF will be positive (correlated); if they have opposite signs, the CF will be negative (anti-correlated); and if they sometimes have the same sign and at other times have opposite signs, the CF will be negligible (uncorrelated).

For quantum systems that have a constant relative phase (after taking the average of multiple measurements), the fluctuations around this average look like experimental background noise when observed in a single measurement. In these systems, the interplay between two types of noise contains information about higher-order CFs (those of order greater than one). First, there is quantum-measurement noise — individual quantum measurements have a fundamental noise owing to relations similar to the Heisenberg uncertainty principle, which constrains the precision with which the position and momentum of quantum objects can be measured. Second, there is thermal noise, which results from extra motion present in systems at non-zero temperatures. Schweigler *et al.* generated a huge amount of data to evaluate the combination of these sources of fluctuations. This allowed the authors to calculate higher-order CFs that are required for testing theoretical models of such quantum systems.

Schweigler and colleagues' experiment consisted of a pair of weakly interacting one-dimensional quantum fluids — comprising thousands of ultracold rubidium-87 atoms — that behave in a wave-like manner (Fig. 1). The authors used a measurement technique known as matter–wave interferometry[5] to determine the CFs of the system; the interference between the two waves produced an interference pattern whose fringes (bright or dark bands) corresponded directly to the relative phase between the waves.

The authors calculated 'disconnected' CFs, in which the information present in lower-order CFs was removed. In many systems — for example, atomic gases ultracooled to a phase of matter known as a Bose–Einstein condensate[6] — only first- and second-order disconnected CFs contain useful information. However, Schweigler *et al.* evaluated disconnected CFs up to tenth order. They found that these contain information that is not present in any combination of lower-order CFs, highlighting the complexity of their system. Furthermore, the authors showed that the CFs were in agreement with predictions of the sine-Gordon quantum field theory[3], rather than with those of more-conventional and simple models of 1D quantum fluids[7].

Although Schweigler and colleagues' study represents a powerful first demonstration of their technique, only a tiny fraction of the information present in their CFs was used. An nth-order CF is an n-dimensional function of the positions at which the measurements are taken, but the authors fixed all but two of these quantities — they restricted their study to 2D parameter spaces or, even more restrictively, looked at simple averages over all the positions. These simplifications made the authors' data easily tractable, but simultaneously erased most of the information present in their CFs. A crucial next step will therefore be to develop the theoretical and numerical tools required to interpret all the data present in these CFs and to fully characterize the corresponding quantum systems.

Moreover, the physics describing the authors' weakly interacting 1D quantum fluid was not under debate. However, their methodology might in future be applied to strongly interacting systems in which the underlying physics is not established. In particular, their technique is broadly applicable to 1D systems including disordered quantum systems of interacting atoms far from thermal equilibrium, in which the unknown physics of many-body localization[4] is likely to be in play. ■

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AGEING

Tools to eliminate senescent cells

Ageing and many diseases are partly driven by the accumulation of damaged cells that no longer divide. It emerges that these senescent cells can be eradicated in mice using a drug that interferes with the activity of the protein FOXO4.

MANUEL SERRANO

If cells incur too much damage, they undergo either a self-elimination process known as apoptosis or a self-disabling process called senescence. Senescent cells can be long-lived, and so accumulate in aged and damaged organs[1]. The elimination of senescent cells is known[2–6] to increase healthy lifespan and reduce the severity of age-related diseases in mice. Writing in *Cell*, Baar *et al.*[7] expand our understanding of this phenomenon. They report that senescent cells depend on the transcription factor forkhead box protein O4 (FOXO4) for their survival, and show in mouse models that both age-associated defects and tissue dysfunction caused by chemotherapy can be reversed by pharmacologically perturbing the function of this protein.

Senescent cells forcibly block their own capacity to proliferate while programming themselves to secrete signalling molecules — a phenomenon known as the senescence-associated secretory phenotype (SASP). It has been proposed[8,9] that the normal function of the SASP is to restore tissue function in two ways: first, by stimulating less-damaged neighbouring cells to engage in tissue repair; and second, by attracting inflammatory cells to eliminate senescent cells and turn off SASP-mediated signals. However, this restorative process may fail when the extent, duration or frequency of damage exceeds repair capacity, or when reparative and inflammatory cells become unresponsive to the effects of the SASP. The end result is an aberrant accumulation of senescent cells that, contrary to their initial purpose, aggravate tissue dysfunction.

In the past two years, it has become clear that senescent cells have distinct molecular vulnerabilities that can be targeted by senolytic compounds — pharmacological agents that preferentially kill senescent over non-senescent cells[2]. Senescent cells express high levels of pro- and anti-apoptotic factors, and are therefore poised on the brink of cell death[4,5]. This is the basis for prototypical senolytics, which inhibit members of the survival-promoting BCL-2 protein family to tip cells into apoptosis. A senolytic based on a combination of two drugs has also been found, but the molecular basis for its activity remains to be elucidated[2,6].

Baar *et al.* set out to learn more about the mechanism by which senescent cells restrain themselves from undergoing apoptosis. Gene-expression data revealed that the transcription factor FOXO4 is upregulated in senescent cells compared with normal cells. The authors further showed that downregulation of FOXO4 using an inhibitory RNA molecule triggered apoptosis in senescent but not in normal cells, whereas downregulation of other