of the important structural information about the sample, but the phase at different image points is not ordinarily recorded on an electron micrograph. However, it can be found using a process known as focal series reconstruction[3,4], or by creating interference between the scattered wave and a known (unscattered) reference wave, as is done in an imaging technique called electron holography[5].

Van Dyck and Chen suggest that it is possible to calculate the heights of atoms from the image plane using only one viewing direction, if this phase can also be determined. The authors point out that the phase speed — the rate at which the phase changes with scattering angle — near the image of a particular atom is approximately proportional to the height of that atom. This approximate proportionality then allows the height to be determined, in rough analogy to Hubble's law. However, it should be noted that the proportionality is strictly valid only in the vicinity of the atom's projected position in the image plane, and that its value is approximate because of aberrations in the microscope's lenses. Therefore, the local and approximate constant of proportionality allows only the height of that particular atom to be measured.

In applications of holography that have captured the public's imagination, a ghostly three-dimensional image of a macroscopic object is reconstructed from the information given by a two-dimensional interference pattern (the hologram) of two laser beams. In this form of imaging, which was first proposed[6] by the physicist Dennis Gabor to image microscopic objects using electron waves instead of light beams, the macroscopic object may be regarded as an ensemble of point scatterers, and the fact that fringes in the interference pattern overlap is no obstacle to correctly reconstructing the spatial positions of these point scatterers. In this technique, the three-dimensional nature of the image automatically gives information about the third dimension. This is also the basis of atomic-source holography[7], which has been used, for example, to determine the positions (including the heights) of atoms adsorbed on a surface.

Van Dyck and Chen propose that knowledge about the third dimension can instead be obtained by first reconstructing the normally invisible phase of the electron wave, and then exploiting the analogy with Hubble's law. They demonstrate their technique for atoms in a system composed of two layers of graphene — a one-atom-thick, honeycomb-like lattice of carbon. But for the proposed technique to be more generally applicable, it will be necessary to extend the algorithm to reconstruct truly three-dimensional objects, as Gabor envisaged. ■

Dilano Saldin *is in the Department of Physics, University of Wisconsin-Milwaukee, Milwaukee, Wisconsin 53211, USA.*
e-mail: dksaldin@uwm.edu

1. Van Dyck, D. & Chen, F.-R. *Nature* **486,** 243–246 (2012).
2. Hubble, E. *Proc. Natl Acad. Sci. USA* **15,** 168–173 (1929).
3. Coene, W. M. J., Thust, A., Op de Beeck, M. & Van Dyck, D. *Ultramicroscopy* **64,** 109–135 (1996).
4. Hsieh, W.-K., Chen, F.-R., Kai, J.-J. & Kirkland, A. I. *Ultramicroscopy* **98,** 99–114 (2004).
5. Lehmann, M. & Lichte, H. *Microsc. Microanal.* **8,** 447–466 (2002).
6. Gabor, D. *Nature* **161,** 777–778 (1948).
7. Saldin, D. K. *Surf. Rev. Lett.* **4,** 441–457 (1997).

PLANT IMMUNOLOGY

A life or death switch

The identification of two receptors for salicylic acid reveals how the hormone controls cell death and survival during plant immune responses, in tissues close to and distant from the site of infection. SEE LETTER P.228

ANDREA A. GUST & THORSTEN NÜRNBERGER

Immunity to microbial infection is an inherent feature of multicellular organisms. In plants, immune responses are activated when cellular receptors recognize microbial proteins (effectors) that betray the invader to the plant's surveillance system[1,2]. This activation requires the plant hormone salicylic acid, which is produced on microbial attack[3]. But how plants detect the hormone, and how it performs its immunity-associated functions, has remained unclear. On page 228 of this issue, Fu *et al.*[4] report the identification of two salicylic acid receptors in the model plant *Arabidopsis thaliana*, and provide a fascinating explanation of how the hormone controls both cell death at the site of infection, and cell survival and immune activation in non-infected tissues.

In plants, effector-triggered immunity (ETI) is often accompanied by programmed cell death (PCD) at the infection site. In addition to participating in local immune responses, PCD triggers long-lasting immunity against a broad spectrum of microbes throughout the plant — a protective mechanism referred to as systemic acquired resistance[3]. Salicylic acid participates in these immune responses by controlling the movement of a protein called NPR1 (non-expresser of pathogenesis-related genes 1) from the cell cytoplasm to the nucleus[5]. Once in the nucleus, NPR1 regulates the expression of plant defence genes. Because mutant

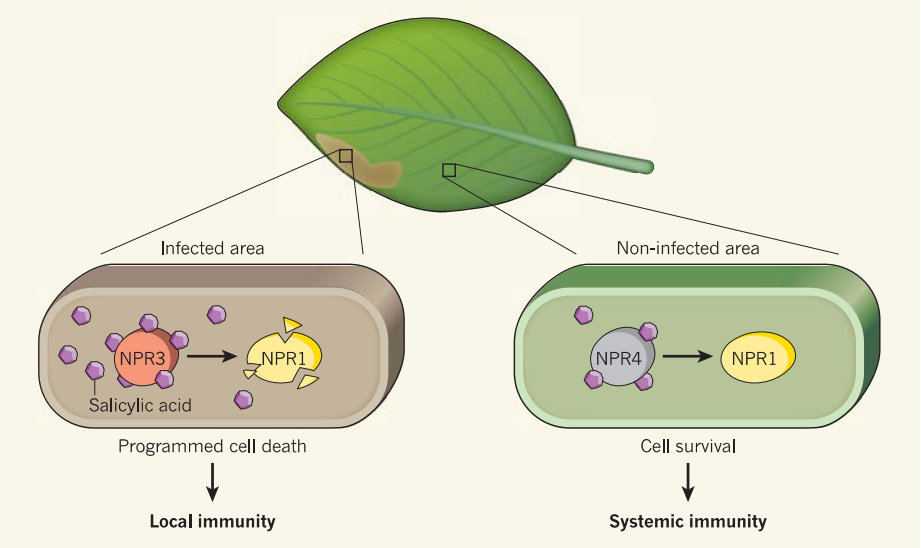

Figure 1 | Salicylic acid-mediated control of plant cell death and survival. On microbial infection, levels of the plant hormone salicylic acid increase, with its concentration decreasing gradually with increasing distance from the site of infection. Fu *et al.*[4] show that at high salicylic acid concentrations — typically found in infected areas of the plant — the receptor NPR3, which binds salicylic acid with low affinity, mediates degradation of the cell-death suppressor NPR1 (left panel), thereby favouring programmed cell death and local effector-triggered immunity. However, at the lower salicylic acid concentrations typically found in cells distant from the infection site, salicylic acid cannot bind to the low-affinity receptor NPR3, so cell death is blocked. In these cells, salicylic acid instead binds to the high-affinity receptor NPR4 (right panel), blocking degradation of NPR1, and thereby favouring cell survival and the expression of genes associated with systemic immunity.

plants that are insensitive to salicylic acid and plants that lack NPR1 exhibit similar immune defects, NPR1 was previously proposed[6] to be a salicylic acid receptor. However, Fu *et al.*[4] did not detect any physical interaction between salicylic acid and NPR1, suggesting that NPR1 does not serve this receptor function.

What, then, could be the bona fide salicylic acid receptor mediating local and systemic immune activation in plants? The research group presenting the current paper has previously shown[7] that the proper functioning of NPR1 requires that the protein is broken down by cellular protein-degradation machinery called the proteasome. So Fu and colleagues hypothesized that adaptor proteins that link NPR1 to the proteasome might be receptors for salicylic acid. Two members of the NPR protein family, NPR3 and NPR4, exhibit a protein-domain structure that is characteristic of such adaptor proteins, leading the authors to surmise that these proteins could be the proteasome adaptors that mediate NPR1 degradation. To validate this assumption, the researchers demonstrated that NPR1 is degraded by the proteasome in wild-type *A. thaliana* plants, but not in plants in which the genes for NPR3 and NPR4 have both been knocked out.

Fu and colleagues used *in vitro* protein–protein interaction studies to assess the effect of salicylic acid on the formation of protein complexes between NPR1 and NPR3 or NPR4. The authors found, surprisingly, that salicylic acid promotes NPR1–NPR3 interaction, but disrupts formation of the NPR1–NPR4 complex. Thus it seems that salicylic acid interacts physically with NPR3 and NPR4 in a receptor-like manner, but that this interaction has opposing effects on the adaptor proteins' interactions with NPR1. The authors also found that although NPR3 and NPR4 both bind to salicylic acid, NPR4 binds with greater affinity than does NPR3. Hence, *Arabidopsis* plants contain two salicylic acid receptors, NPR3 and NPR4, which differ in their affinity for the hormone and in their roles in NPR1 degradation, with NPR3 mediating NPR1 breakdown only in the presence of salicylic acid and NPR4 only in its absence.

What are the biological consequences of NPR3- or NPR4-mediated degradation of NPR1? Fu and colleagues found that both local PCD and local ETI responses to bacterial infection were compromised in plants lacking the genes encoding both NPR3 and NPR4. The impairment of PCD, combined with the fact that NPR1 accumulates in the mutant plants (because it cannot be degraded) suggests that NPR1 suppresses PCD in wild-type plants. Because salicylic acid levels are highest at infection sites[8], Fu *et al.* propose that binding of the hormone to the lower-affinity receptor NPR3 mediates NPR1 degradation and de-repression of PCD and ETI in infected cells (Fig. 1).

However, infection causes salicylic acid levels to increase systemically as well as locally, with its concentration decreasing gradually with increasing distance from the infection site[8]. In cells farther away from the infected area, salicylic acid levels are likely to drop below the concentration required for NPR3-mediated NPR1 degradation and, thus, PCD. Fu and colleagues propose that, in these cells, salicylic acid binds instead to the higher-affinity receptor NPR4, which inhibits NPR4-mediated NPR1 degradation and thereby facilitates NPR1 accumulation, cell survival and subsequent salicylic acid-dependent gene expression (Fig. 1). Consistent with this model, the authors showed that NPR1 levels are lowest in cells undergoing PCD and highest in cells surrounding PCD lesions.

Several mutant plants that exhibit runaway PCD have been identified[9], and the question of how plants control PCD has been a major area of research. Fu and colleagues' findings provide compelling evidence that salicylic acid acts as an immune signal to determine cell fate in plant immunity. Studies investigating plant proteins associated with abnormal PCD should now examine whether these proteins might contribute to the functionality of NPR3 or NPR4.

Salicylic acid is the only major plant hormone for which the receptor has remained elusive. Fu and colleagues' demonstration that the two salicylic acid receptors control distinct defence strategies by de-repressing local cell death and immunity at the infection site in one case, and systemic immunity remote from the infection site in the other, is reminiscent of the de-repression of physiological programs enacted by other plant hormones, such as auxin, gibberellic acid and jasmonic acid[10]. However, NPR3 and NPR4 are the first plant-hormone sensors for which differences in binding affinity have been shown to mediate differential control of plant responses. Because most plant hormones regulate multiple aspects of plant life, it is certainly possible that other plant hormone receptors use a comparable mode of action. Consistent with this idea is the recent identification[11] of auxin hormone-binding proteins that have different ligand affinities, suggesting that plants also have means for differential sensing of auxin[1]. ■

Andrea A. Gust *and* **Thorsten Nürnberger**
are in the Centre of Plant Molecular Biology, Department of Plant Biochemistry, University of Tübingen, D-72076 Tübingen, Germany.
e-mails: nuernberger@uni-tuebingen.de; andrea.gust@zmbp.uni-tuebingen.de

1. Dodds, P. N. & Rathjen, J. P. *Nature Rev. Genet.* **11,** 539–548 (2010).
2. Jones, J. D. & Dangl, J. L. *Nature* **444,** 323–329 (2006).
3. Spoel, S. H. & Dong, X. *Nature Rev. Immunol.* **12,** 89–100 (2012).
4. Fu, Z. Q. *et al. Nature* **486,** 228–232 (2012).
5. Mou, Z., Fan, W. & Dong, X. *Cell* **113,** 935–944 (2003).
6. Cao, H., Glazebrook, J., Clarke, J. D., Volko, S. & Dong, X. *Cell* **88,** 57–63 (1997).
7. Spoel, S. H. *et al. Cell* **137,** 860–872 (2009).
8. Enyedi, A. J., Yalpani, N., Silverman, P. & Raskin, I. *Proc. Natl Acad. Sci. USA* **89,** 2480–2484 (1992).
9. Lam, E. *Nature Rev. Mol. Cell Biol.* **5,** 305–315 (2004).
10. Robert-Seilaniantz, A., Grant, M. & Jones, J. D. *Annu. Rev. Phytopathol.* **49,** 317–343 (2011).
11. Calderón Villalobos, L. I. *et al. Nature Chem. Biol.* **8,** 477–485 (2012).

ASTRONOMY

An infant giant

Spectroscopic measurements of a galaxy that shines brightly at submillimetre wavelengths place it in the middle of a nascent galaxy cluster at a scant one billion years after the Big Bang. SEE LETTER P.233

ALBERTO D. BOLATTO

As in many scientific fields, but perhaps more than in most, advances in technology frequently drive progress in astronomy. The deployment of a new instrument or a capability can afford a completely different view of the Universe, opening a window onto an aspect of reality that was previously unsuspected or only theorized. One such advance occurred in the late 1990s with the advent of large-format submillimetre-wave cameras — particularly SCUBA, the Submillimetre Common-User Bolometer Array mounted on the James Clerk Maxwell Telescope in Mauna Kea, Hawaii — and the resulting discovery of a class of luminous yet elusive galaxies. On page 233 of this issue, Walter *et al.*[1] describe an analysis that advances our understanding of this family of galaxies and closes a chapter on the story of their origins.

Early on, images taken with SCUBA revealed a population of galaxies that shine brightly at submillimetre wavelengths, prosaically named submillimetre galaxies (SMGs). One of the first deep SCUBA images to uncover SMGs was obtained[2] in 1998 through observations of the Hubble Deep Field (Fig. 1), which is perhaps the most emblematic patch of sky observed by the Hubble Space Telescope. Surprisingly, SMGs were very faint, or