tion is a critical one because the delay before the gene shuts down is what allows protein levels to oscillate with a 24-hour rhythm. The researchers are also on the trail of other proteins that seem to control the *kaiA* gene and help regulate *kaiB* and *-C* as well.

While Ishiura and his colleagues work to fill out the picture, researchers in the field will want to put this new revelation into its evolutionary context. They already knew that the clock proteins of fruit flies and mammals are strikingly similar, making it clear that these clocks evolved from the clock of a common ancestor (*Science*, 5 June, p. 1548). But the *Neurospora* clock has only weak similarities to the animal clocks, raising the possibility that it might have had an independent origin. Researchers disagree about that but say that the cyanobacteria discovery confirms at least two independent origins for clocks.

More may be in the offing. Just this June, researchers got their first glimpse of a plant clock when two teams, one led by John Harada at the University of California, Davis, and the other by Elaine Tobin at UC Los Angeles, identified two different mutations that disrupt the circadian rhythms of the plant *Arabidopsis*. Both affect transcription-control proteins known as MYB proteins, which are unrelated to any known clock proteins. That begins to smell like yet another independent clock, says Steve Kay of The Scripps Research Institute in La Jolla, California.

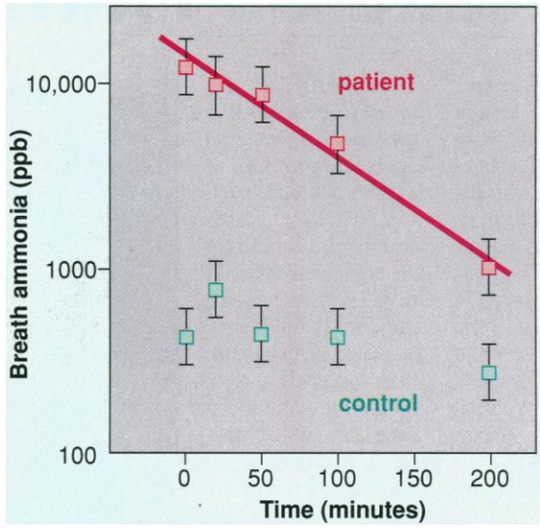
Yet Mother Nature didn't veer far from her tried-and-true system for telling time when she built the *Arabidopsis* clock: The MYB proteins both apparently go back and turn off their own genes. Perhaps, says Kay, feedback on gene transcription has always won out over other possible mechanisms because proteins that regulate their own production are common and therefore readily available to be crafted into clocks. Alternatively, speculates clock researcher Michael Young of Rockefeller University, "maybe this is the only way you can make a clock." **–MARCIA BARINAGA**

MEDICAL TECHNOLOGY

Breathalyzer Device Sniffs for Disease

BOSTON—A whiff of a patient's breath can sometimes be enough to tell a doctor what's wrong. The fishy smell of compounds called amines can indicate kidney problems, while the sweet smell of acetone can mean diabetes. Now two scientists have developed a machine that could turn this practice into a high-tech diagnostic technique, they announced at the American Chemical Society meeting here last week.

In just minutes, the device can analyze a puff of breath for the trace gases that signal diabetes, kidney failure, ulcers, and possibly even cancer. Commercial versions could be available within a few years, providing fast, noninvasive diagnosis. "These are very exciting results," says Michael Henchman, a chemist at Brandeis University in Waltham, Massachusetts, who is not involved in the work. "[This] technique could be as important to medicine as MRI [magnetic resonance imaging]."



SOURCE: D. SMITH/KEELE UNIV.

Telltale breath. Breathalyzer tracks declining ammonia levels—a sign of kidney failure—in a patient undergoing dialysis.

The telltale compounds find their way into the breath when they build up in the blood. As the blood circulates through the lungs, gases in the lungs and blood equilibrate, and the breath carries them out. But developing a diagnostic device that's better than a physician's nose at picking up these wafting fumes has not been easy.

Researchers have tried sniffing out illness, for example, with an instrument known as a gas chromatography–mass spectrometer, or GC-MS. But a GC-MS has trouble dealing with some of the complex mixtures of trace chemicals in the breath. To convert the uncharged organic compounds into charged ions that can be propelled through the mass spectrometer by electric fields, the device bombards the compounds with electrons. The bombardment often breaks down different trace gases into similar smaller components. "It makes it impossible to deconvolute your data" to determine the exact parent compounds, says David Smith, a chemical physicist at Keele University in Staffordshire, United Kingdom.

Two decades ago, when Smith was studying trace gases known to be present in interstellar gas clouds, he developed a gentler way to attach a charge to molecules. His device, known as a selected ion flow tube, or SIFT, reacts compounds in a test sample with carefully selected ions instead of electrons. The reactions change the original compounds only slightly, and each one produces a unique signal in a mass spectrometer.

Three years ago, while working on his technique during a brief stint at the University of Innsbruck in Austria, Smith realized that the same technique might be useful for sorting out the chemicals in breath. Smith and Patrik Spanel, a physicist with the J. Heyrovsky Institute of Physical Chemistry in Prague, Czech Republic, teamed up to adapt the SIFT technique. But they soon faced a new challenge: The ions they intended to react with the trace compounds also reacted with substances that are abundant in breath, such as oxygen, nitrogen, water, and carbon dioxide, which depleted the ions and yielded confusing results. So Smith and Spanel identified a new set of ions—HO_3^+, NO^+, and O_2^+—that don't react readily with the basic ingredients of breath.

Instead, they found that each ion reacted only with certain trace breath components, producing a unique chemical signature for each molecule. And because the SIFT device can generate all three ions simultaneously and feed them into the reaction tube one right after the other, Smith and Spanel were able to obtain complete profiles of all the target compounds from just a single breath. Smith says that he and Spanel have already converted their instrument from a hulking tabletop device to a portable machine that can be wheeled into hospital rooms, and they are currently working to shrink the equipment further.

When Smith and Spanel tested their instrument on patients with various disorders, the results jumped out. Patients with kidney failure, for example, showed levels of ammonia more than 10 times higher than those in controls, because of the waste compounds in their blood. "It essentially delivers an instantaneous diagnosis," says Henchman. The device enabled researchers to watch those levels fall to normal as the patients received dialysis treatment (see graph).

Smith also reported that the machine can gauge a subject's stress level by tracking isoprene, as well as track markers for diabetes and ulcers. Preliminary data even suggest that it could detect hydrocarbons (he declined to say which ones) associated with bladder and prostate cancer. In addition, Smith believes the new machine will prove to have a versatile nose for trouble and could monitor air quality and food freshness as well as disease. **–ROBERT F. SERVICE**