Small strip, big opportunities

For thousands of years, urine analysis has served as an indicator for diseases. And today, urine strips are still a common method of medical diagnosis. An invention by Chris Zimmerle will help to increase the reliability of results in the future.

The idea is simple: to find out what's going on inside the body, look at what flows out of it. It's therefore no surprise that early civilizations and doctors in the Middle Ages believed that urine could serve as an indicator for disease. The latter used visual inspections, odor tests or even tasting for a first diagnosis of all kinds of illness. As knowledge about anatomy, physiology and organ functions grew, analysis of urine and its chemical constituents also evolved, delivering more accurate evidence of possible diseases – especially after the invention of the microscope.

Today, visual inspections, smell tests and tasting are no longer the preferred methods for urinalysis; instead, testing is now done with strips. Once urine comes into contact with these test strips, the strips undergo a chemical reaction resulting in color changes. This makes strips an easy-to-use and fast method not only for home pregnancy tests – one of the best-known applications – but also to detect a variety of ailments like kidney and liver disease, diabetes, and urinary tract infections.

Today's urine strips are remarkably sophisticated, but far from perfect. "We're still innovating", says Chris Zimmerle, a scientist at Siemens' Healthcare Diagnostics team in Elkhart, Indiana. "With all the changes in technology we've seen in the last years, while the strips themselves have remained similar, the technology to measure and analyze them in new ways has greatly improved."

Zimmerle and a small team of nine people in Elkhart work in the Point of Care field for urine strips and diabetes testing. They focus their efforts on improving the test strips themselves, as well as the instrument systems used to measure results from the strips. What drives their research is one simple goal: reliability of results. Not only would a false-negative result be undesirable – indicating that a patient is healthy when in fact he is not – but also a false-positive, giving evidence that the patient may be ill and leading to follow-up tests. Although the reliability of the Siemens urine strips is good, their goal is to constantly try to improve the accuracy.

One threat that can affect the results is high humidity, which can quickly damage urine strips. This could, for instance, occur when a strip container was not completely closed after use. Very humid, tropical conditions can also cause damage. But thanks to an invention by Chris Zimmerle, there is now a way to determine if a result has been compromised. Although his invention is invisible to the human eye, it can make a big difference: An Infrared ID band was applied to the Siemens Multistix urinanalysis strips, making it possible to identify the strip type and also to minimize potential false-positive results.

In addition to this ID band, strips may contain up to ten pads measuring parameters such as glucose, bilirubin, blood and pH, allowing detection of a broad range of conditions. Once the strip is dipped into the urine sample, a chemical reaction begins causing those pads to change color. The strip is then inserted into an analyzer – a small, portable device – and an automatic check is initialized. The analyzer can detect strips that have been compromised by humidity and, in these instances,

generates a printed error message instead of reporting inaccurate results. In a recent controlled study, approximately 98% of all strips that had been exposed to high humidity were detected and an error message was generated, thus preventing inaccurate reporting.

The trick is that the presence of the ID band allows one of the existing reagent pads to serve as a humidity indicator: When exposed to high humidity, this reagent pad can appear as a (false-) positive result. Once the strip is inserted into the analyzer, the strip type is recognized – thanks to the ID band – and automatically activates additional optical measurements in order to find out whether the strip was affected by humidity.

Chris Zimmerle is an expert in this specialized research field. He has already registered 17 inventions that are protected by 49 individual patents and 14 IPR families. However, he didn't begin his career with an interest in urine analysis. Instead, he landed in it almost by accident. He studied Biochemistry at Wright State University, Ohio, and holds a Ph.D. in Biomedical Sciences. He went on to do post-doctoral studies at Washington University. Zimmerle started working for Siemens Healthcare more than 25 years ago in immunoassay development before transferring to urine chemistry development in the early nineties.

At that time, state-of-the-art technology was nothing more than "single-point" instruments that could only read one small area at a time. Zimmerle and his co-workers found this unsatisfactory. Their solution was innovative but highly effective: they took an inexpensive document scanner, turned it upside down and developed software to read the results on the urine strips available at that time. The advantage: by using scanners, and later cameras, results could be delivered much faster and more accurately.

While the majority of Zimmerle's work has been with traditional urine chemistry reagent strips, the release of the CLINITEK Status instrument in 2002 was an important step forward, making it possible to read immunoassays (a biochemical test that measures the presence of an analyte through the use of an antibody or immunoglobulin). One of the immunoassays Chris has worked on is used to detect human chorionic gonadotropin (hCG), a protein released in the urine during pregnancy.

Recent instruments Zimmerle has been working on demonstrate what state-of-the-art technology can do. Everything that was once visualized by eye can now be analyzed by cameras, making it possible to detect color development more accurately and reliably by removing errors caused by the human eye, lighting conditions, or strip reading times. Zimmerle's work resulted in the novel calibration of the CLINITEK Novus analyzer. Several issues had to be resolved to obtain accurate results from the camera contained within this system. Zimmerle explains: "It is absolutely necessary that the measured color is the same across different instruments. That is why we need to calibrate the cameras in order to 'define' a color that is reproducible. Only then can different instruments interpret the results on the pads in the same way".

Much of this research involves a combination of biochemistry, computer science, and some understanding of optical measurements and color. This was a natural extension of much of Zimmerle's graduate and postgraduate work which centered around computer simulations of biological processes.

But research is always ongoing, and more innovations in this field can be expected. “Things are becoming more complex – for the better. This is because technology allows us to do a lot more”, says Zimmerle. He calls this “data mining” and explains: “The strips can deliver up to twelve readings. When testing specimens with new technology, we get a massive amount of data. Even if we’re getting ‘only’ twelve results, our newest urinalysis instrument is actually collecting 96 readings on every single sample. This results in thousands of data points for a typical clinical study. There can be clinical interferences and correlations in this data that can be used, the trick is finding it.”

Zimmerle’s fascination for future technologies is not confined to his work. He is a big fan of science shows on TV. It’s therefore no surprise that the father of two boys is also being kept busy by another project, which he calls “project ‘home improvement’”. A couple of years back, he started to build a home theatre in his basement. Often on the program: science fiction movies.