



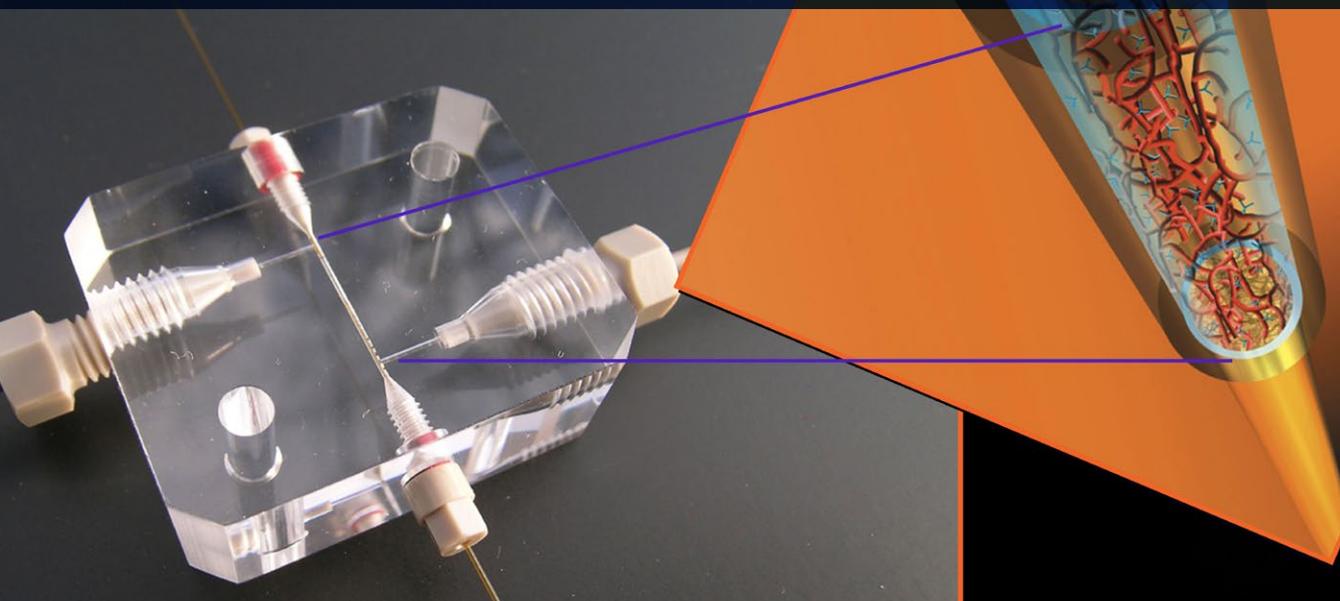
Dr Norberto Guzman

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Dr Daniel Guzman

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# Improving diagnostic testing and disease analysis with IACE

## Research Objectives

The development of accurate and affordable healthcare approaches that benefit patients around the world.

## Detail

### Bio

#### Norberto A Guzman, PhD, MSc

Dr Guzman is currently Chief Scientific Officer and Director of Research at Princeton Biochemicals Inc, Princeton, New Jersey, USA. His interest is primarily in biomedicine and biotechnology with emphasis in protein biochemistry and immunochemistry.

#### Daniel E Guzman, MD

Dr Guzman is currently a clinical instructor at the Department of Medicine, School of Medicine, University of California, San Francisco, California, USA. His interests are primarily in hospital medicine, diversity and inclusion, biomedical and chemical engineering, biomarker discovery and detection, and microfluidics.

### Funding

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### Collaborators

Terry Phillips, Tim Blanc, Fernando Benavente.

Above: The analyte concentrator–microreactor (ACM) device illustrating the internal channel, where one or more biorecognition affinity capture ligands (antibodies, lectins, aptamers, others) are immobilised to a matrix (beads, monoliths, sol-gels) or directly to the walls of the channel, as seen in the expanded view. Adapted from *Electrophoresis*, 29(16) with permission from John Wiley & Sons.

## References

- Guzman, NA, Guzman, DE, (2021) Immunoaffinity Capillary Electrophoresis in the Era of Proteoforms, Liquid Biopsy and Preventive Medicine: A Potential Impact in the Diagnosis and Monitoring of Disease Progression. *Biomolecules*, 11(10), 1443.
- Guzman NA, Guzman, DE, (2020) A Two-Dimensional Affinity Capture and Separation Mini-Platform for the Isolation, Enrichment, and Quantification of Biomarkers and its Potential Use for Liquid Biopsy. *Biomedicines*, 8(8), 255.
- Guzman, NA, Guzman, DE, (2018) From a Central Laboratory to the Bedside: A Point-of-Care Instrument for Monitoring Wellness and Disease Using Two-Dimensional Immunoaffinity Capillary Electrophoresis Technology. *Archives Biomedical Research*, 1 (001).

## Personal Response

***IACE promises a more accurate and affordable approach to disease diagnostics: what do you think is the biggest barrier to its widespread adoption, in both high- and low-income countries?***

“ One of the biggest challenges is that ELISA is a mature business and conveniently used technique worldwide, but unfortunately many tests result in erroneous data. Current and expected technological improvements of IACE will lead to better accuracy in diagnosis and prognosis, and to a better understanding of the underlying mechanisms of disease. IACE is a cost-effective technique with a more comprehensive approach to obtaining accurate results than ELISA which, in the near future, will be used routinely in many clinical settings worldwide. ”

# Improving diagnostic testing and disease analysis with IACE

Current immunosorbent tests used for medical diagnosis are often unreliable, fraught with unacceptable rates of false-positive and negative results. Much of this unreliability stems from the geometry of microtiter plates, but more importantly, the lack of recognition that antibodies are always capable of binding a spectrum of related substances. Several researchers have shown that separating sample components after capture, using immunoaffinity capillary electrophoresis – IACE – enables more specific biomarker binding and detection. The improved accuracy of this IACE technique has facilitated new disease research and can also be incorporated into a low-cost point-of-care medical device to deliver diagnostic testing to remote areas.

Accurate diagnosis is crucial to delivering targeted healthcare. However, current laboratory diagnostic tests, such as the most widely used unidimensional enzyme linked immunosorbent assay (ELISA), are not always accurate, which can result in inappropriate or inadequate treatment if a patient is misdiagnosed. This potential inaccuracy in medical testing fosters a lack of confidence in the healthcare system and results in medical errors. It also increases the cost of medical care by necessitating additional testing.

ELISA was first described in 1971 and had a monumental impact on diagnostics. However, at that time protein chemistry was in its infancy. Subsequent analytical advances in protein chemistry have revealed complexities never imagined in the 1970s. At the onset of ELISA implementation the dogma was ‘one-to-one’, in other words, that each antibody

is highly specific and capable of binding only one particular antigen. Proteins are perhaps the most common antigen target of ELISA antibodies but only in the last decade have scientist begun to appreciate the complexity of protein variants. Shocking to scientists at the time, the Human Genome Project revealed that only about 20,000 genes were identified, when far more were expected, to account for biological complexity. Today, the scientific community is beginning to think in terms of ‘proteoforms’, and that proteins are more complex than a singular product of a gene. Genetic variants, alternate gene splicing, and post-translation modifications, are now known to yield a spectrum of highly similar protein variants recently termed proteoforms. This new understanding of protein complexity necessitates re-evaluating the old ELISA dogma of one-to-one specificity, and acceptance of the fact that many molecular structures can be bound in

an ELISA. Deciphering those structures is where IACE becomes an essential step forward in improving diagnostic accuracy by enabling, for example, the determination of which proteoforms may be associated with a disease state.

Many diseases are known to affect humans, but a specific diagnostic test is only available for a small portion of these. The key to precise detection is the development of a specific biomarker(s), such as a particular proteoform produced at key stages of the disease, including before its clinical manifestation. ELISA works by attaching antibodies to the bottom surface of a well on a test microtiter plate. These bound or ‘captured’ antibodies have traditionally thought to bind specifically to only one type of target – the disease antigen intended to be detected by the test. If the appropriate antigen binds to the captured antibody, it is then detected by attaching another antibody linked to a colour-producing enzyme. There is no question that ELISA has been an invaluable diagnostic tool and remains widely used to produce rapid diagnostic results. However, we must accept that its accuracy has serious limitations and that we have a tool to remedy those limitations.

## FALSE RESULTS

These immunoassays are commonly used in laboratories to study the stages of disease progression and inform treatment strategies for affected patients. Antibodies and other affinity biorecognition capture agents are mistakenly considered to be specific to just one antigen; in reality, however, antibodies are capable of binding to an array of related substances. It is this indiscriminate binding that can lead to false results. Immunoassays can also yield false negative results if the antigen breaks free from the binding site at some point during the experiment, or if the target antigen is not sufficiently abundant in the sample to be detected.

US researchers Dr Norberto Guzman and Dr Daniel Guzman believe all these challenges can be addressed by a new two-dimensional approach, immunoaffinity capillary electrophoresis – IACE.

## IMMUNOAFFINITY CAPILLARY ELECTROPHORESIS – IACE

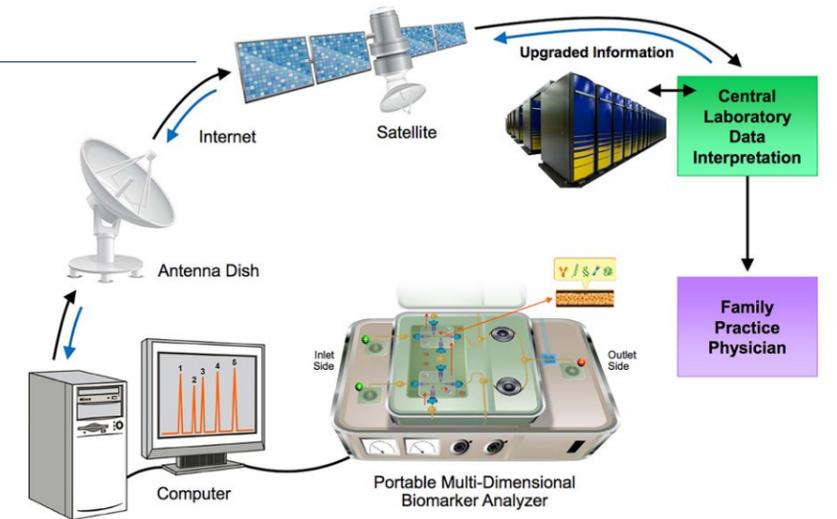
A two-dimensional immunoassay diagnostic technology in which the captured substances or cellular entities (eg, biomarkers) are eluted and then separated, so each substance or cellular entity can be identified and quantified separately.

IACE uses a capillary fitted with an affinity chamber placed prior to the separation portion of the capillary. In the concentration step, the sample is drawn into the capture chamber, where it is concentrated and isolated from unrelated sample components. In the separation step, captured substances are eluted and separated by high-resolution capillary electrophoresis. This critical second dimension is what enables the discernment of related substances, such as proteoforms or proteoform distributions, and potentially reveals new insights to disease states. The biomarkers separated in the second step can then be measured by detectors incorporated into the system. IACE enables clinicians to identify and quantify captured molecules and correlate them to diseases.

## IMPROVED ACCURACY AND APPLICATION

The fact that IACE separates target biomarkers from other sample components makes it far more accurate than previous diagnostic immunoassays such as ELISA; IACE has proven to be faster, more reliable, and more reproducible than other diagnostic methods. The added detection capability of IACE enables researchers to quantify biomarkers throughout a patient’s disease progression.

IACE technology can be used in medical research settings to not only identify key biomarkers found in the body during certain stages of disease progression, but also to capture potential disease-causing agents, such as toxic metabolites, to study their specific role in causing disease. For example, the



Schematic representation of an IACE biomarker analyser connected via Internet to a central laboratory, equipped with a supercomputer and artificial intelligence for more efficient patient diagnosis, data analysis, and interpretation. Computationally intense tasks are becoming essential in the field of medicine, including its use for early an accurate diagnosis of diseases. Reproduced from *Archives of Biomedical Research* 1(1), under *Creative Commons Licence 4.0*

peptide immunosuppressant drug called cyclosporin can be processed by the body into multiple different metabolites, some of which are toxic. An IACE analysis of metabolite ratios in a patient sample can be used to determine what ratio or concentration of each component correlates to a certain disease outcome. These metabolites are indistinguishable with ELISA but can now be studied in detail. This advanced IACE technology has already been used to accelerate pharmaceutical R&D by providing new precision and insights into how

laboratory testing is often prohibitively expensive, and therefore inaccessible to resource-limited patients or those living in poverty. IACE provides a cost-effective, compact, and highly sensitive technology which addresses these issues in healthcare diagnostics.

IACE can be incorporated into a point-of-care device for ‘in-home’ use; in fact, it can be used virtually anywhere. Furthermore, the IACE device can be deployed in remote locations and the data can be electronically transmitted to

## IACE provides a compact, cost-effective, and highly sensitive technology which addresses accessibility issues in healthcare diagnostics.

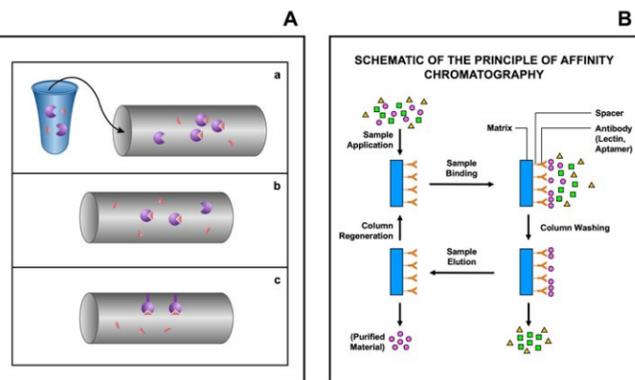
a new drug is absorbed, distributed, metabolised, and excreted (ADME). The high resolution of IACE permits the separation of a myriad of proteoforms of significant importance in the diagnosis, which in turn enables disease monitoring, and informs treatment options and efficacy of treatment.

## ACCESSIBLE, AFFORDABLE HEALTHCARE

Perhaps one of the most important applications of portable IACE analysis devices is in making healthcare more accessible. Many low-income countries struggle with the high cost of healthcare and general lack of resources. Diagnostic

a central laboratory for interpretation. For example, paramedics in an ambulance could begin testing en route to the hospital and awaiting physicians could be assessing critical parameters before the patient even arrives. This combination of accurate diagnostics and telemedicine approaches amounts to a significant benefit in all healthcare settings.

The last piece of the puzzle is for clinicians and scientists to understand and embrace this new technology, so that they can move beyond the traditional unidimensional immunoassays of the 1970s and work toward delivering better targeted healthcare worldwide.



A. Schematic diagram of the three main modes of affinity capillary electrophoresis, two modes of free-resolution affinity capillary electrophoresis (a and b), and immobilised affinity capillary electrophoresis (c). Adapted from *J Chromatography B* 715(1), with permission from Elsevier.

B. Schematic representation of the principle of the technology known as affinity chromatography.



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