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Technology Brief

Introduction: NanoEngineering Corp's innovative viral-pathogen recognition technology holds significance for the COVID-19 era. It relies on self-contained ion-mobility analyzer with extended size-range for precision measurement of nanoscopic virion-analytes. It comprises a small, inexpensive, very rapid, portable, integrated ESCRIM™ system and software. ESCRIM stands for: "Electro-Spray Charge-Reduction (Vir)Ion Mobility" nano-size measurement.

Background: Current challenges in state-of-the-art in viral disease diagnosis via PCR genetics-chemistry are that it requires many hours or days to complete in centralized, sterile, clinical-laboratories with cost ≥$20 per analyte. PCR analysis is inherently retrospective -- unable to detect *unknowns*. While exquisitely sensitive, PCR is prone to amplify contaminant signals while missing the dominant pathogen virus – resulting in false readings; this weakness can only be mitigated by *quantitative* PCR at even greater cost in time and expense. It's also cost-prohibitive to maintain PCR technology's "Readiness" to address public health emergencies and bio-defense needs (epidemics). This is because "libraries" of short shelf-life PCR reagents comprising virus-specific PCR diagnostic kits must be stored under refrigeration and constantly replenished at the point-of-care at enormous ongoing expense – *whether they are used or not*.

Description: NanoEngineering Corporation's (NEC) innovative virus-particle mobility-size analysis technology offers rapid means to overcome these limitations of PCR analysis in a portable manner with simple logistics for use at point-of-care at low cost to <$1 per analyte. NEC's ESCRIM™ virion detection and size analysis tool quickly surveys ALL virus-sizes quickly in order to recognize the size of the dominant virus species present in abundant numbers (infections), *including unknowns.* This is accomplished in a single scan that can be completed within five minutes in non-sterile conditions to generate electronic size-distribution spectra. Cost of storage for rapid deployment with first responders is minimal.

Bacterial infections are easy to see under microscopes. In contrast there is no simple way to analyze viral infections in a routine manner. Virus particles (virions) are too small to see optically (limit ≥ 300 nm) -- yet they are too large for mass spectrometers (≤15 nm). NEC's ESCRIM™ high resolution (vir)ion mobility size-analyzer easily fills this unmet need. ESCRIM™ provides speedy particle-size analysis over virus size ranges with <1 nm precision, and is able to readily distinguish one species from another (Table 1); note that the variability in literature values cited underscores the present difficulty in making precision measurements in this size-range. NEC's technology offers means to enhance the precision and accuracy of these size measurements.

Nature aids this endeavor in that virus-particles within a species are monodisperse (size-pure). "Signature" virion size-data can thus be used for initial virus species identification. A representative DMA virus-spectrum for Hepatitis B was collected in a 5-min. scan is shown in Fig, 1. The Hepatitis sample was furnished by Indiana University and required minimal additional sample processing prior to particle mobility size analysis.

Table 1: Nominal Virus Sizes

Virus Species Name	**Diameter** (nm)
Rhinovirus	20-30
Norovirus	23-40
Polio	≈30
Zika	40-43
rubella	40-80
dengue	≈50
west nile	≈50
hepatitis C	55–65
rotavirus	≤76
influenza	80-120
SARS-Co-V2 (COVID-19)	77-125
adenovirus	90-100
HIV	110-128
Lassa	110-130
hantavirus	120-160
epstein-barr	122-180
respiratory syncytial	150-250
herpes	155-240
smallpox	250-300

ESCRIM™ technology would provide a front-end screening step for preliminary targeting of more expensive, confirmatory PCR analysis. With its low-cost operating characteristics similar to a conventional ion-mobility spectrometer or clean-room particle counter, the NanoRanger™ offers potential for robust service in both laboratory and field analyses. NEC has licensed this patented high-resolution ESCRIM™ technology from Yale University. NEC has co-developed it with Yale for virus size surveys. NEC now has an ESCRIM™ system ready for sale to early adopters (Figure 2).

Complements PCR: ESCRIM™ technology would provide an independent measurement that can serve front-end screening step for preliminary targeting of more expensive, confirmatory PCR analysis. This triage promises to extend the effectiveness of PCR analysis.

R&D Partners**:** Scripps Research Institute (FL); Brookhaven National Laboratory; BVS Inc. (insect virus analysis experts).

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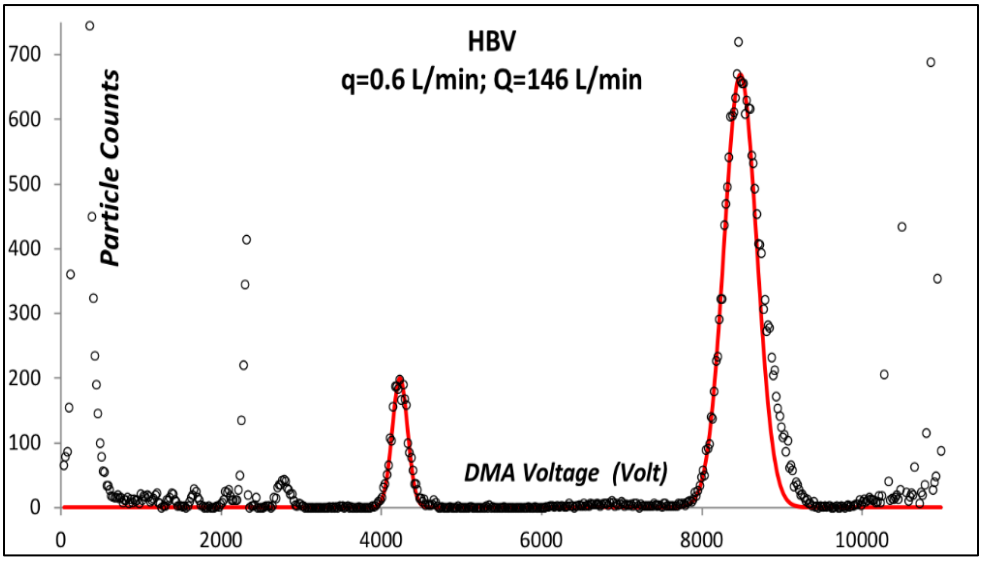

Figure 1. Hepatitis B virion-counts as a function of instrument voltage. ESCRIM ™ Spectral peak at 8200 volts are from singly charged virions -- starkly evident above background. Double-, triple- and quadruple -charged virions appear at ½, ⅓, ¼ voltage values.

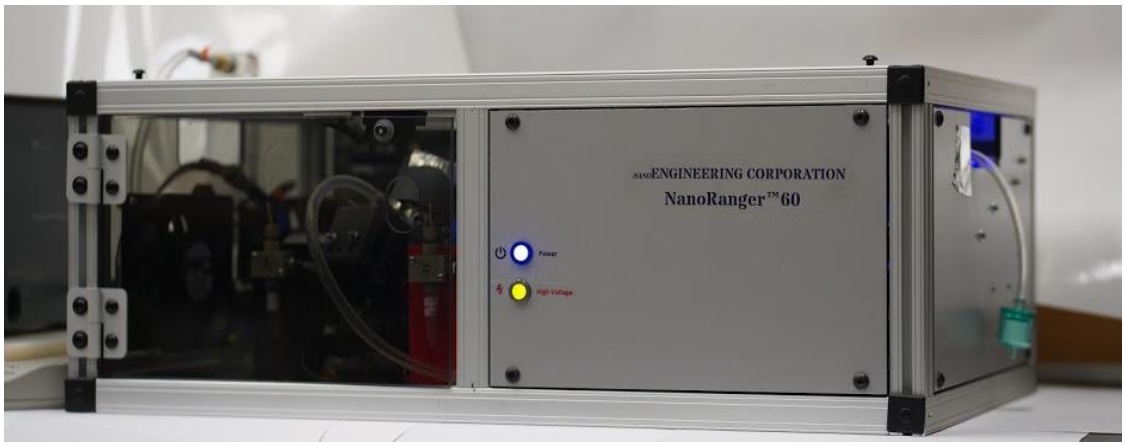

Figure 2. NEC's portable, table-top ESCRIM™ for virus analysis; biofluid-sample virion spectrum data acquisition with user's USB-connected computer and controls software. Low logistics cost: No PCR chemicals