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# Diagnostic Platform for Current Health Status Monitoring

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# Diagnostic Platform for Current Health Status Monitoring

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## Military Relevance:

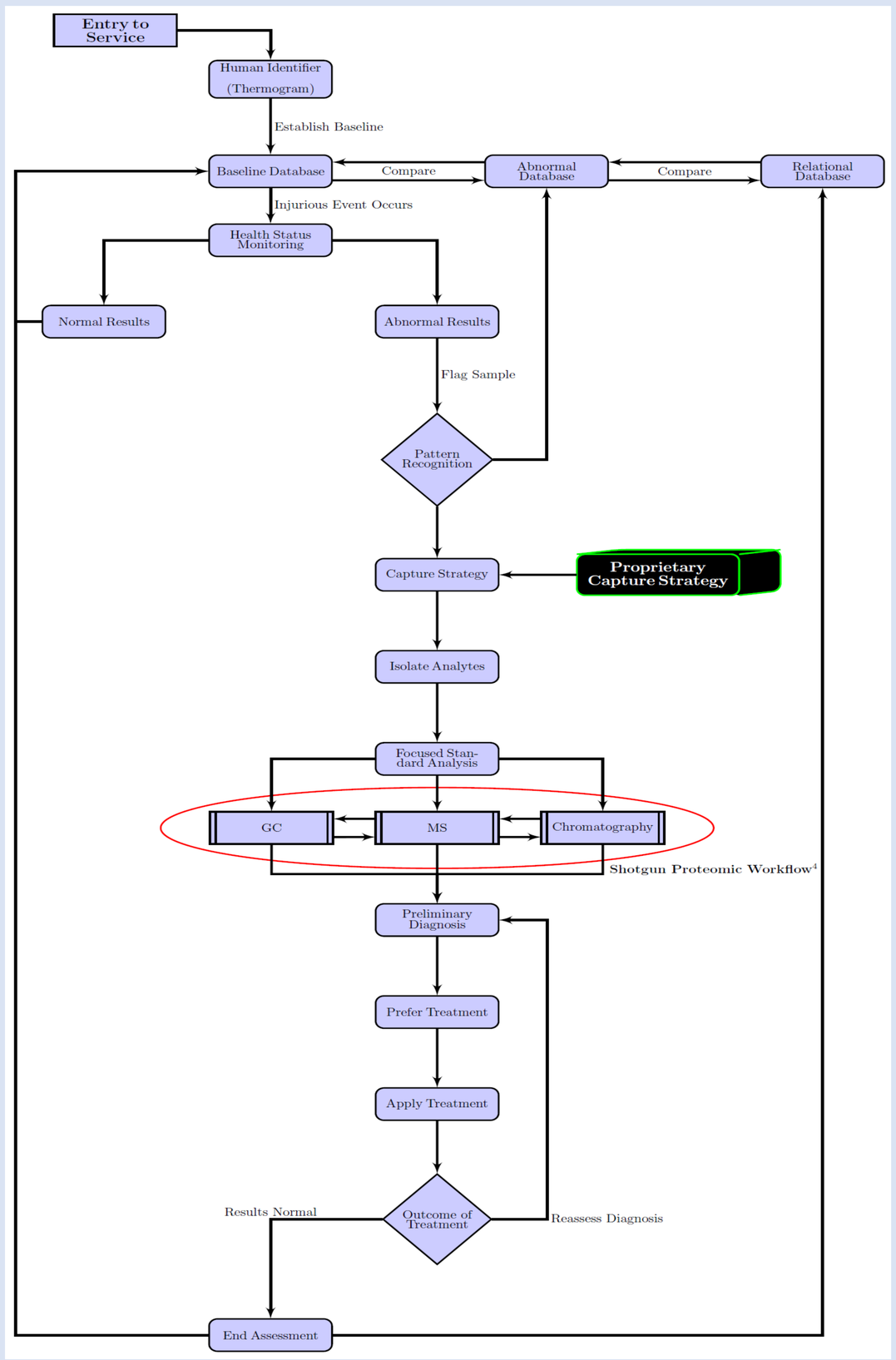
Our diagnostic platform can quickly ascertain general health status without specific reagents or assays. It provides a fast and minimally invasive means for assessing and monitoring health status of military personnel and civilians in war possibly affected by chemical, biological or physical warfare agents and other consequences of war.

## Abstract:

Our approach is based on physical measurements of blood plasma and exploits the plethora of information contained in the human plasma proteome, as a reporter of human health status. The assay involves collection and analysis of thermograms of plasma from human blood measured by differential scanning calorimetry (DSC).

Plasma thermograms arise from the temperature-induced denaturation profile of proteins within blood plasma measured by DSC. This insightful measurement thereby provides a snapshot of the current state of the human plasma proteome which directly informs on overall systemic health. Such measurements have been shown to be highly accurate and sensitive indicators of health status. Remarkably, plasma samples from healthy "normal" individuals display a signature thermogram distinct from thermograms for samples from diseased individuals.

Attractive features of the plasma thermogram diagnostic platform include the fact it is based on a novel technique, distinct from current genetic biomarkers and other molecular diagnostic approaches. The assay requires a small quantity of material (100 µL per sample), has quick turnaround time (less than 2 hours) and very low test COGS. Assay results are quantitative, robust and reproducible due to fundamental properties of proteins in the plasma sample. The assay can be automated for high-throughput applications.




| Project Goals | | |
|---|---|---|
| | Objectives | Result |
| 1 | Rapid Sample Processing | < 2 hour turnaround[1] |
| 2 | Scalable | Automatable for high-throughput application |
| 3 | Small sample volume required | 100µL of plasma/serum |
| 4 | Positive discrepancies between normal and unhealthy people | Reproducible results for asymptomatic states.[1] |
| 5 | Significant differences between disease and normal baseline | Quantitative similarity for the same diseases and significant differences for other specific diseases.[2] |
| 6 | Biomarker discovery and isolation | Successful separation of specific analytes from whole plasma.[3] |
| 7 | Development of automated system with minimal user input | Proof-of-concept turnkey prototype in development |

## Experimental Results:

For an individual plasma (or serum) sample the normalized plasma thermogram is a plot of the "excess specific heat" versus temperature measured by differential scanning calorimetry (DSC). Such a measurement provides a snapshot of the physical state of the sample. The average plasma thermogram for 100 clinically normal people is shown in Figure 1. Regions indicated on the plasma thermogram correspond to the melting of individual proteins comprising sample. Clearly the plasma of heathy individuals provides a thermogram that varies very little from sample to sample, which provides a statistically robust "normal" baseline for comparisons.

Plasma thermograms for specific diseased samples are statistically more similar within each disease state and statistically different from the average normal thermogram. As shown in Figure 2, for 1,278 diseased samples from over 15 different diseases, all but 12 differed more than one standard deviation from the average normal thermogram.

Specific examples shown in in Figure 3 are for three commonly misdiagnosed diseases, i.e. Rheumatoid Arthritis (autoimmune), Lyme Disease (infectious) and Systematic Lupus (autoimmune), that often do not present with obvious clinical symptoms. Average thermograms for at least five patients in the three diseased states are clearly different from one another, and display remarkable statistical differences from the normal baseline thermogram.

These results clearly demonstrate the powerful utility of plasma thermograms for assessing the current health status of people.

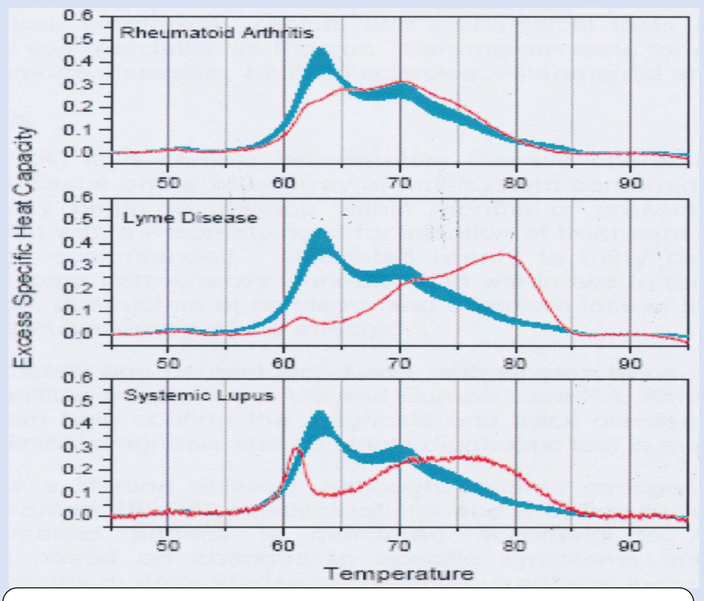



Figure 3: Comparison of plasma thermograms from diseased plasma with Normal (cyan line).

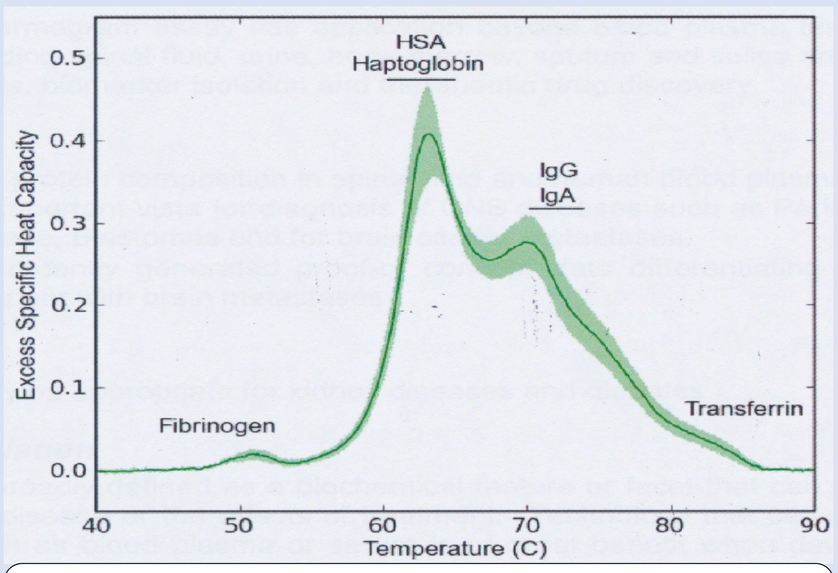



Figure 1: Average (raw) DSC thermogram for "normal" individuals.

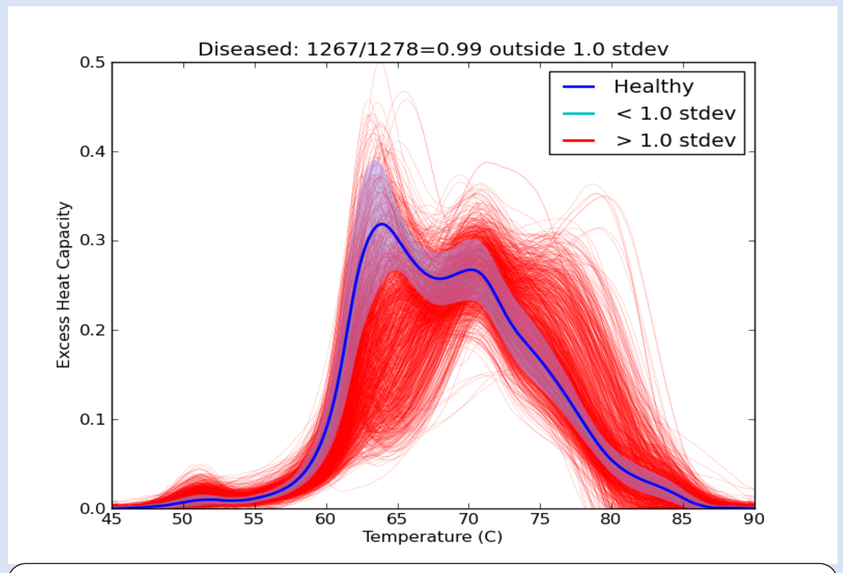



Figure 2: Disease thermograms are statistically different than healthy

## References:

**[1]** Wisniewski, Mark A., et al. "Differential scanning calorimetry in molecular diagnostics." *IVD Technology* 17.6 (2011): 29-34.
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**[3]** Koslen, Megan M., et al. *In preparation (2017)*
**[4]** De Geyer, Philip E., et al. "Plasma Proteome Profiling to Assess Human Health and Disease." *Cell Systems 2.3 (2016) 142-143.*

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