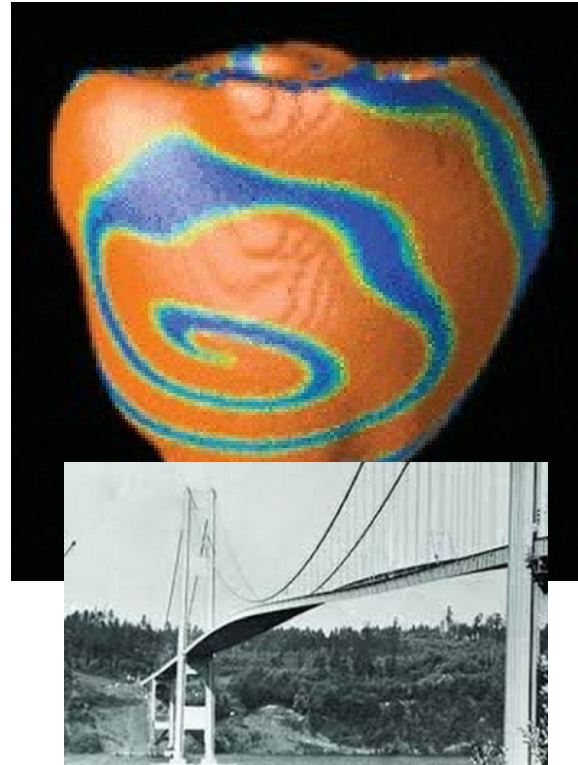# AIM-ing-AHEAD, Population Health Equity Bioinformatics, and New Directions in
Epidemiological Planning and Pandemic Prevention
Quantum, yes § NpC, certainly § M&M, absolutely critical

Martin Dudziak, PhD
Director and Senior Research Scientist
TETRAD Institute of Complex System Dynamics
07.July.2022

We are faced with
New and Old Non-linear Challenges
In Public Health for an inseparable-connected
World Community

We have the means and capabilities
We do not depend upon "AI" and "Silicon Valley"
But we need to address
Key Threats and Principle Tools

Consider first
Emergent Changes in the Biosphere
And in the
Health Patterns of modern Homo sapiens

Climate Change

Overpopulation

Over-urbanization and de-Naturing

Lifestyle (nutrition) changes

~~~~~~~~~

What Tools we have today that are most effective

vs.

Tools that seem "Wow" but are often not effective
in present and often biased state of development

Quantum computing – Turing and "Gödelian"
Supercomputers – Turing
Network Computers – MIMD PDP BOINC

Emergent Stressor-driven Dysautonomia
CNS – Arrhythmia – Autoimmune - Inflammation
POTS – CF/ME – MS – AFIB - PASC

M&M – Migration and Mutation
Environment and Climate Nonlinear Changes
Habitat Disruption
Massive Interface and Exchange
Novelty Breeds Contempt and Adaptation

I

M&M – Migration and Mutation
Environment and Climate Nonlinear Changes
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M&M – Migration and Mutation

Virus – bacteria – eukaryotic-organism parasites

Flora and fauna

Carriers – the vectors

Faster turn-around in natural mutation

Disruption of habitat ==> Adaptation, Evolution

Migration in response to climate/environment changes

Migration in response to food and water source changes

The Human Presence – urbanization, travel, shipment, wastes

Mutation in response to species-mixing

More change on the Outside ==> More Change on the Inside!

A Brief List

Coronaviruses – COVID-19 was a lightweight compared to SARS-1, MERS

Influenzas – H5xx, H7xx, H9xx

Ebola   Hanta   Zika   HIV

Yersina pestis – primed for a return in a Big Way

Cholera   Measles   Monkeypox

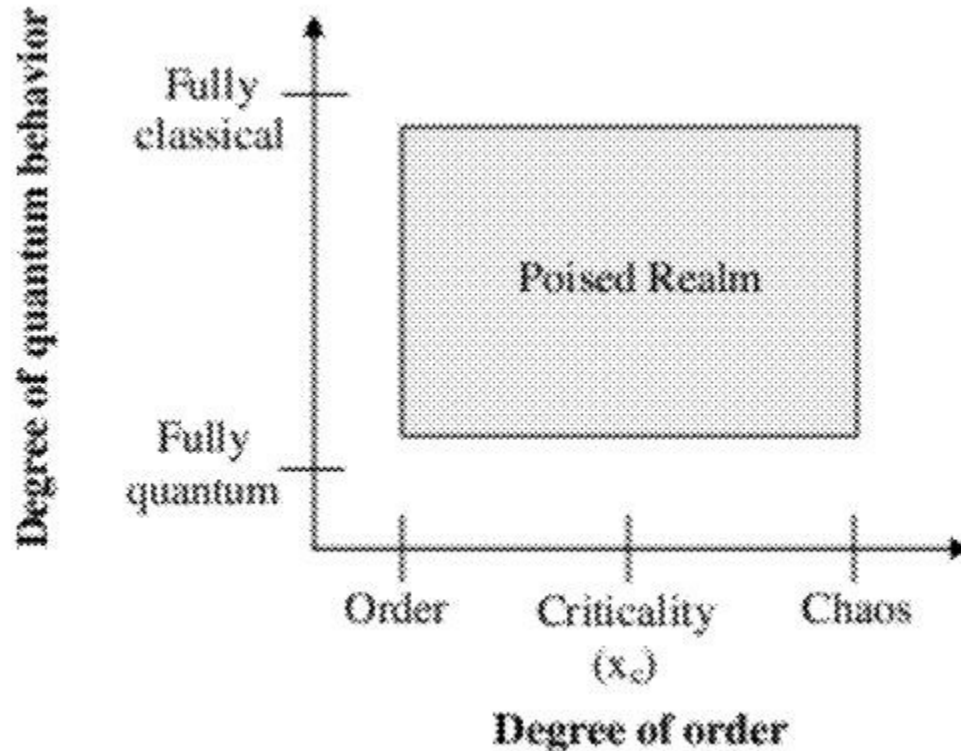Chagas (*Trypanosoma cruzi*)   Tick-borne diseases (multiple)

Meningitis   Yellow fever   ***ZOONOTIC Diseases***

II

Quantum computing – Turing and "Gödelian"
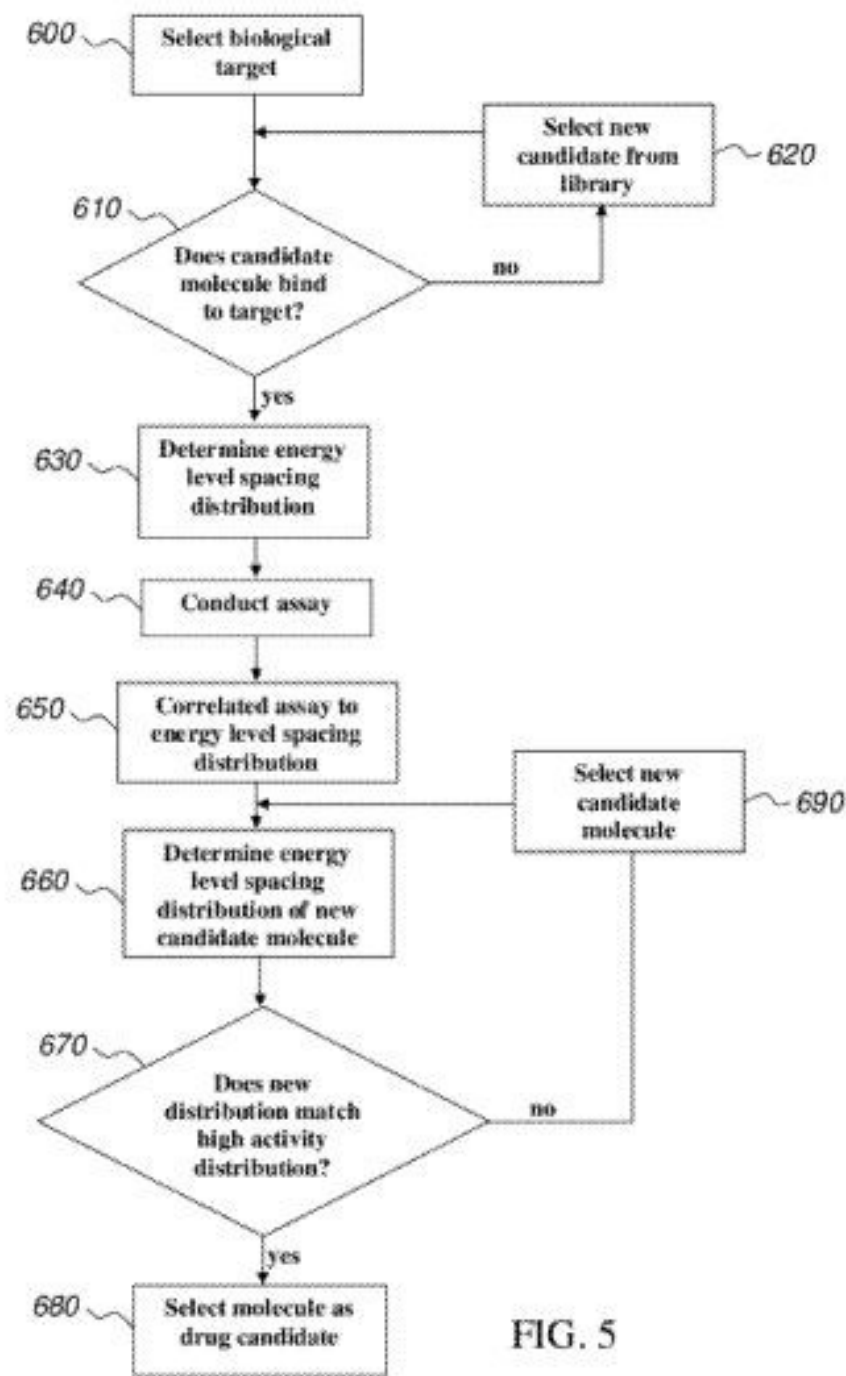Supercomputers – Turing
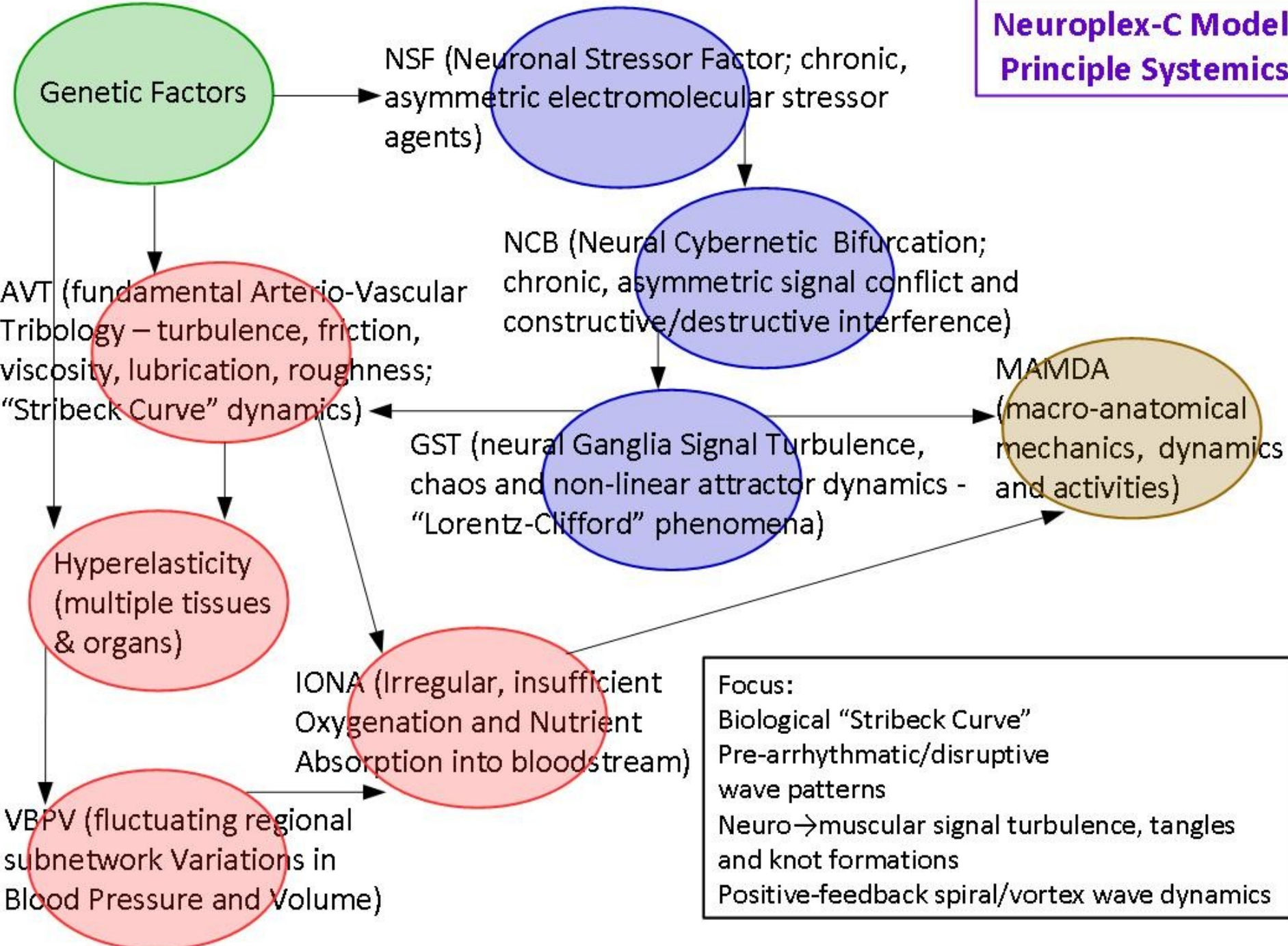Network Computers – MIMD   PDP   BOINC

FIG. 5

III

Emergent Stressor-driven Dysautonomia
CNS – Arrhythmia – Autoimmune - Inflammation
POTS – CF/ME – MS – AFIB - PASC

Neuroplex-C Model
Principle Systemics

Genetic Factors

NSF (Neuronal Stressor Factor; chronic, asymmetric electromolecular stressor agents)

NCB (Neural Cybernetic Bifurcation; chronic, asymmetric signal conflict and constructive/destructive interference)

AVT (fundamental Arterio-Vascular Tribology – turbulence, friction, viscosity, lubrication, roughness; "Stribeck Curve" dynamics)

MAMDA (macro-anatomical mechanics, dynamics and activities)

GST (neural Ganglia Signal Turbulence, chaos and non-linear attractor dynamics - "Lorentz-Clifford" phenomena)

Hyperelasticity (multiple tissues & organs)

IONA (Irregular, insufficient Oxygenation and Nutrient Absorption into bloodstream)

VBPV (fluctuating regional subnetwork Variations in Blood Pressure and Volume)

Focus:
Biological "Stribeck Curve"
Pre-arrhythmatic/disruptive wave patterns
Neuro→muscular signal turbulence, tangles and knot formations
Positive-feedback spiral/vortex wave dynamics

PC -psycho-catalyst -
Psychological origins:
neurological processes
involving classical emotive
and cognitive functions

Genetic factors linked to
either IAI direct-effects,
or production of NSF, or
reaction to specific CC or
AEC stimulant sources

BMC -behavioral-mechanical-
catalyst - biomechanical
origins:
patterns of chronic movement
and/or static postures

**Neuroplex-C Model
Chronic Stressors
leading to
Inflammatory-and
Autoimmune type
(IAI) Processes [1]**
~~~~~~~~~~~~~~~~~
**ANCES - Autonomic
Neurophysiological
Control and
Electrochemical Stress**

+

NSF (Neuronal Stressor Factor;
chronic, asymmetric (equilibrium-
disrupting) electromolecular stressors)

CC – chemical-catalyst -
External origins:
physical substances affecting
ANS/CNS through
exposure or ingestion,
Voluntary or involuntary

NCB (Neural Cybernetic Bifurcation;
chronic, asymmetric signal conflict and
constructive/destructive interference)

MAMDA
(macro-anatomical
mechanics, dynamics
and activities)

=

AEC -acusto-electronic-catalyst -
Acoustic/electromagnetic
origins:
noise, light, other EMF

GST
(neural Ganglia Signal Turbulence,
chaos and non-linear
attractor dynamics;
"Lorentz-Clifford" phenomena)

Adhesions and other connective tissue aberrations (+ and – growth effects) - a major common element in these slow-evolving conditions

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Neuroplex-C Model Chronic Stressors leading to Inflammatory-and Autoimmune type (IAI) Processes [2]
**~~~~~~~~~~~~~~~~~**
ANCES - Autonomic Neurophysiological Control and Electrochemical Stress

1. Quantum computing – Turing and "Gödelian"
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Additional
Background and Reference Material
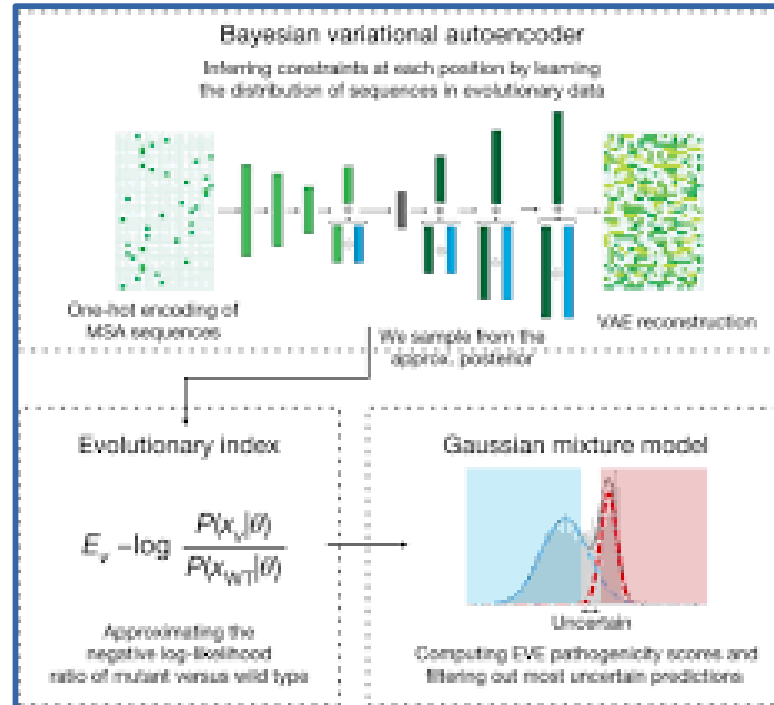
PHIBER as a Key Tool to *AIM AHEAD*

PHIBER = Population Health Informatics Biomedical Equity Resource
AIM AHEAD = Artificial Intelligence and Machine Learning for Advancing Health

Review: Four Goals of AIM-AHEAD

Partnerships, Research , Infrastructure, Data Science Training

Population-tuned, objective, unbiased Intelligence

A resource that can be used to address both explicit and deeply-hidden inequities in healthcare that are unraveling our Society

NIH's AIM-AHEAD program →
increase the participation and representation of researchers and communities underrepresented in

development of AI/ML models
+

enhancement of AI/ML capabilities,
beginning with electronic health record (EHR) data.

Lack of Diversity = and → Incomplete Data and Inbalanced AI Logics
Both are killers for any healthcare system that must rely extensively, heavily upon statistical data and AI/ML reasoning

The consequences are NOT ONLY continued health disparities and inequities for underrepresented communities, but serious long-term degradation and degeneration of the Whole Population and its socioeconomic stability.

Underrepresented communities have untapped potential Not only to contribute new expertise, data, recruitment strategies, and cutting-edge science to the AI/ML field, but also to Better Understand the psychophysical and socioeconomic Situations of those underrepresented and poorly understood communities!

To build powerful AI (and more – even true "sients") that will serve humanity best and not in a stilted, biased way, we need to have a "spectrum" of colors of Mind, not only a few "bands"!

PHIBER as a Key Tool to *AIM AHEAD*

PHIBER – Population Health Informatics Biomedical Equity Resource

What it is and how it employs Synthetic Intelligence to Improve Population Health Equity through assessment of Health Risks and identification of Proactive Diagnostics

Our focus began with our long-standing permanent work in Chronic Neural Stressor Agents within Dysautonomic and Arrhythmic Disorders

To properly real-ize the theory and make the models in order to achieve improvements in early diagnostics and non-invasive therapeutics, we Need

Significantly More, Better, and Comprehensive (population-diverse, equitable) health records, assessments, prognostics, both quantitative and qualitative.

Thus a truly accurate (equitable)
Population Health Informatics Biomedical Equity Resource (PHIBER)

About the Lead Researcher:

Martin is principal investigator in the PHIBER Project and the primary architect of systems and algoirithms employed in PHIBER. With a PhD in theoretical and computational physics, he has taught in several US and European universities, within physics, biomedical engineering, and computer science, and he has worked in several multinational corporations and non-profit organizations, focused upon both research and applications. His particular interests and accomplishments concern non-linear, chaotic, stochastic and turbulent systems within physical and biological environments, including cybernetic, sensor-fusion and control applications.

About TETRAD Institute:

A private, not-for-profit research organization established by several scientists to address problems in fundamental sciences concerning complexity, self-organization, emergence, and non-linear turbulent systems. Projects have been typically organized by collaborative teams of specialists from international backgrounds. Past and concurrent projects have focused upon fundamental theoretical physics, quantum biology, quantum computing, and synthetic intelligence.

Collaboration and consortium people - interactive research in this Project:

Harvard
SUNYAB
Johns Hopkins
Meharry
U-Arizona

Karlinska
Oxford
Göttingen

Zaragoza

PHIBER Pilot Project 2022-23

Neuro-Cardio-Autoimmune range of disorders (primarily) [NpC]

Environmental Toxin Exposures
(especially chronic, long-undetected, quasi-trace amounts)
    e.g., Cr, Co, Ni, As, Cd, Hg, Tl, Pb and U

Black, Native/Indigenous, Migrant/Refugee population subgroups

Pilot-project focus region →
(especially) Michigan, Chicago,
Ohio, Tennessee, Virginia

♦ **Define the Datasets**
♦ **Define the Sources and Build the Infrastructure**
    ● **actual/past-acquired data**
    ● **realistic, near-term acquirable accurate data**
    ● **long-term possible and work-to-goal data**
♦ **Define and Build the Intelligence Engine (pattern recognizer/make/predictor)**
♦ **Put tools and resources into Hands of People and start using them productively**

PHIBER Pilot Project – Three Specific Aims

[1] Aim #1 An intelligent knowledge base usable by all.
Flexible architecture and implementation that can be employed throughout all public and private healthcare networks for earlier detection of indicators and "look-ahead, heads-up" conditions.
Goal: Works with Epic, Allscripts, Cerner, McKesson and the rest

[2] Aim #2 Machine learning that enables discovery and innovative reasoning.
Bayesian, neural network (VAE, GAN, others) and formal logic systems.
Goal: Inductively provable to be unbiased across population variances

[3] Aim #3 An adaptive, expansive, open-ended architecture for radical public health situations.
Detection of higher-risk and newcomer pathologies earlier, faster,capable of alleviating burdens of the health system due to extraordinary social and healthcare system destabilization such as acute, high-transmission pandemics (e.g., COVID-19), capable of rapid innovation and adaption to dramatic nonlinear conditions.
Goal: Be better than what we had for COVID-19 and up to the present, for general public health and especially public-assistance populations

To understand how people are so easily and subtly affected, so badly in the long run, with such comorbidity-intensive diseases – cancer, cardiovascular arrhythmia and cognitive neuropathy – from environmental toxins that are often treated as sub-trace amounts, or not detected properly or ignored or hidden (the last two are major problems in several modern nations including USA) ----

---- It merits to examine some fundamental etiologies that involve:

- Fundamental biophysics
- Including novel theoretical directions of research in

Coherent quantum entanglement, entrainment and resonance (CQER)
Think of it as non-Turing quantum computation at the macromolecular scale involving signal propagation in protein arrays including microtubules and intermediary filaments

This is how a variety of seemingly disparate and multi-scalar STRESSORS act over different scales of time to create
Neuromuscular (including cardiovascular) dissonance and dysfunction
Herein is where environmental toxins as well as psychological duress and abuse all work to degrade cognitive, muscular and regulatory functions in the organism

Foundations, Priors, and Pertinent Background - Neuroplex-C Project:

An interdisciplinary project investigating common underlying etiologies in multiple disorders and diseases characterized as dysautonomia, arrhythmia, and including several autoimmune classifications.

The initial focus has been on cardiac arrhythmia including SVT, AFIB and syndromes such as POTS. This has expanded with findings emerging from COVID-19 and PASC ("Long COVID").

Variances in pathologies and in population demographics point to the need for integrating more extensive biometrics including genomics and proteomics, in a comprehensive manner across all population groups (racial, ethnic and socioeconomic).

Objectives include modified and expanded diagnostic testing, innovative non-invasive therapeutics, and broader public health education to address contributing factors of stress, nutrition, and lifestyle practices.

Adhesions and other connective tissue aberrations (+ and – growth effects) - a major common element in these slow-evolving conditions

AVT (fundamental Arterio-Vascular Tribology – turbulence, friction, viscosity, lubrication, roughness; "Stribeck Curve" dynamics)

Hyperelasticity (multiple tissues & organs)

IONA (Irregular, insufficient Oxygenation and Nutrient Absorption into bloodstream)

VBPV (fluctuating regional subnetwork Variations in Blood Pressure and Volume)

SVT + other tachycardia

POTS

AFIB

ME/CFS

Aspects of EDS / hypermobility
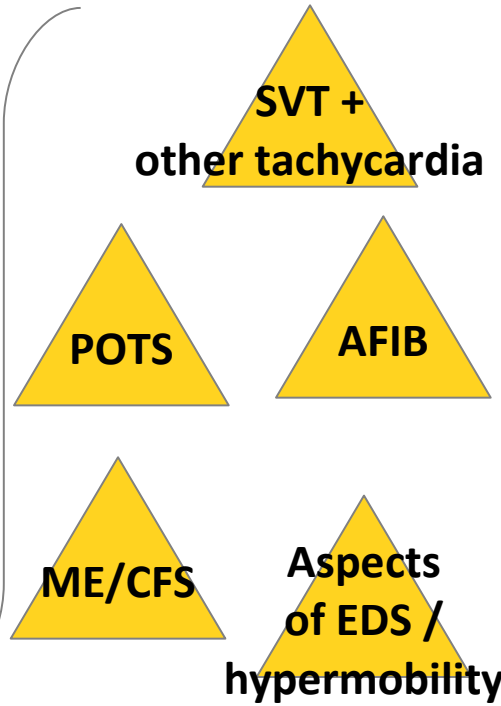
Certain Inflammation Extremes (esp. cardio, pulmonary, GI tract)

Aspects of aneurysm

Aspects of atherosclerosis

Aspects of MALS

Precursors of MS

Precursors of Alzheimer's

Precursors of Parkinson's

Neuroplex-C Model Chronic Stressors leading to Inflammatory-and Autoimmune type (IAI) Processes [3]
~~~~~~~~~~~~~~~~
ANCES - Autonomic Neurophysiological Control and Electrochemical Stress

Certain Inflammation Extremes (esp. cardio, pulmonary, GI tract)

+

Sustained Stressor Agents (esp. Psychological Catalysts; PC)

+

Acute High-Impact Infectious Disease (like COVID-19)

➡️

Higher risks, and recurrence, and intensification of pre-existing:

POTS

AFIB

ME/CFS

Precursors of MS

Aspects of aneurysm

Aspects of atherosclerosis

Aspects of MALS

Neuroplex-C Model Chronic Stressors leading to Inflammatory-and Autoimmune type (IAI) Processes [4]
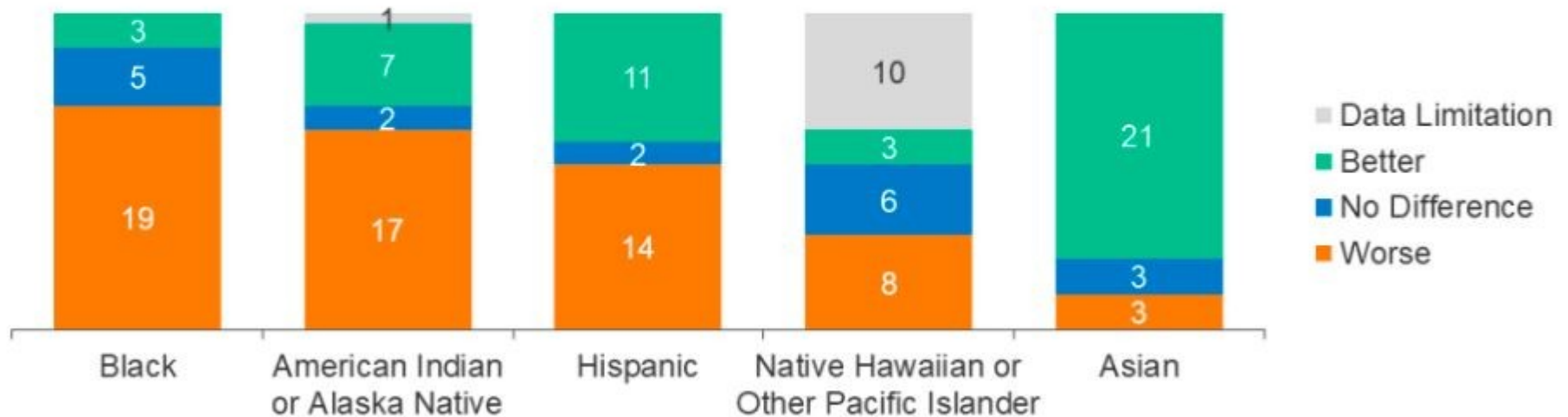~~~~~~~~~~~~~~~~
ANCES - Autonomic Neurophysiological Control and Electrochemical Stress

Figure 2

People of Color Fare Worse than their White Counterparts Across Many Measures of Health Status

Number of health status measures for which group fared better, the same, or worse compared to White counterparts:

Note: Measures are for 2018 or the most recent year for which data are available. "Better" or "Worse" indicates a statistically significant difference from Whites at the p<0.05 level. No difference indicates no statistically significant difference. "Data limitation" indicates data are no separate data for a racial/ethnic group, insufficient data for a reliable estimate, or comparisons not possible due to overlapping samples. Persons of Hispanic origin may be of any race but are categorized as Hispanic for this analysis; other groups are non-Hispanic.

KFF

4 - Integral importance of large-scale population-based bioinformatics:

Significance of Population Health Equity and Diversity Biometrics for Improved Early Diagnostics and Proactive Treatment and Positive, Sustainable Survival

Issues:

► Incomplete Data being collected from virtually all patients at risk

► More people than ever at risk due to:

♦ COVID-19 and PASC

♦ Massive Stress, Anxiety, Passive/Active Abuse, *Social Deconditioning*

♦ Variances between Racial and Ethnic Groups – Not Understood, Not Examined, Not Considered

♦ Social / Institutional / Professional Prejudices toward Most-At-Risk Population Sub-Groups for many dysautonomic/autoimmune conditions

► Need for Massive Biometrics including Behavioral & Genetic Data in order to:

♦ Ascertain genetic etiology and amplification factors

♦ Understand the psychosocial, nutrition, lifestyle factors

♦ Develop personalized plans for individuals at risk and in general

♦ Overcome medical/healthcare prejudices and discrimination which result in misdiagnosis and ignoring problems until Too Late

**More Issues that Demand Population Health Equity and Diversity Satisfaction:**

This is about BOTH

♦ Inequities in diagnostic and therapeutic medicine AND

♦ The GAP in understanding the variances between multiple genotypes and beahavior/lifestyle types which is Required in order to Answer the many questions raised and implied by this Project and many others in related fields

►Massive Statistics of a different "order" than what are typically queried or discussed by healthcare providers – particularly in USA

► Yes, anonymity and privacy can be preserved and protected – including for critical data pertaining to lifestyle including mobility functions

► COVID-19 and PASC must be addressed head-on because This is a Large and Multi-Generational Problem we now face

► Psychological Dynamics including parent-child, adult-adult, and societal factors of abuse, bullying(!) and other discrimination – spanning indeed all races and demographics and arguably intensifying in the 2020s – this must be included in the Data Collection and the Biometric Resources to be assembled

► This must Not be yet-another-exercise in building a huge database and then it sits there and is used by (maybe) only a handful of researchers

► **Population Health Equity Biometrics Resource** (PHEBR) **can and must be a Tool for Social Health Change including Policy and Practice (not only "research")**

4 - ADaM and EVE and the Engine:

The main tasks:

VLDB (Very Large DataBase) operations

ETL ("extract-transfer-load")

Communication asynchronous Parallel Processing ("cloud" and "feed" tasks)

Pattern recognition, error-correction and fitting, classification
Pattern simulation, mimicking and projecting
Probabilistic reasoning, estimation, outcome prediction

VAE (Variational auto-encoder) and GAN (Generative Adversarial Network) methods
- well-proven, robust, widely used including in image/text recognition and
simulation, and in medical imaging and EHR modeling

Figure 5. Using the VAE/GAN model to reconstruct dataset samples with visual attribute vectors added to their latent representations.

Using the VAE/GAN model to reconstruct dataset samples with visual attribute vectors added to their latent representations.

[14]

Figure 7: **Image generation** qualitative results, showing five sampled results for two different images. **Top:** Ours, **Middle:** SinGan [24], **Bottom:** ConSinGAN [28].
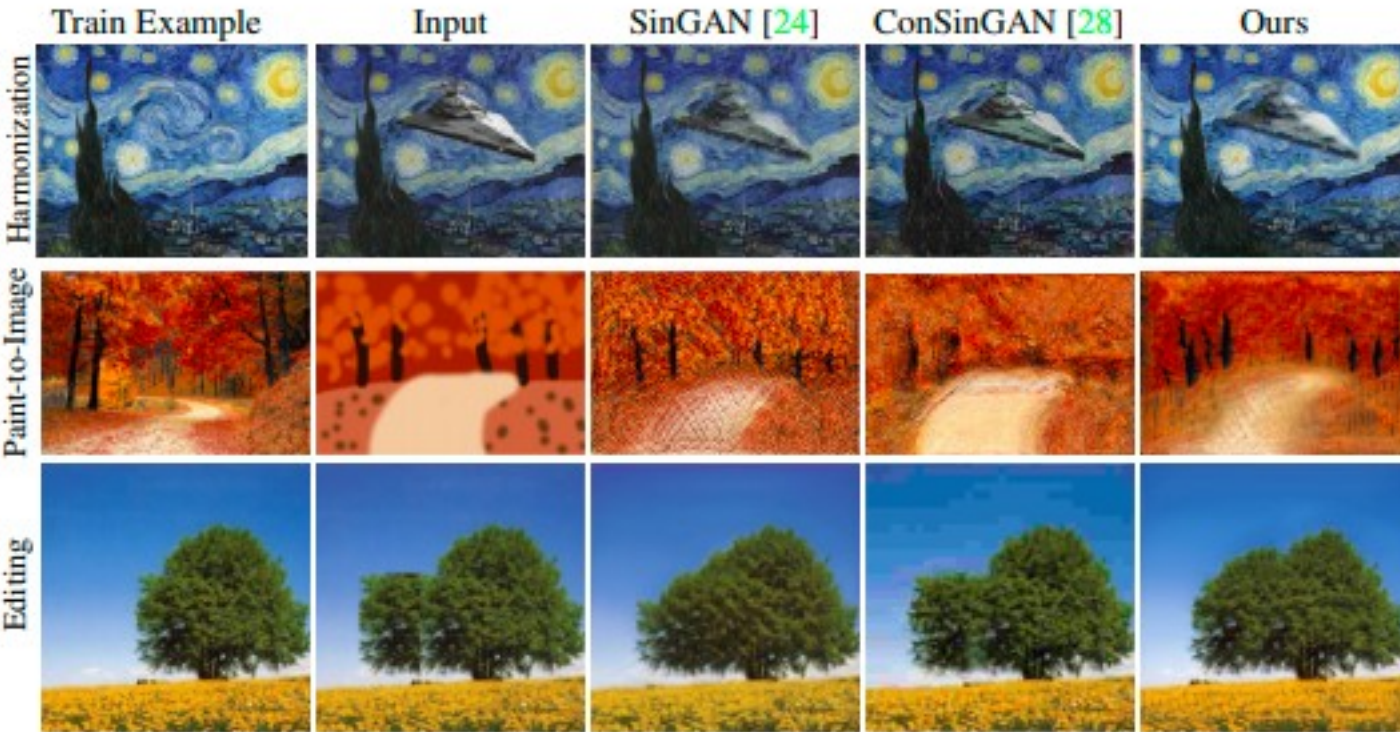
Figure 8: Additional image applications comparison: harmonization, paint-to-image and editing.

[15]
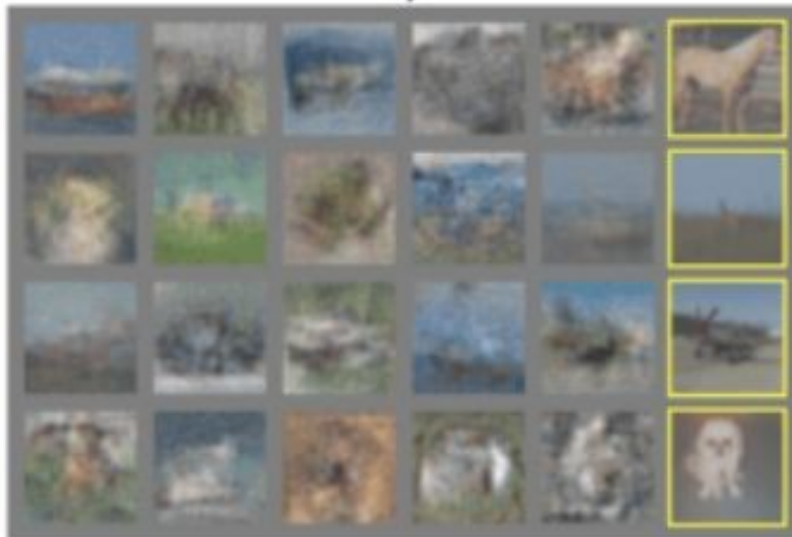
Examples of GANs used to Generate New Plausible Examples for Image Datasets. Taken from Generative Adversarial Nets, 2014.

[16]

What is and how to build the PHEBR

Prime Objectives:

[1] Resource for Identifying and Reducing Health Inequities (Inequialities) for Affected, Vulnerable, and Ignored Minorities and Population Sub-Groups
This, of course, pertains to many (all) aspects of healthcare

[2] Assist genomics-focused research "across the board"

[3] Assist in the challenge of identifying "earlier than later" the at-risk populations for "neuro-cardio-plus" disorders, including other autoimmune types

[4] Other objectives include the benefits to healthcare industry entities: pharmaceutical, medical device, hospital, insurance, others

Clinical medical statistics – massive data sources – properly anonymized (no privacy issues) originating from public/private institutions

Focus upon Classes of Populations considered to be
(known/definite → potential-at-risk) for NPC-category health issues

VLDB ADW
"Active Data Warehouse"

Applications (SI ("AI")) and other Use-Cases
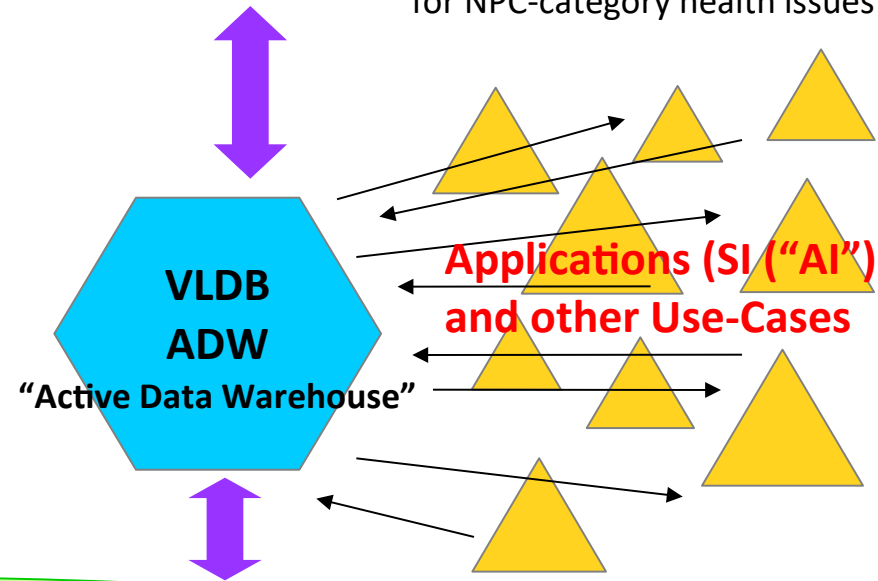
Human-Machine Users (Agents) – different use-cases, objectives, applications
♦ Genomics, genetic engineering, diagnostics, therapies, pharma, devices
♦ Public health (equity/inequality problem; pandemic prevention/containment)
♦ Identifying and refining relations and etiologies of NpC-type disorders and diseases

The PHEBR is a kind of "New Genesis" for studying links between poorly-understood and syndrome-categorized disorders and diseases ----
What better way to do this than to "couple" together ADAM and EVE? 😊 😄

ADAM and EVE

AdaM – Active Data Mover – a VLDB Engine

GOAL with PHEBR:

Adapt EVE logic (Bayesian + NN pattern detection) to task of seeking and identifying patterns within massive data streams of clinical-origin patient medical histories for:

♦ Indicators of risk conditions and causal relations on the basis of acquired data sets in PHEBR

♦ Missing-gaps - types of data to pursue and collect through future clinical measurements (e.g., behavioral, lifestyle)

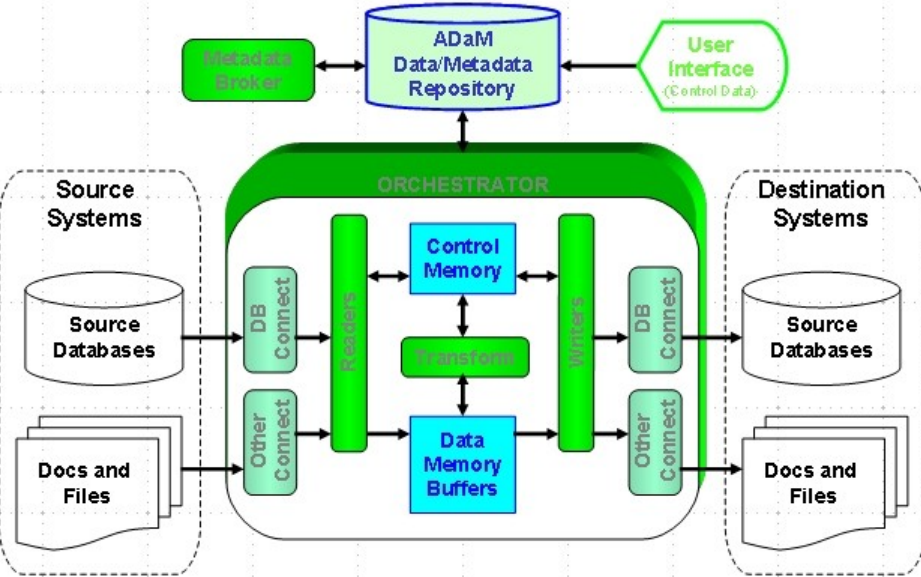♦ What-Ifs and Hypotheticals pertinent to NpC for investigation and evaluation and linkage with genetic modeling systems like EVE (HMS/OATML)

eve
evolutionary model of variant effect

Marks Lab - Harvard Medical School
OATML - Oxford Applied and Theoretical
Machine Learning Group

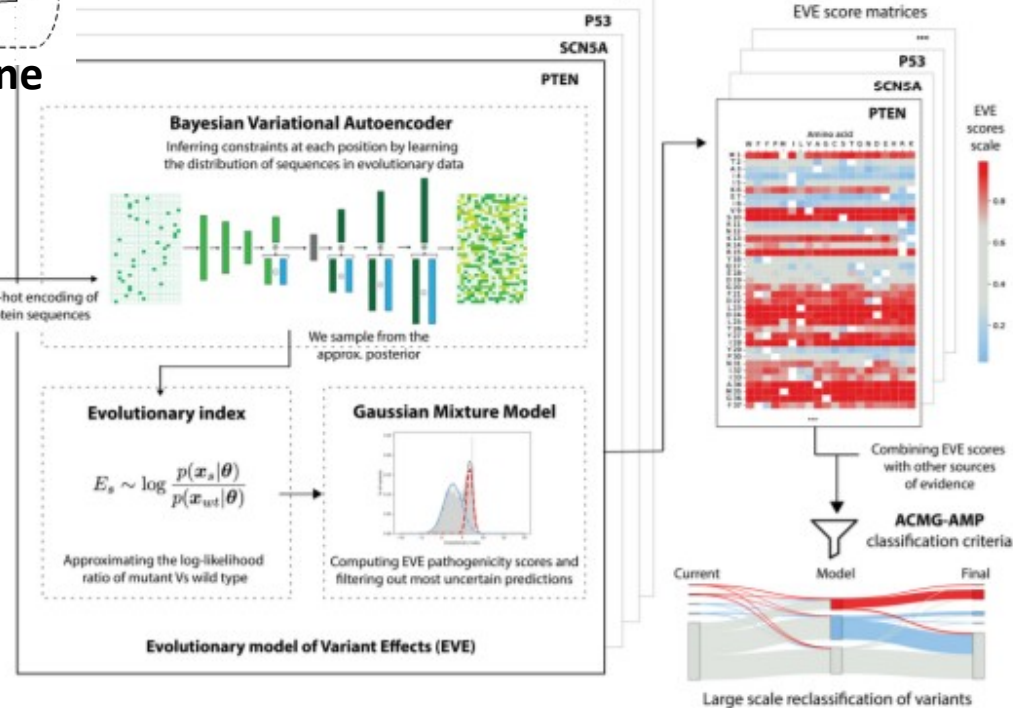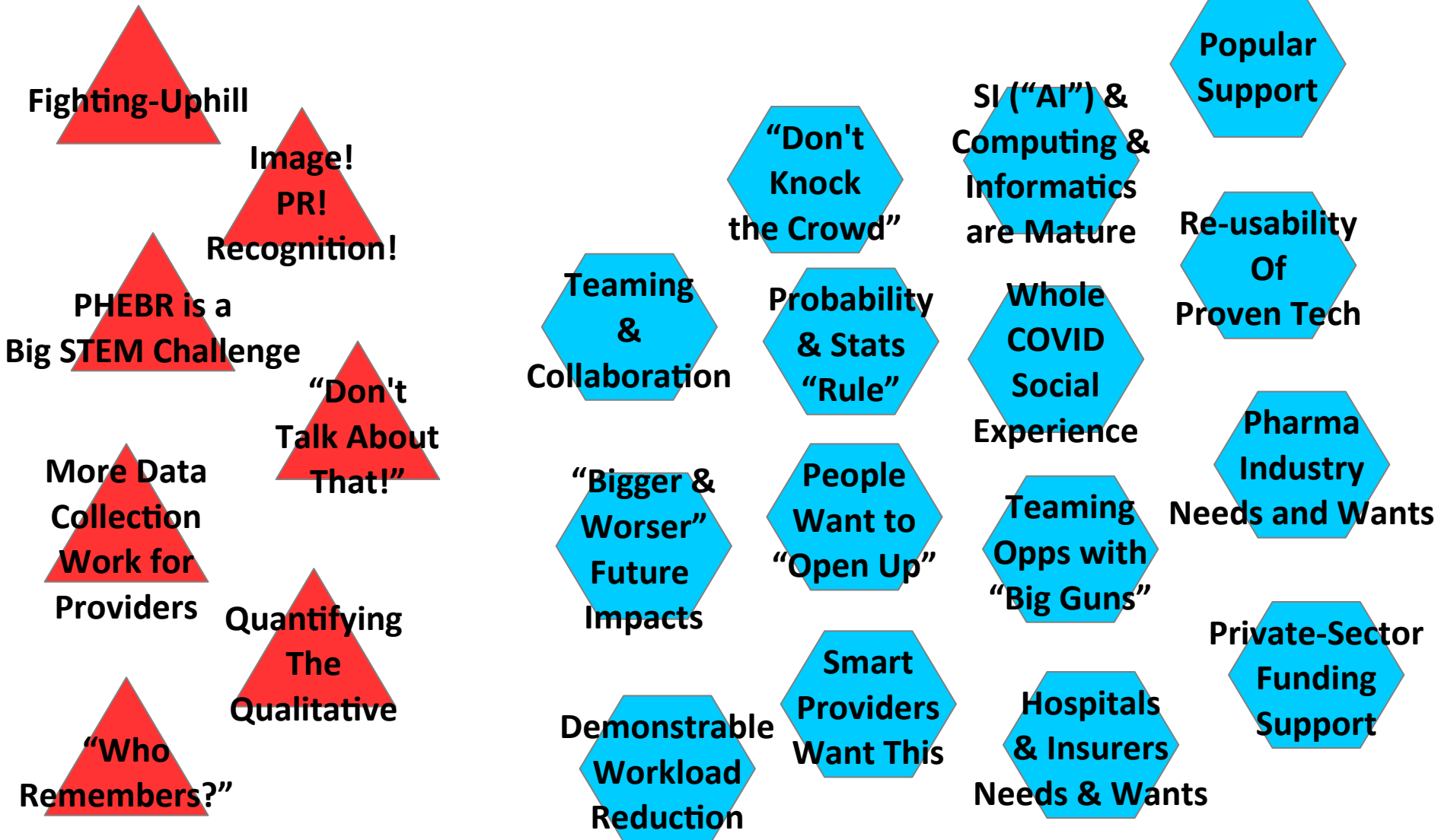**Evolutionary model of Variant Effects (EVE)**

<u>5 – Implementation ("PHIBER-*alpha*"):</u>

- acquiring datasets of disparate and varied patient group types
- acquiring real-time per-patient increments
- training the system using VAE, GAN and other algorithms for both data correction and simulated data element creation
- identifying target patient types for follow-up provider-led actions
- recommending follow-up inquiries, observations and diagnostics-to-therapeutics action
- providing a logical and systematic basis to proceed into a fuller-scope development of the PHIBER for use on a national+ scale

During this Pilot Project, our focus will be upon the following population and biomedical metrics:

- Environmental toxins originating in mining, smelting, and waste removal and disposal processes connected with principally uranium and other toxic metals
- Health risks primarily linked with cancers and birth defects
- Black, Native and specific disadvantaged other minority populations in pre-identified, previously-studied communities within socially and economically disadvantaged regions ("Appalachia-plus") of Tennessee, Kentucky, West Virginia, Virginia, Illinois, Ohio, and Michigan.

5 - Challenges and opportunities in population health equity and diversity:

Fighting-Uphill

Image! PR! Recognition!

PHEBR is a Big STEM Challenge

"Don't Talk About That!"

More Data Collection Work for Providers

Quantifying The Qualitative

"Who Remembers?"

Teaming & Collaboration

"Don't Knock the Crowd"

Probability & Stats "Rule"

"Bigger & Worser" Future Impacts

People Want to "Open Up"

Demonstrable Workload Reduction

Smart Providers Want This

SI ("AI") & Computing & Informatics are Mature

Popular Support

Re-usability Of Proven Tech

Whole COVID Social Experience

Teaming Opps with "Big Guns"

Pharma Industry Needs and Wants

Hospitals & Insurers Needs & Wants

Private-Sector Funding Support

OASIS
Social Intelligence Architecture

Terra
(instantiation of) OASIS Environment

... multiples possible

OASIS *Archipelago*
a taxonomy of intelligence systems
OASIS (Terra) →
    IID (PHEBR) →
        SIA (Debora)

IID
Intelligence Information Domains

PHEBR
Population Health Equity Biometrics Resource

... multiples possible

Seldon
Prediction Engine

SIA
Sient Intelligence Applications

Debora
Psychosocial Safety & Security

... multiples possible

Based upon and built from OASIS core components, each Oasis World (e.g., Terra) provides the matrix for personal and interpersonal dataflow. This contributes (with many other data streams) to an IID (e.g., PHEBR) which has a domain focus (e.g., health). Together these work and work with SIA systems – applications such as Debora, each of which has a focus on a population type and specific attributes and their predictive (future-possible-likely) values.

Team Members, Collaborators, Advisors, Assistants

Rachel Roman, RN, NP

Kevin Ciresi, MD

Alexa Alexberg, RN (Karlinska Institute and Hospitals)

-- with collaborative engagement and assistance from --

Svetlana Blyshstein, MD (SUNYAB/Amherst)

Tae Chung, MD, PhD, Taylor Bopp, and the Chang Lab and Clinic (Johns Hopkins)

Yarin Gal, PhD (Oxford U)

Stuart Hameroff, MD, PhD (U of Arizona)

Daniel Lee, PhD and his Lab (NYU)

Stefan Luther (Göttingen U and Hospitals)

Pedro Marijuan (Zaragoza U)

Deborak Marks, PhD (Harvard U)

Jorge Navarro (Zaragoza U)

Ottorino Ori, PhD (Parma U)

Ulrich Parlitz (Göttingen U and Max Planck Institute for Dynamics & Self-Organization)

Lauren Stiles, PhD (Dysautonomia International Foundation)

Thank You!