PHIBER as a Key Tool to AIM AHEAD

PHIBER – Population Health Informatics Biomedical Equity Resource



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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)

NIH's AIM-AHEAD program \rightarrow

increase the participation and representation of researchers and communities currently underrepresented in

> development of <u>AI/ML models</u> +

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

Lack of Diversity = and \rightarrow 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"!

Review: Four Goals of AIM-AHEAD

Partnerships, Research, Infrastructure, Data Science Training

How PHIBER serves and meets these objectives:

Partnerships – Institutes including TETRAD, Companies, working with Universities and Medical Schools, and with Hospitals and Social-Service Organizations that focus upon Minority Population Situations + Needs + Wants

Research – SI (AI/ML), VLDB, ETL, PDP, UEX

Infrastructure – PHIBER is more than a data resource and knowledge base - it becomes the skeleton and muscles of a Health Intelligence Infrastructure

Data Science Training – interns and apprentices including middle/high school students in Buffalo, later in Navajo Nation and other predominantly Black, Native People, Migrant and Refugee communities

PHIBER as a Key Tool to AIM AHEAD

Population Health Informatics Biomedical Equity Resource



Population-tuned, objective, unbiased Intelligence

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

Format of the Presentation:

- 1 Introduction to PHIBER the Three Specific Aims
- 2 People Health Crises Who, where, what, why
- 3 Datasets Challenges, Help-Network, Accuracy

4 – ADaM and EVE and the development of VAE+GAN algorithm sets to build a realistic "population of opportunity" for modeling and predicting

- 5 Implementation Building PHIBER-*alpha* in the Pilot Project
- 6 Application How PHIBER will be used and useful afterwards
- 7 Conclusions

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:





<u>1 – Introduction:</u>

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

MMC-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

Thus... Neuroplex-C (NpC) $\rightarrow \rightarrow \rightarrow$

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.



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

BMC -behavioral-mechanicalcatalyst - biomechanical origins:

patterns of chronic movement and/or static postures

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

AEC -acusto-electronic-catalyst -Acoustic/electromagnetic origins: noise, light, other EMF Genetic factors linked to either IAI direct-effects, or production of NSF, or reaction to specific CC or AEC stimulant sources 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 (equilibriumdisrupting) electromolecular stressors)

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

> MAMDA (macro-anatomical mechanics, dynamics and activities)

GST (neural Ganglia Signal Turbulence, chaos and non-linear attractor dynamics; "Lorentz-Clifford" phenomena) Copyright © 2022 TETRAD Institute 14 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) NCB (Neural Cybernetic Bifurcation; chronic, asymmetric signal conflict and constructive/destructive interference)

> MAMDA (macro-anatomical mechanics, dynamics and activities)

GST (neural Ganglia Signal Turbulence, chaos and non-linear attractor dynamics; "Lorentz-Clifford" phenomena) Neuroplex-C Model Chronic Stressors leading to Inflammatory-and Autoimmune type (IAI) Processes [2]

ANCES - Autonomic Neurophysiological Control and Electrochemical Stress

Hyperelasticity (multiple tissues & organs)

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

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





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.





Source: Emily E. Petersen et al., "Racial/Ethnic Disparities in Pregnancy-Related Deaths-United States, 2007-2016. "Morbidity and Mortality Weekly Report 68, no. 35 (September 6, 2019): 762-65.

INFANT MORTALITY RATE



Source: "Infant Mortality and African Americans," U.S. Department of Health and Human Services. Office of Minority Health, https://minorityhealth.hhs.gov/omh/browse.aspx?lvl=4&lvlid=23.





"Exploring persistent racial/ethnic disparities in lead exposure among American children aged 1–5 years..." (Teye, Yanosky et al) – reference [6]

Nationwide, Black people are exposed to greater-than-average concentrations of a dangerous form of pollution known as PM 2.5. People of color face more exposure from almost every type of source, while white people are less exposed.



"People of Color Breathe More Hazardous Air...." (Tabuchi and Popovich) --- reference [7]



"Radioactive pollution is a serious threat to the welfare of the Navajo people. Some Navajo miners were exposed to high levels of radioactivity in mines and mills. One 1959 report found radiation levels ninety times acceptable limits (LUHNA, 2002 (more info)). Of the 150 Navajo uranium miners who worked at the uranium mine in Shiprock, New Mexico until 1970, 133 died of lung cancer or various forms of fibrosis by 1980." [9]



Claim (by author)

Given estimates that 85% of Navajo homes in the Navajo Nation (AZ and NM) contaminated with Radioactive Uranium, the Native Peoples of the Dine Nation, the Navajo, are likely exposed on a constant, daily, 365-days/year basis to <u>Significantly Higher Radioactivity</u> than the standardized and generally accepted estimates made by DHS and CIA regarding potential radiation levels which might have come from so-called "dirty bomb" nuclear terrorism. Significantly higher. [Those official estimates are classified and unpublishable.]

<u>3 – Datasets – Challenges, Help-Network, Accuracy:</u>

[1] Existing EHR Records from reliable sources (public hospitals and medical centers)
 – these will be incomplete with respect to overall PHIBER dataset structure, but useful for principal medical data types.

[2] Existing minority-specific, disease-specific, toxin/agent-specific studies (pubic sources) – these will also be principally medical-only data types.

[3] Limited new interview-based studies (selected minority populations within the Pilot Project region of focus, through proactive community organizations) – these may include qualitative behavioral data types.

Current (ongoing) tasks in Phase 1:

Discussions with Black, Native/Indigenous and Migrant/Refugee Health Agencies and Community Organizations for defining sources of accurate data as EHR or in alternative formats of data entry

Developing interactive apps for personal entry of data by sample (volunteer) population groups.

Simulation of data for purposes of developing and refining the analytical software to be applied to such data.

Preliminary PHIBER Dataset Elements:

Fieldname (* = time-series potential/typical)	Type (Numeric/Image/Text/Block N/I/T/B)	Source Type (Quant-numeric /Qual-text n/t)	Data Source (I=instrumental D = dialog/document O=observation)
Age	N	n	D
Sex/gender	Ν	n	D
Race	N	n	D
Ethnic origins	N	n	D
Genome sequence data and analyses if available	В	n/t	Ι
Weight *	N	n	I
BMI *	N	n	Ι
Blood pressure *	N	n	I
Pulse *	N	n	I
Blood oxygenation *	N	n	I
Breathing force *	N	n	I
Body temperature *	N	n	I
Alliergies *	N	n/t	D
Immunizations *	N	n/t	D

Fieldname (* = time-series potential/typical)	Type (Numeric/Image/Text/Block N/I/T/B)	Source Type (Quant-numeric /Qual-text n/t)	Data Source (I=instrumental D = dialog/document O=observation)
CBC *	N	n	I
HbA1C *	N	n	I
Glucose/albumin *	N	n	Ι
Disease history *	Т	t	D
Procedures *	Т	t	D
Active diagnoses *	Т	t	D
Family medical background (history) *	Т	t	D
Nutrition and substance- intake history *	T	t	D
PCR and/or ELISA tests for specific pathogens *	N	n	Ι
SIMOA (single-molecule array) * [multiple types]	N/B	n	Ι

Fieldname (* = time-series potential/typical)	Type (Numeric/Image/Text/Block N/I/T/B)	Source Type (Quant-numeric /Qual-text n/t)	Data Source (I=instrumental D = dialog/document O=observation)
EEG *	В	n	I
EKG *	В	n	Ι
Echocardiography *	N/B	n/t	I
MRI, CT, other ultrasound and <u>radiological</u> imaging *	I/B	n/t	Ι
Transcranial magnetic stimulation (TMS) *	B	n	Ι
Ultrasound therapeutics *	I/B	n/t	I
Economic (financial)	В	n/t	D
Education	Ν	n/t	D
Geo-spatial	Ν	n/t	D
Community	В	n/t	D/O
Therapy assessments * (Type 1 in basic	T/B	t	D/O

Fieldname (* = time-series potential/typical)	Type (Numeric/Image/Text/Block N/I/T/B)	Source Type (Quant-numeric /Qual-text n/t)	Data Source (I=instrumental D = dialog/document O=observation)
Self-assessment and caregiver assessments pertaining to levels of chronic psychosomatic stress * (Type 2 in basic classifications – see [1])	T/B	t	D/O
Indicators from self- assessments and questionnaires * (Type 3 in basic classifications – see [1].)	T/B	t	D/O
Other Data types * (Type 4 in basic classifications – see [1].)	T/B	n/t	I/D/O

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

<u>lssues</u>:

- 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

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 <u>Tool for Social Health Change</u> 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]

393 9 7 0 2 b) a) . 1 11

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

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

Applications

and other Use-Cases

ADW "Active Data Warehouse"

VLDB

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? (3) (2)

ADAM and **EVE**

 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)

evolutionary model of variant effect

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

P53

EVE score matrices

<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-totherapeutics 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 preidentified, 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:

The person who says it cannot be done Should not interrupt the person doing it. Chinese Proverb

Data-Set and Software Open Distribution to AIM-AHEAD Consortium

At the completion of this pilot project, the datasets we will have acquired and organized, and the software code (source) employed within the PHIBER, will be fully available to members of the AIM-AHEAD Consortium, with ample support in the form of documentation and assistance from our team for consortium members to make use of these resources.

6 - Application and Uses:

Testbed for entire AIM-AHEAD Consortium community

Try it, use it, bang-on-it - adapt and improve

Specifics for evolving partners

- Meharry and HBCU medical school network
- Buffalo East Side community health network ("St. Ann's" new center)
- Navajo Nation in cooperation with IHS (Indian Health Service)
- Society of Refugee Healthcare Providers
- U. S. Committee for Refugees and Immigrants
- Racial Health Equity
- Center for Black Health
- Kaiser Family Foundation
- Quanterix, Inc.
- Epic. Inc.

Progress into a Beta Version

- Expanded datasets including behavioral and qualitative assessment data
- Expanded refinement (training) of the VAE+GAN neural networks

7 – Conclusions:

- ◆ PHIBER is an excellent path for establishing a necessary and currently absent core for comprehensive health metrics that include critical behavior, lifestyle and also SIMOA-type metrics for earlier diagnostics and evaluation.
- ◆ Major need for consistency among healthcare providers within informatics will engender automatically improvements in population health equity.
- ♦ Increased public awareness + more intelligent computational tools \rightarrow awareness and receptivity among both healthcare providers and the general-public population.
- ◆ Public health education is the KEY this is needed "on both sides".
- ♦ Understanding NpC type of underlying "inflammatories" can help with other "mainstream" inflammations (e.g., from infectious diseases).
- ◆ COVID-19 and PASC have amplified the whole problem of autoimmune and arrhythmia for multiple generations.
- ♦ EVE and tools in SI ("AI") and VLDB can help to rapidly build a multi-valued PHEBR.

Next Steps Now

- Do the defined work for the Pilot Project
- Participate and engage with AIM-AHEAD Consortium members
- Build solid networks with Black, Native, Migrant, Refugee communities
- Plow, sow, cultivate, harvest, disseminate!

Team Members, Collaborators, Advisors, Assistants

Rachel Roman, RN, NP Kevin Ciresi, MD Michael Passov

-- with collaborative engagement and assistance from --

Alexa Alexberg, RN (Karlinska Institute and Hospitals) 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) Wang Qingguo (Meharry Medical College) Lauren Stiles, PhD (Dysautonomia International Foundation)

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VAE-GAN was introduced for simultaneously learning to encode, generating and comparing dataset samples. In this blog, we explore VAE-GANs and the paper that introduced them : *Autoencoding beyond pixels using a learned similarity metric.* https://wandb.ai/shambhavicodes/vae-gan/reports/An-Introduction-to-VAE-GANs--VmlldzoxMTcxMjM5

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Thank You!

