Abstracts and Notes under development pertaining to TBD/TND/ICMC Projects

mjd version 1.1 31.Dec.2020

Preface

These are very rough notes for some upcoming papers, project reports to sponsors and partners, and ideas for more organized and focused project endeavors. There are references to concepts, terms, investigative studies, and particularly work by others, but here things are without specific or formal refs and bibliographies in place. This is not a formal paper but only a set of notes, even though some of us tend to be more formal and organized with writing our "notes". We aim to accommodate other people (readers, constructive critics and potential partners) and we also think of future uses such as in publications and lectures. So... please be patient with the "rough unpaved roads" here!

Origins and Future Directions

Much of what's here originates over the past twenty-plus years and involves several individual researchers and groups. Some are connected presently or in past years with TETRAD Institute or the affiliate partner company, Intelligence Renaissance Industries, or some individuals involved in these two entities. Many others are mutually unknown to each other and not connected or even interested in theory (or at least our avenues).

Increasingly, much of this new and exploratory work which has roots in physics and mathematics, now shows indicators of promising relevance to biology, neurophysiology and practical medicine, especially in addressing a combination-set of autoimmune and neuro-linked syndromes (most of which have never been associated with one another; e.g., MS, Alzheimer's, Parkinson's, and POTS, just to name four). This draws in much from the past two decades and particularly the past 5-10 years, with the growth of solid empirical research in molecular biology and genetics, empowered by nanoscale and higher-resolution imaging and signal measurements, and also through extensive clinical studies, especially those concerning electromagnetics, optics and non-pharmaceutical therapies, and also the careful integration of self/group-directed mindfulness and a variety of psychophysical disciplines with advanced imaging, molecular diagnostics, and therapies including both pharmaceuticals and surgery.

Some among us are theoreticians working on the integration of some findings from “far and wide” in biomedical and psychiatric disciplines, looking for a better and more comprehensive understanding of causes, and others of us are experimentalists seeking to integrate their findings within such a broader and more comprehensive theoretical foundation.

Some of us are more in the theoretical space, others more “applied” and with some emphasis upon either design and development of devices and drugs, or in the clinical uses thereof. The results thus far are still in very raw and primitive states, but we want to express some ideas sooner than later so that we can team up and collaborate with others who know more, especially in the clinical practice domains.

One last point. Currently, we at TETRAD have been involved in a new multi-project Program, known as **New Horizons: Beyond 2020 Vision.** What is mentioned here about certain bio/medical investigations does fit within this broader Program, for which we are in various discussions and negotiations for sponsorship, grants, and other forms of long-term support for a growing, diversified community of researchers and clinicians. As we enter into the calendar year 2021, we are hopeful that what we have done and are working on now will interest others with whom we can join forces so that together we will reach some solid answers that help people live healthier and happier lives.

1. Abstracts and Overviews

These may turn into papers for publications and/or presentation. These are extended intro/abstract forms and not final “abstracts”.

Disruption of Autonomic Control Functions through Informational Storm Events Triggered by Chronic Sustained Stressor Agents

We examine the balance between sympathetic and parasympathic control networks and the effects of deregulation brought on by chaotic signal conflict and a “double bind” bifurcation syndrome, contributing to noise and informational heat dissipation. This complex of conflicting and negating signal action compounds a signal weakness effect that operates at the level of energy transfer propagated as biosolitons through protein chains, in turn affecting adversely protein conformational dynamics and the geometrical behavior of DNA helical structures within protein sheaths. Further, we explore the role of both neurochemical and bioelectromagnetic stressor agents as the principal class of factors responsible for the mechanics of such neurosystem disruption. We introduce an explanation for the biophysics by which such stressors directly and adversely affect biosoliton signal propagation in proteins and nucleic acids, demonstrating a causal path from such stressors (both external stimuli and internal psychological triggers) to what can be termed “informational storms” within the autonomic neural networks. Such storms, analogous to cytokine storms within the context of infectious disease, encode and reinforce cycles of behavior including the emergence of chronic positive feedback loops related to the informational storm events and signal weakness effects. We explore how these cyclical, “chreode-like” formative processes thereby create and reinforce epigenetic effects of activation and deactivation for particular immediate-early expression genes that are centrally responsible for control of both FF (fight-or-flight) and RR (relaxation response) systemic behaviors, principally through regulation of cortisol and DHEA metabolism and homeostasis. We further argue that the long-term deregulation and loss of efficient signaling, and the positive feedback loops that result, is a strong model for explanation of the neurodynamics involved in a number of disorders of the autonomic nervous system, leading to significant pathologies of the cardiovascular, gastrointestinal and endocrine systems. We claim that a combination of psychological and physiological behaviors, supported by appropriate pharmacological agents but strongly resting upon techniques including exercises to develop conscious control of several generally-considered autonomic functions, can lead to long-term control that dampens and subdues the signal weakness and informational storm phenomena sufficiently to reverse the observed positive feedback loops and create an effective pathway to reduce the overall dysautonomic behaviors.

2. Somewhat-related abstracts and summaries

[2.1]

Topological Connectome and the Etiology of Neurodegenerative and Neurorestorative Processes with implications for Autoimmune Disease and Traumatic Injury

M Dudziak, E Deli

Abstract

The 50 Brodmann areas of the cerebral cortex is divided into around 500 smaller cortical patches, made up of macro columns, mini-columns, layers, and finally neurons. A fractal structure is characteristic of both the structural and functional organization of the brain. While active neurons give rise to extracellular fields, feedbacks to the neurons can alter their behavior, even without a physical connection between the neurons. Changing the synaptic weight between neurons changes the global character of the neural system, the ability to respond to future stimuli. Many levels of feedback loops, such as the cortico-thalamic loop, give rise to a complex regulation. At every organizational level, the topology of the electric activities is characteristic of the neuronal regulation and complexity. Network topology measures represent the best computational method for the grading of levels of consciousness [1]. Memory loss in dementia contributes to disorientation in space, time, and identity, leading to insecurity, and anxiety, which only intensify cognitive disturbances. For example, repetitious thoughts indicate susceptibility to anxiety, and depression. In multiple sclerosis, Parkinson's, Alzheimer's, and other psychological and interpersonal disorders, disturbances in spatial orientation have also been noted [2,3]. Disturbances in navigation altered neurogenesis and significantly reduced neural stem cell production [4], indicating the close relationship between conceptual and spatial deficiencies. The possible connection between spatial deficiencies and topological alterations might offer early diagnostic markers and novel targets for mental diseases.

[2.2]

Topological Information Processes in Viral-Host Interaction and Membrane Penetration: common natural biocomputation processes underlying certain contagious and autoimmune diseases and adaptive mutation

M Dudziak, E Deli, G Vattay, O Ori, D Sabov

Abstract

A model incorporating principles of topological order and efficiency shows utility for demonstration of a mechanism present in both viral entries for certain agents including coronavirus, influenza and filovirus types such as ebola, and also in non-infectious disorders and diseases associated with autoimmune reactions, particularly within the brain and central nervous system. This process can be described as a type of natural biocomputation involving extensive molecular surfaces. It appears to fit with observations of surface protein changes within viral envelopes and primary structures involved in entry to target host cells, and it involves an iterative changes within viral protein conformation and surface topography that can be associated with underlying mutations within the viral strain. Similar processes appear to be present in the phenomenologically distinct and non-viral initial inflammatory stages of neurons affecting axons, both myelin sheaths and interior microtubule chains, leading to neuronal degeneration that triggers subsequent normative engagement of the immune system response. The apparent computational process is similar to certain non-Turing quantum computing models and leads to consideration of an underlying common mechanism within certain biological structures that involves the interaction among non-smooth manifolds and the optimization of surface-fitting that is consistent with Ricci Flow models for deformation and maintainability of topological consistency.

[2.3]

I. Program/Project Overview II. Specific "lead" paper and presentation (Spring 2020, Berlin)

I. Program/Project Overview

Impact of Environmental, Ecological, and Socioeconomic Changes in Early 21st Century on Viral and other Microbiological Disease, Epidemiology, Public Health Response and the Pharmaceutical Development Practices

Preface

We will show the underlying causes for why recent (2002+, particularly) epidemics and pandemics have decisively different characteristics that bear important, even critical, consequences for human health and social stability. In so doing we will show certain relationships active between such phenomena as viral mutation, new infectious vectors, novel routes and accelerations of transmission, higher virulence and the general-population disposition to more severe complications in personal and social health management for certain infectious diseases. We will show connectivity between hemifusion, endocytosis and other forms of viral entry, viral replication, consequent systemic over-reactions including cytokine storm inflammation, and also connectivity and common elements between these pathogenic processes and certain foundations for autoimmune reactions and related pathologies in signaling, communication and recognition that lead to autoimmune reactions and prolonged cellular component degradation in both neural and non-neural cellular types. We will describe how certain fundamental processes are biomolecular manifestations of a generalizable type of non-Turing computational paradigm, one which can be employed in both models, simulations and the design of corrective therapies, including pharmacological design and implementation, and also in an architecture for synthetic computation algorithms and machines designed and constructed along principles similar to those employed within the biology of viruses, bacteria, cells, and complex multi-celled organs and autonomous-behaving organisms.

Within this is clearly a well-defined place and pathway for the other research initiatives and projects which actually provide the foundations for what is going into these works – namely, everything concerning what we abbreviate as RTD, TBD, ICMC, and also GCM.

II. Specific "lead" paper and presentation (target presentation Spring 2020)

The Initial Presentation and Short Introductory Paper

Changes Afoot in the Kingdom: New Epidemiological Dynamics - the Confluence of Climate, Socieconomics, and Global Patterns upon Future Drug Discovery, Design, Testing, Trials and Implementation

[tentative team of co-authors]

M Dudziak R Roman E Deli R Csencsits (others TBD)

Abstract

Several very closely coupled behavioral changes on international, transcontinental and global scales have converged within recent decades, all of which involve greater movement, displacement and

interfacing of different species of organisms which include humans, livestock breeding animals, and a variety of microorganisms that have high potential for infectious disease. These changes are closely coupled with population rise and density in close-habitation urban metropolis regions, greater affluence and resulting travel, both short-range frequent commuter distances and long-range commercial and leisure travel, especially by air. This set of changes in the underlying ecosystem and in socioeconomic patters can be linked to an increased variety and virulence within certain infectious disease agents. The overall changes are unpredicted and unexpected in most current models influencing healthcare planning and in particular public health including epidemiological management, that have emerged within the current two decades. These encompass and bring together mutual effects and often nonlinear impacts, attributable to the new dynamics of climate change, agriculture and food industry, transportation of good and movement of people, as well as interpersonal proximity, contact and exchange of personal physical media. The consequences are enormous for not only basic epidemiological models and response to epidemic and pandemic-potential infectious diseases, but also the fundamental models, systems, regulations and actual practices involved in drug research and discovery, design, testing and trials and product introduction and implementation within both institutional and private uses. We introduce some of the observed factors, relations and consequences, and we identify new pathways by which the medical establishment – public and private – including the pharmaceutical industry as a community – can more effectively prepare and establish the type of resilience necessary for reducing the personal and socioeconomic destructive impacts of epidemic and pandemic outbreaks, while simultaneously advancing the overall health of all segments and diversities of the global population.

So, as Henry V said to his army a few years back --
"The game's afoot: Follow your spirit..."

[2.4]

Quantum Biology, Cellular Communications, Genetic Control, Disease, Injury, Disorder, Aging

A brief memo

M. J. Dudziak, PhD IIS 27.June.2016

The processes by which a complex living organism (e.g., human) reacts to acute injury (including severe tissue trauma and damages from infection including inflammation) are not dissimilar to processes (functions) that pertain to other forms of severe biosystem stress including disorders and diseases such as cancer, cardiovascular disease, fatigue, and most broadly and open-ended of all, the processes of aging.

These processes – both negative (debilitating) and positive (healing) - involve chemical and electromagnetic interactions that influence, among other things, gene activation and the intercellular signaling that is mediated by molecules know as exosomes.

These processes involve multiple levels of molecular, intercellular, and regional tissue relationships and communications. Central and fundamental is a phenomenon that is loosely termed quantum entanglement (QE; also coherent quantum entanglement resonance, CQER), and the experimental evidence is now emerging to match the theoretical models. QE occurs within nucleic acids (e.g., DNA) and proteins, but at different scales. At one level, it involves coherence between segments of DNA that are responsible for variations in how DNA folds and shapes itself as a long “string” and this in turn has a role in the control of gene activation.

One of the phenomena of special interest is that which involves generation and transmission of intercellular signals through molecules known as exosomes. Such molecules execute important communications from one region of the body to another and there are extensive research findings which demonstrate the role of exosomes in the body's self-healing process.

We begin to believe and assert that there are ways to influence these processes using a variety of stimuli besides those which involve chemical agents (drugs), stem cell treatments, or invasive surgeries. Such stimuli may act as catalysts, accelerators, and enhancers for pharmaceutical, stem cell, and other medical treatments, and in some cases they may be sufficient or preferable as therapies without other procedures such as drugs and external agents, or surgical procedures.

The theoretical models and the emerging experimental evidence include the results of clinical studies - in particular within the domains of neurodegenerative disease and neurorestorative therapies (e.g., for conditions such as stroke, traumatic brain injury, and cognitive disorders such as Alzheimer's). The models and experiments indicate the realistic possibility of developing systematic treatments with value for multiple aspects of healthcare - prevention, deceleration, and palliative treatment for different diseases, and also restoration of various healthy functions. Such therapeutic methods promise to be attractive medically from the standpoints of having low complexity, risk, cost, and high value for the patient.

In summary, the living organism is resilient and has plasticity, adaptability, and the power to restore balance, equilibrium, and wellness, more than we have estimated previously. The basis for this systematic power is in great part rooted in highly integrated systems of intercellular signaling and communication. These systems are implemented through both chemical signaling agents such as exosomes and by bioelectromagnetic fields. Together, such fields and signal transmissions interact with intracellular structures and ultimately affect the activation and deactivation of genetic information sequences in DNA. This process is believed to be effected within cells through the medium of very basic biophysical mechanisms that involve molecular-scale quantum entanglement, as well as fundamental physical mechanisms known as solitons and phonons.

This new direction of basic research and applied medical technology holds promise for how we can address a number of diseases and disorders (such as those previously mentioned) and for reducing and even to some extent reversing – in substantive and lasting ways - the effects of such disorders upon patients who have suffered from such conditions. The implications of this molecular and cellular biology for practical medicine and healthcare are potentially immense and offer promises for new treatments for major diseases, disorders, injuries, and for creatively addressing aspects of slowing the process of aging.

[2.5]

Generalized Heterogeneous Computing Machine – Quantum Non-Turing Computing based upon Biology and the Brain

Abstract

This report presents the fundamental architecture of the GCM (hardware and software), a design for a computing system encompassing topological cortical columns using physical microdevices and circuits and incorporating simultaneous perturbation stochastic approximation (SPSA) models. The architecture employs PPC (protein (peptide) polymer conjugates), conformally arranged, in topological ordering that on the macro scale resembles origami, quipu and other knotted string-like structures, within graphene layers for conductive logic and for i/o connectivity to “heterogeneous” Turing-machine computing devices (bit-based and qubit-based). The implementation of this architecture involves multi-material multi-layer 3D printing (graphene, silicon, metals, and PPC).

The primary logic employed within the GCM is derived from network dynamics of the neural connectome and involves the autonomous formation of resonant patterns of activation and deactivation with topological defor-

mations, employing SPSA and the emergence of chreodic topological features that maintain persistence over time and are “eigenstructured” topologies, resistant to variations in spatial deformations and resistant to noise introduced both internal and external to the GCM system.

The GCM is capable of learning and introducing self-critical, self-adjusting innovations through exposure to diverse and widely-varied stimuli forms. Decoherence problems as in quantum Turing-machine computers is not a problem but a necessary ingredient for cognitive invention and memory (reconstruction) retention. The formal basis for the GCM is consistent with observed neurobiology and with fundamental RTD (Reflexive topological Dynamics) physical theory and principles of emergency of order and structure from randomness.

Applications for the GCM include tasks in drug design, n-body cybernetics and control, and other challenges in pattern discovery within physical and life sciences, robotic navigation, and the study of psychosocioeconomic dispositions and trends for behavior of large populations.

[2.6]

Integrative Reflexive Information using NfL and fMRI with phenomenological monitoring for optimization of therapeutics in multiple sclerosis and related neurological diseases

Abstract

The role of nutrition, physical fitness and cognitive exercise as both prophylactic and therapeutic aids pertinent to neurological diseases, including those of autoimmune characteristics, has been demonstrated but has generally been inadequately studied in the context of patients outside of strict control groups, often undergoing a history of varying treatments and often subject to variations in medication and lifestyle changes. Correlation of environmental and behavioral factors, both in etiology of disease and in treatments leading to comparative cures, long-term remissions and/or reduced progressions, needs closer monitoring of both direct neurological function and patient-interactive behaviors. Limitations on types and frequencies of significant observation, such as offered in particular by neurofilament light (NfL) and functional MRI (fMRI) testing, has contributed to the current deficit in understanding how certain modalities of lifestyle, diet, and exercise affect progressions of diseases such as multiple sclerosis, dementia, and Parkinson's. A program involving coordination and control of frequent multi-sensor diagnostic imaging and chemical analysis in conjunction with lifestyle and activity monitoring using wearable and telepresence technologies has been designed for inclusion with pharmaceutical regimens within both clinical trials and sustained patient practice. This program is conducted in combination with nutrition, physical fitness, and psychological practices that complement administration of pharmaceutical treatments. The initial phase is focused upon incorporation of monthly and bimonthly examination using NfL and fMRI in addition to conventional MRI. Non-pharmaceutical therapeutics introduced include transcranial magnetic stimulation (TMS) and photobiomodulation (PBM) in addition to exercise and dietary practices previously shown to have bearing on both avoidance and mitigation of neurological disorders of these types. Initial patient populations are within RRMS and SPMS multiple sclerosis groups and with long-term engagement underway for next-phase studies.

[2.7]

Brain is not a Turing Machine and AI is a limit-case of adaptive logic

M Dudziak, E Deli, O Granichin, G Vattay (others tbd)

Abstract

Thermodynamics is a rapidly changing field that promises the development of novel techniques and applications. The brain's synaptic network displays a topological character, which is related to psychology. Cortical activation compresses information and builds an evoked potential. The frequencies of the brain's evoked cycle reflect the energy need of synaptic changes. Deep learning can also be divided into phases that consist of compression of information and relaxation, which culminates in representation. Just as backpropagation in current neural networks, feedback loops in the brain improve performance. The brain's biggest loop is the evoked cycle. It is centered on the resting state, which is maintained by self-regulation. Self-regulation is an essential quality of neural systems that perform computations with thermodynamic efficiency in orders of magnitude greater than current supercomputers. Subjective perception of stimulus is an appropriate Fourier transform of the input. The resulting temporal organization orients the mental world orthogonally to the physical environment. Temporal orientation allows biological systems to form memory, learning, and evolution. As material systems observe the principle of least action when moving in space, intelligent systems might balance their action repertoire between the past and the future. Thus, generalization is a type of memory that boosts the ability to handle future challenges. The resting state permits the gradual evolution of the system in time and engenders the brain's temporal orientation. In a temporal system, quantum phenomena such as, entanglement forms in time and therefore is resistant to spatial disturbance. The later quality is perhaps the most essential advantage of brain-like quantum systems. A self-regulating system herein that can change and learn in response to the environment, and it may be suitable as the evolvable elements for future for thermodynamic computers.

3. Appendix – some background material

Two other specific components of the **New Horizons: Beyond 2020 Vision** Program are briefly summarized here.

ICMC_TBD

Immuno Cyto Molecular Computation/Communication and Topological Biomolecular Dynamics
Research is focused upon two principle areas:

[a] VESID (Viral Entry Structural Integrity Disruption) – design of prophylactic and therapeutic medications for interruption and prevention of host cell entry processes via specific targeting of viral envelope topological structures. VESID is based upon topological models of cellular and viral signaling and recognition which contribute to the mechanics of infection, inflammation and immune response. VESID is not a vaccine nor a form of medicine for advanced viral infection such as in deeper lung regions with consequent inflammation and other pathologies. VESID is a combination of proven and established compounds for oral and nasal administration, and it is principally a prophylactic and early-stage defense against a virus (first target, SARS-CoV-2 from COVID-19; others to follow later).

Related background information: www.intelrenaissance.com (see "VESID")

[b] Topological order and efficiency, conformal geometries, and biosoliton dynamics within autoimmune disorders, with special attention to multiple sclerosis, dementia and dysautonomia pathologies. The medical domain of special study is that of Neuronal Electrochemical Stressors disrupting biosolitonic molecular signaling. Such disruption progressively leads to accelerative demyelination and microtubule brittleness and fragmentation and the foundational stages of MS, AD and other ND disorders. We are also engaged in examination of similar topological-metabolic relationships and etiologies involved with such conditions as dysautonomia, POTS and MALS. We are finding evidence that disruption of normal autonomic regulatory functions is linked with chronic, sustained counter-active signaling, leading to a type of "double-bind" phenomenon of conflicting and mutually negating command and control actions between sympathetic and parasympathetic networks. Among the results can be spurious growth and decay of neural pathways which in turn by repeated conditioned response lead to disorders such as tachycardia and other dysfunctions of the autonomic system.

ACCOMPLISHMENTS TO DATE
We have shown in models, in theoretical work, how VESID can function at the molecular (protein-lipid level). We have shown the projected success of a mix of compounds that are known to be safe for human consumption. Certain of these have been employed for medical purposes, and certain of these are compounds found in ordinary human diets. We have shown that these compounds will remain sufficiently long in nasal and throat passages and will make contact with incoming viruses that travel in those passages. We have shown that there will be sufficient levels of contact between these compounds and the viruses in those regions in order to effect molecular bindings with viral . Our theoretical and modeling work has provided the basis for the claim that VESID can provide a

substantive and strong defense against COVID in ways that support all current and traditional methods (e.g., face masks, accurate personal hygiene, social distancing) and that, very importantly, reduce the risks of contagion that do exist even with such precautionary and preventive measures. We believe that VESID can serve, in combination with healthy practices including such precautions, to enable communities and societies to practice lighter, safer and more socioeconomically proactive measures, all of which support not only economies but the psychological and social well-being of the populations.

STATUS NOW

With VESID we are now ready to proceed to experimental verification in vitro and then in vivo. All advance preparations for clinical trials have been planned and arranged in the full expectation that the next immediate experimental phase will be successful. We have made already arrangements for the types of clinical trials to be employed, regarding population demographics and especially social (environmental) settings, since the nature of such clinical trials will involve, necessarily, people operating within social groups and different locations.

In other TBD research such as the emerging branch of study for dysautonomic conditions we are precisely at the point of transforming theoretical studies into models that can be brought together with clinical data and ongoing medical studies.

CHS

(Community Health Sustainability)

The integration of BioProtection practices and methods, MedAtrium mobile diagnostics and therapies, Eyrie public activity and resource management informatics and VESID medicinal solutions, tailored and optimized for specific civic and social entities. MedAtrium constitutes a highly modular and reconfigurable architecture for rapid-deployment medical diagnostics and therapeutics, oriented to large-scale public needs in epidemic, pandemic and other emergency response situations. BioProt incorporates informational methodologies, physical procedures, and social education in order to address multi-origin, multi-agent problems of microbially-transmitted infectious disease and other health conditions through the environments of homes, schools, workplaces, and other sites of human congregation and interaction. Eyrie provides an open, secure, publicly-acceptable, privacy-protective informatics environment, usable by any members of the public and also any professional individuals and institutions, capable of performing the essential and necessary functions of finding, organizing and sharing information important in public health and individual health response to epidemic, pandemic and similar health and safety crisis situation.

Related background information: www.intelrenaissance.com (see all product and research components)

ACCOMPLISHMENTS TO DATE

All components and the integrated system architecture for CHS have been carried through the respective R&D stages and all components have received appropriate regulatory and licensing

approvals, in most cases for a matter of years, as far back as 2008. We and our partners have built what needs to be employed today and going forward. Visit the IRI website to learn more about what we have now – Bioprot, MedAtrium, Eyrie, and all our knowledge and people-experts for building CHS for anyone. There is all that reported on the site and in related docs.

STATUS NOW
The project team has been completely ready to proceed with virtually any civic, corporate, or other public/private entity, for implementing customized solutions. The immediate challenges have been not in technology nor service abilities but in the fact that so many communities and institutions have been in a state of confusion and lack of resources for beginning these measures such as what CHS can provide, because of the intensity of the COVID pandemic.

4. Suggestions for Next Steps

Meet, discuss common points, intersects, overlaps, and paths for collaboration.
Do some seminars and workshops. Bring one or more of us to you. Best if in-person, but people can attend via teleconferencing as well.
Explore the ways what we are doing and the directions we are pursuing can fit in and support your work.
Get support from multiple sources including the private sector where we have strong indicators for what we can do together.
Collaborate on the paths that make the most sense and offer the greatest value.

5. Contacts

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