Yahriel's 4A's: An Independent Interdisciplinary Field

1. Aerospace-Aeronautical Systems

2. Anthropology-Engineering

3. Applied Science, Technology, and Society (STS)

4. Anatomy and Artificial Intelligence

By Yahriel Salinas-Reyes

A proposed thesis submitted to the graduate faculty in complete fulfillment of the requirements for the degree of

DOCTORATE OF NEUROSCIENCE AND BIOMEDICAL DATA-SCIENCE/INFORMATICS

The student author, whose presentation of the scholarship herein will be reviewed by the program of study committee, is solely responsible for the content of this thesis. The Graduate College will ensure this thesis is globally accessible and will not permit alterations after a degree is conferred.

Undergraduate Institution: Iowa State University of Science and Technology

Ames, Iowa

2023

Bachelor's: Aerospace and Aeronautical Engineering ('23)

Master's: Applied Science and Technology ('23)

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NATURE'S CHAOS GAME: AN EXISTENTIALIST APPROACHINFORMED BY MATHEMATICS AND NEUROBIOLOGY

INVESTIGATOR: *Yahriel Salinas-Reyes*
RESEARCH MANUSCRIPT

i.
DEDICATION

I dedicate my thesis primarily to the two most important people in my life - my nurturing mentor known as The Cyclone of Education, and my to my lifelong supporter, and companion, Don Yahriel Salinas-Reyes - An embodiment of Chaos, Order, Logic, and Madness. I miss you both incredibly, and I promise to make good on my word to make you both proud.

I am deeply grateful to my family in the United States, Mexico, and El Salvador for bearing with me patiently as I worked on my thesis. I dedicate this work to all of you. Your unconditional love and strong show of support are the only things that kept me going every time I wanted to give up. To my parents, Sonia Reyes-Alvarenga and Oscar Salinas-Millan, your daily phone calls and pep talks kept me grounded and pushed me closer to the finish line. To my sister Lizbeth Salinas-Reyes, who would chide me every week and guilt trip me for being away from home - your prayers and love have kept me safe here. To my family Abigail Salinas-Reyes, Samuel Salinas-Reyes, Delmy Salinas-Reyes, and La Raza - thank you for seeing the best in me. You have never failed to cheer me up.

Lastly, to my supporters - thank you for being patient, caring, understanding, and being invested in me and my thesis. I am incredibly lucky to have you all, and I couldn't have done this without you.

Yahriel Salinas-Reyes 2023

Personal Statement

Yahriel Salinas-Reyes, Fulbright-Garcia Robles Open Study/Research Award
Molecular & Systems Bioengineering towards Neuroscience

In the realm of mathematics, the concept of chaos game originally alluded to a method of generating fractals—intricate geometrical patterns that seem to symbolize the fractured nature of reality itself. The intricate dance of numbers, shapes, and chaos mirrors my own journey through life, marked by a tapestry of neurological and neurodevelopmental challenges.

My story is one of resilience, determination, and an unquenchable thirst for knowledge, and has been anything but conventional. From an early age, I grappled with ADHD, PTSD, anxiety, and autism. These neurological conditions, instead of being impediments, have become the driving force behind my academic pursuits. I realized that within the chaos of my mind, there was an unexplored realm of creativity and analytical thinking. However, life had more challenges in store. Hearing loss and a speech impediment made communication a daily struggle. But rather than let these barriers silence me, I embraced the power of written expression. Writing became my voice, a medium through which I could convey my ideas, emotions, and discoveries. As I embarked on my academic journey, I encountered a myriad of obstacles that tested my resolve. Financial challenges loomed large, threatening to derail my dreams of higher education. Yet, I persevered, seeking scholarships and part-time work to support my studies. I also navigated the language barrier, as English is not my first language, and adapted to the demands of college life in a new world. Physical health issues further complicated matters. Sciatica, a debilitating condition, left me bedridden and unable to attend classes. Still, I did not relent. I leveraged technology to engage with coursework remotely, demonstrating my unwavering commitment to my education. In the midst of these personal challenges, I took on the role of the primary caretaker for my mother, who battled severe health issues. This responsibility, while emotionally taxing, underscored the importance of resilience and compassion. It reinforced my belief in the power of empathy and understanding, qualities I have carried into my academic pursuits. The most recent chapter in my life introduced a new set of challenges—adjusting to mental health medications and diagnoses. While the journey to stability has been arduous, it has deepened my empathy for those facing similar struggles and ignited my interest in the intersection of mathematics and mental health. My experiences have shaped my academic journey and my aspirations. I am driven by a passion for fractal mathematics, drawn to the beauty of patterns that emerge from chaos. I see parallels between the complexity of fractals and the human mind, and I am determined to explore these connections. Through these trials, I discovered a profound truth: our stories are woven into the tapestry of science and art. We tell stories to make sense of the world, to illuminate the unknown, and to connect with others. In Mexico, I hope to immerse myself in the rich mathematical heritage of the country, studying under esteemed mentors who can help me unlock new dimensions of fractal mathematics. I envision collaborative research projects that bridge the gap between mathematics and neurodiversity, shedding light on the intricate patterns of the human mind. My story is one of resilience, determination, and an unshakable belief in the transformative power of education. Amid the chaos of life's challenges, I have emerged as a passionate scholar, ready to contribute to the world of mathematics and advocate for the value of neurodiversity. I am eager to embark on this Fulbright journey, where I can explore the marvel of the human spirit, using mathematics as my compass to navigate the intricate patterns of our world. Together, we will write a new chapter in the wondrous story of human ingenuity, science, and nature itself.

Statement of Grant Purpose

Yahriel Salinas-Reyes, Host Country: Mexico, Field: Molecular & Systems Bioengineering

Project Title: Unraveling the Molecular Code of Natural Antidepressants in Grapes

In the ever-evolving world of scientific inquiry, certain moments emerge as profound intersections of human ingenuity, scientific inquiry, and the enigmatic wonders of nature. Encapsulated within this project is one such moment. With a central focus on unraveling the molecular code of grapes to find the compounds responsible for its potential natural antidepressant properties, Yahriel Salinas-Reyes aims to foster innovation in treatments for mental health disorders and conditions. Also encompassed in the project is an investigation into the nature of schizophrenia and the complexities of neuroplasticity, in hopes of advancing understanding of the mental illness. The overarching goal is to address the mounting global health crisis presented by mental health disorders, including depression and schizophrenia, which have surged to an unprecedented global health crisis significantly diminishing the quality of life for millions and placing immense pressure on healthcare systems worldwide.

At its core, the project is driven by the ambition to conduct a comprehensive molecular analysis of grapes, with a particular emphasis on understanding the genetic and molecular mechanisms governing the synthesis of antioxidants. Grapes have garnered scientific interest due to their potential health benefits and their recent recognition as potential natural antidepressants. Yahriel's unique background in aerospace engineering and micro-electro-mechanical systems (MEMS) equips him with the precision and expertise required to delve into the microscopic realm of chromosomes and molecules—an essential prerequisite for unveiling the genetic secrets grapes hold. To fulfill the project's objectives, advanced techniques in molecular biology and biotechnology systems engineering will be employed. The primary goal is to pinpoint the specific compounds within grapes responsible for their potential antidepressant properties, involving their isolation and characterization to illuminate their mechanisms of action within the brain. The aim is to identify practical applications for mental health treatment by comprehending the genetic and molecular foundation of natural antidepressant production in grapes.

Concurrently, this research adopts a multifaceted approach to unravel the complexities of schizophrenia, a debilitating and chronic mental disorder characterized by symptoms such as delusions, hallucinations, disorganized speech, and cognitive deficits. At the heart of schizophrenia's enduring enigma are Bleuler's four A's: Alogia, Autism, Ambivalence, and Affect blunting. Extensive research has explored the etiology of schizophrenia, leading to the emergence of three prominent theories: genetic, neurodevelopmental, and neurobiological. Each theory offers a distinct perspective on the origins of this complex disorder, making it challenging to pinpoint a single causative factor. Nonetheless, neurobiological theory has gained prominence due to its comprehensive approach, explaining schizophrenia as a result of abnormal brain dysfunctions or structural anomalies. This theory stands on solid scientific ground, holds promise in guiding treatment strategies, transcends cultural and demographic boundaries, and raises fewer ethical concerns compared to alternative theories. Structural and functional abnormalities in key brain systems (i.e., the prefrontal & medial temporal lobes) play a pivotal role in the manifestation of schizophrenia symptoms that are integral to working memory and declarative memory processes. The disrupted functioning contributes to cognitive impairments and emotional dysregulation in individuals with schizophrenia. In the quest to understand schizophrenia, neuroplasticity—the brain's remarkable capacity to adapt and reorganize itself in response to learning, experiences, and environmental changes—emerges as a crucial factor operating at various levels, from synaptic plasticity, where the strength of connections between neurons is modified, to large-scale changes in brain structure and function. In the context of schizophrenia, neuroplasticity offers hope for improving cognitive functioning and overall quality of life for affected individuals. Research has shown that cognitive remediation therapies— which harness neuroplasticity—can lead to improvements in cognitive domains such as memory, attention, and problem-solving, mitigating some of the cognitive impairments associated with the disorder.

This project is founded on the belief that nature holds the key to addressing complex health challenges, including mental health disorders like depression and schizophrenia, and seeks to explore the potential of grapes as a source of natural antidepressants.. One intriguing entry point into the complex world of grape biochemistry is through the study of yeast used in wine production, which plays a pivotal role in the fermentation process, and influences the composition of compounds within grapes. Scientific evidence unveiled that certain molecular compounds in the antioxidants act as natural antidepressants but there lacks initiative to utilize these antioxidant agents in psychiatric institutions and practical methods. By employing advanced techniques such as neuroimaging, fractal geometry, and spectral analysis, the project aims to unveil underlying patterns and causative factors associated with depression and related mental health conditions. The significance of this research extends far beyond the development of new treatments. It encompasses a broader understanding of the intricate relationship between food, biochemistry, and mental health. This knowledge has the potential to inform dietary recommendations that promote mental well-being, potentially reducing the global prevalence of these disorders.

Yahriel, and the research team at the university Tecnológico de Monterrey endeavor to decode the molecular secrets of nature to improve the human condition, particularly for individuals affected by schizophrenia and other mental health disorders. Yahriel's work represents a convergence of scientific rigor, interdisciplinary collaboration, and a profound commitment to the betterment of human well-being. Furthermore, this research holds the potential to strengthen international collaborations between the U.S. and Mexico. By conducting research at Tecnológico de Monterrey, Yahriel can contribute to the exchange of knowledge and ideas between the two countries, fostering a stronger global community which reflects the essence of the Fulbright mission, emphasizing mutual understanding and collaboration between nations. Yahriel Salinas-Reyes' Fulbright-Garcia Robles Open Study/Research Award proposal represents a unique and ambitious endeavor to explore the natural antidepressant properties of grapes. Grounded in the principles of interdisciplinary research, this project not only has the potential to transform mental health treatment but also to deepen our understanding of the brain's plasticity. It is a testament to the power of collaboration and cultural exchange in the pursuit of knowledge and the betterment of human well-being. Yahriel's unwavering commitment to utilizing opportunities to their fullest and to serve as a cultural diplomat, bridging gaps between different fields and nations, promises to unlock the molecular code of nature and take meaningful strides toward a healthier and more fulfilling world for all. Yahriel's proposal represents a remarkable opportunity to weave together science, innovation, and compassion in the quest to decipher the extraordinary truths hidden within the universe's code.

Tecnológico de Monterrey

Monterrey, Nuevo León, México
September 28, 2023

Dear Fulbright Program and National Geographic Society,

I am writing to you today with the distinct privilege of welcoming Yahriel Salinas-Reyes as a visiting fellow and proudly assume the role of his research advisor at Tecnológico de Monterrey, in the Molecular and Systems Bioengineering Research Group and the FEMSA Biotechnology Center. This opportunity represents a watershed moment in the pursuit of knowledge and global collaboration. Allow me to express my unwavering confidence in Yahriel's ability to not only excel in this role but to make a transformative impact on the fields of neuroscience, molecular sciences, and systems biotechnology.

In case he's accepted into your programs, Tecnológico de Monterrey stands ready to provide Yahriel with the resources, mentorship, and collaborative environment he deserves to excel in his chosen path. We are unwavering in our conviction that Yahriel's transdisciplinary approach, his unwavering analytical mindset, and his ceaseless thirst for knowledge will not only elevate our research community but also harmonize seamlessly with the mission of the Fulbright Program and National Geographic Society. Together, we shall forge connections, advance knowledge, and safeguard the wonders of our world. Thank you for considering Yahriel's application, and please do not hesitate to reach out to us if you require any additional information or should any questions arise.

Sincerely,

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Nature's Chaos Game: An Existentialist Approach Informed by Mathematics and Neurobiology

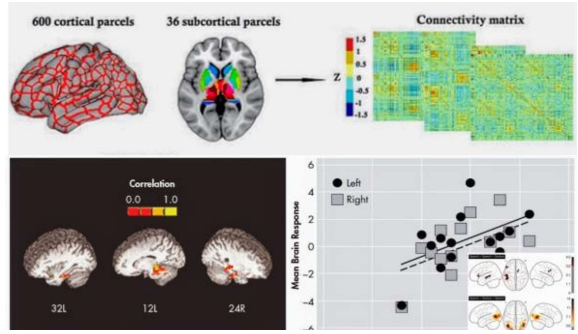

Figure 1. Morphological-Anatomical Features Connectivity

Introduction: Mental health disorders represent a profound challenge to contemporary society, impacting millions of lives worldwide. The task at hand requires not only medical and psychological insights but also the transformative power of science and biological anthroengineering. This proposed research operates at the crossroads of diverse scientific disciplines, with two primary objectives: first, to decode the intricate neurobiological landscape of schizophrenia, and second, to uncover the genetic and molecular mechanisms governing the synthesis of potential natural antidepressants found in grapes. Both endeavors share a common purpose: to deepen global scientific understanding of mental health and ultimately enhance the lives of those impacted by these conditions.

Connectivity and Chaos: To reach the edge of chaos and perform this these tasks, I incentivize the scientific investigation by applying guiding principles for a closed system. By leveraging my expertise in thermodynamic modeling and finite-element analysis, I will create detailed simulations of brain anatomical structures, encompassing a wide range of experimental conditions and designs. Let Σ be smooth oriented surface that is bounded, $\partial\Sigma \equiv \Gamma$, then we invoke boundary conditions. Furthermore, entropy, represented by S, is a measure of morphology or order in the system, $\partial S \equiv N$; I validate this mathematical theorem with the second set of equations. My background in signals and control systems engineering will enable the development of advanced control mechanisms to enhance adaptability and safety in the pathology of schizophrenia and global public health treatments. Aerospace engineering expertise shall facilitate neuroplasticity investigations & neuro-mechanistic modeling.

Governing Equations: [1] ***Energy:*** $\Phi_E = \oiint E \cdot dA$, [2] ***Mobility:*** $\iint_\Sigma (\nabla \times F) \cdot d\Sigma = \oint_{\partial\Sigma} F \cdot d\Gamma$, and [3] ***Continuity:*** $\iiint_V (\nabla \cdot F)\, dV = \oiint_S (F \cdot \hat{n}) \cdot dS$.

Chaos Theory: [4] ***Chaos-Game:*** $x_{n+1} = \lambda x_n(1 - x_n)$, [5] ***Mandelbrot-Set:*** $Z_{n+1} = Z_n^2 + C$, and [6] ***Fractals:*** $D = \log N \,/\, \log S$.

Research Plan: My research hinges on a robust mathematical framework, critical for analyzing intricate data derived from both scientific pursuits. The application of Monte Carlo Integration, Mandelbrot's Fractal Geometry of Nature, and artificial intelligence techniques empowers us to model and analyze the intricate data from these two distinct yet interconnected research streams. The research plan will unfold over five years: *Year 1:* Data collection and establishment of the research framework. *Year 2:* Neuroimaging and genetic data analysis. *Year 3:* Development of mathematical models. *Year 4:* Validation of models and refinement of findings. *Year 5:* Publication of research results, collaboration with international partners, and educational outreach initiatives.

Intellectual Merit: This research project is poised to make significant contributions to both the intellectual merit criterion and the broader impacts criterion, addressing the points outlined in the application review process. Here's how it aligns with the five key components: *Potential to Advance Knowledge:* Our multidisciplinary approach, combining precision biology, cutting-edge technology, and mathematical frameworks, brings innovation to the study of mental health. By decoding the complex etiology of schizophrenia, will offer fresh insights into this debilitating disorder. Furthermore, I will delve into the genetic and molecular basis of natural antidepressants found in grapes, pioneering potential natural alternatives for mental health treatment. *Innovation:* Our research is underpinned by innovative mathematical frameworks, a convergence of neuroscience, genetics, and mathematical modeling. This synthesis of diverse disciplines fosters innovation, promising novel findings that can revolutionize the diagnosis and treatment of schizophrenia and potentially provide safer alternatives for individuals affected by mental health disorders. *Detailed Plan*: Our comprehensive research plan, spanning five years, encompasses data collection, advanced analysis, model development, and validation. The plan is characterized by its systematic and strategic approach, with built-in measures of success to ensure the attainment of meaningful results. *Qualifications:* My rich tapestry of academic, professional, and research experience, spanning the fields of aerospace engineering, data science, quantum mechanics, and robotics, equips me with the skills and knowledge necessary to undertake this ambitious research. *Ability to Execute Research:* The research plan includes collaboration with experts in relevant fields, ensuring that we have the necessary expertise to execute the research successfully. Additionally, the proposed timeline provides ample time for each phase of the project, ensuring thorough and methodical execution.

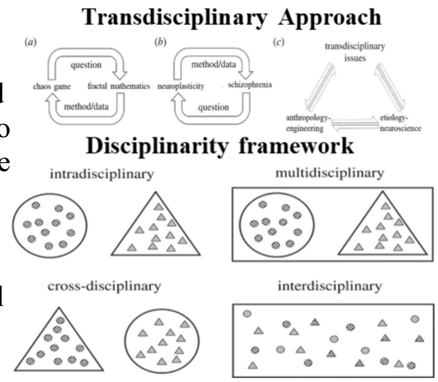

Figure 2. Proposed Existential Approach.

Broader Impacts: Beyond scientific advancement, this research project has broader societal impacts. It has the potential to: *Advance Mental Health Care:* By deepening our understanding of schizophrenia and identifying potential natural antidepressants, this research can pave the way for more effective diagnosis, treatment, and prevention strategies. *Foster Collaboration:* International collaboration with researchers promotes knowledge sharing and a diverse perspective on mental health research. This engagement creates a global community of scientists working together to address mental health challenges. *Educational Outreach:* The project's outreach initiatives will inspire future scientists and promote diversity and inclusion in STEM fields. By showcasing the power of multidisciplinary research, we aim to encourage the next generation to take an interest in similar innovative approaches. *Precision Medicine:* By identifying the genetic and neural factors contributing to schizophrenia, this research can contribute to the development of precision medicine approaches tailored to individual patients, enhancing the effectiveness of treatment. *Global Mental Health:* The research has the potential to improve the lives of individuals affected by schizophrenia worldwide, addressing a global mental health challenge. Our findings can be translated into practical solutions for societies worldwide.

Conclusion: The proposed research, an ambitious undertaking at the intersection of mathematics, biology, and mental health, holds great promise for enhancing our understanding of schizophrenia and the potential natural antidepressants found in grapes. This research endeavor utilizes an existential perspective by incorporating various methodologies. Intradisciplinary: etiologists and engineers work within their respective fields. Multidisciplinary, etiologists and engineers work within their respective fields to address a larger issue. Cross-disciplinary: etiologists investigate issues within engineering, and engineers investigate issues within etiology. Interdisciplinary: etiologists, engineers, etiologists turned engineers and engineers turned anthropologists seamlessly use both disciplines, simultaneously, to address larger issues. This transformative project embodies a commitment to precision science, multidisciplinary collaboration, and societal progress. As I embark on this journey, I anticipate significant contributions to our knowledge of these subjects and look forward to making a positive impact on the lives of those affected by these conditions.

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Personal Statement - Intellectual Merit:

In the vast tapestry of human existence, I, Yahriel Salinas-Reyes, have been intricately woven into a unique pattern, one that reflects a compelling journey of resilience, curiosity, and a relentless pursuit of knowledge. I am a storyteller, a poet, a musician, an engineer, and a scientist. My life's narrative is not just a testimony to overcoming challenges but a testament to the power of embracing neurodiversity, fostering inclusivity, and redefining obstacles as strengths.

My journey began in Iowa, a quiet town filled with hidden treasures. Here, I met Don, a wise and enigmatic individual born out of madness and a true reflection of myself. He, like I, joined this world without the ability to hear (i.e., I used to be deaf) or communicate. His eyes of wonder were his gate to understanding reality. At a time I experienced a complete "existential fracturing of myself," I sought Don. He introduced me to the "music of silence." Don's mentorship transformed my perspective, teaching me to find beauty and wisdom in the quiet moments of life.

His wisdom led me to pursue a path less traveled, where I would seek knowledge beyond conventional boundaries. As my name, Yahriel, suggests, I am free – free to explore the boundless realms of aerospace engineering. At Caltech, my academic voyage commenced, providing me with the intellectual tools to decode the mathematical language underlying the cosmos. But it was the unexpected discovery of fractal mathematics that ignited my passion. Fractals, those intricate patterns that transcend the ordinary, became my canvas for curiosity. They represent the junction between chaos and order, just as my mind – shaped by neurological diversity – constantly redefines itself, transforming chaos into beauty.

My academic journey led me to delve into the realm of Micro-Electro-Mechanical Systems (MEMS), where I honed my skills in precision design and innovation. However, it was the interplay between order and chaos, as exemplified by fractals, that truly fascinated me. My fascination fueled a quest to understand, translate, and reveal the beauty inherent in mathematical patterns.

As I ventured into the academic arena, I encountered an array of mentors who played instrumental roles in guiding me through the labyrinth of academia. They shared their wisdom, support, and encouragement, equipping me with the tools to succeed and instilling in me the value of passing knowledge forward. Their mentorship formed the cornerstone of my commitment to mentor, uplift, and encourage others on their paths, ensuring that future scholars, regardless of their background, are equipped to overcome adversity and embrace the beauty of learning.

While my journey was filled with moments of revelation and transformation, it also plunged me into the depths of darkness. Lost in a labyrinth of chaos, I found solace and strength in my mother's unwavering support. Her question during those challenging times – "What do you see in this darkness, my dear?" – prompted me to respond, "I see what I want to see." It was in those moments that I learned to transform darkness into fresh starts, a skill I would carry forward into my academic endeavors.

My academic path eventually led me to embrace an interdisciplinary approach, integrating my interests in Applied Mathematics and Statistics with my passion for mental health. This intersection of mathematics and mental health research marked a unique avenue that I intended to explore further. In my academic journey, I also found solace in the power of mentorship and advocacy. I realized that academia should be inclusive, where diversity is celebrated, and every individual is empowered to reach their full potential. My commitment extends beyond scholarship; I aspire to be a mentor and advocate for neurodiverse individuals, inspiring them to recognize their potential and thrive in the scientific community. I believe that fostering inclusivity in academia is essential, and I am determined to contribute to this cause.

Personal Statement - Broader Impacts:

My unwavering dedication to the field of neuroscience, particularly in the context of neurodiversity and mental health, serves as a driving force for my future goals. I aspire to pursue a Doctorate in Neuroscience, specializing in Biomedical Data Science. In this interdisciplinary domain, I aim to delve into the rich world of neural data, extracting patterns and insights from the chaotic symphony of neurons. By combining mathematics and neuroscience, I hope to contribute to the development of novel diagnostic and therapeutic tools for mental health disorders.

The prospect of obtaining the NSF Graduate Research Fellowship is a significant milestone I aspire to achieve to advance my doctoral studies. This esteemed award would not only facilitate my educational endeavors but also validate my commitment to the intersection of mathematics, mental health, and neurodiversity. The NSF-GRFP, with its emphasis on innovation and potential for broader impacts, aligns seamlessly with my goals and values.

Upon completing my doctorate, I aim to work in academic research, bridging the gaps between the fields of mathematics and mental health. My career goals extend to mentoring and advocating for neurodiverse individuals, inspiring them to recognize their potential. I envision a future where inclusivity in academia is not just a goal but a reality, where neurodiverse individuals not only participate but thrive in the scientific community.

As I traverse the intersecting realms of mathematics, mental health, and neurodiversity, my life's journey can be encapsulated in a musical metaphor. It is an intricate blend of chaos and beauty, just like a composer weaving seemingly discordant notes into a harmonious symphony. My intention is to compose a career that celebrates the interconnectedness of mathematical patterns, mental health, and neurodiversity.

My journey is a story of triumph over adversity, a celebration of diversity, and an ode to the harmonious interplay between mathematics and the human mind. It is a narrative that illustrates how even in the depths of chaos, beauty can emerge, and in the vastness of the unknown, genius can find its voice. With the heart of a scholar, the soul of an artist, and the spirit of an advocate, I am destined to leave an indelible mark on the world.

Relevant Background:

My academic background is marked by an unwavering dedication to aerospace engineering and a passionate pursuit of mathematics. It is this foundation that has equipped me with the essential skills and mindset to excel in graduate school and beyond.

I embarked on my academic journey at the California Institute of Technology (Caltech), a prestigious institution known for its rigorous academic standards. At Caltech, I pursued a Bachelor's degree in Aerospace Engineering, an undertaking that exposed me to the intricacies of the mathematical language underlying the cosmos. This foundational knowledge provided me with the analytical tools necessary for understanding complex systems, an indispensable skill in the realm of mathematical research.

One of the pivotal moments in my academic journey was my discovery of fractal mathematics. Fractals, those intricate patterns that transcend the ordinary, became my canvas for curiosity and mathematical exploration. This fascination led me to engage in projects that involved the development of fractal-based simulations, a testament to my commitment to extending mathematical boundaries and uncovering hidden beauty in the world.

Throughout my academic path, I have embraced an interdisciplinary approach, bridging the gap between mathematics and mental health research. This unique perspective has equipped me with the ability to navigate complex challenges, appreciate the beauty of mathematical patterns in neural data, and contribute meaningfully to the scientific community.

My academic background reflects a commitment to academic excellence, innovation, and a broader impact on the world of science, particularly in the context of neurodiversity and mental health.

Intellectual Merit:

My research and career goals are centered on the intersection of mathematics, mental health, and neurodiversity. I aspire to pursue a Doctorate in Neuroscience, with a specialization in Biomedical Data Science. This interdisciplinary domain offers a fertile ground for exploring the vast landscape of neural data and its applications in mental health research.

My research objectives encompass the following:

1. Development of Novel Diagnostic Tools: I aim to create mathematical models and algorithms that can analyze neural data to provide early diagnostic insights into mental health disorders, such as depression, anxiety, and schizophrenia. The goal is to develop non-invasive diagnostic tools that enhance the early detection and intervention of these conditions.
2. Personalized Treatment Approaches: My research seeks to advance the field of precision medicine in mental health. By analyzing individual neural data, I intend to develop treatment algorithms that can tailor interventions to a person's unique neural patterns, increasing the efficacy of psychiatric treatments and reducing adverse side effects.

3. Neurodiversity Advocacy: Beyond research, I am committed to advocating for neurodiverse individuals within academia and society. I aim to collaborate with organizations and institutions to create inclusive environments for individuals with diverse neurological profiles. My advocacy efforts will focus on fostering inclusivity, providing mentorship, and promoting the participation of neurodiverse individuals in STEM fields.

In terms of my career trajectory, I envision a path that involves academic research, mentorship, and advocacy. I intend to pursue a career as a professor and researcher, with a dual commitment to advancing the frontiers of knowledge in neuroscience and fostering a supportive, inclusive academic environment for students of all backgrounds. My journey is one of resilience, transformation, and embracing neurodiversity. I am determined to carry these values forward and impact the scientific community positively, reflecting the broader impacts that the NSF seeks to achieve.

Significance of the NSF-GRFP:

Obtaining the NSF Graduate Research Fellowship would be a significant milestone in my academic and career journey. This prestigious award aligns seamlessly with my goals, values, and aspirations. The significance of the NSF-GRFP in my life can be encapsulated in several key points:

Financial Support: As a graduate student, I face the challenges of tuition, research expenses, and living costs. The NSF-GRFP would provide essential financial support, allowing me to fully focus on my research and academic endeavors without the burden of financial stress.

Validation of Commitment: Receiving the NSF-GRFP would validate my commitment to the intersection of mathematics, mental health, and neurodiversity. It would recognize the potential impact of my research and advocacy efforts, bolstering my confidence and dedication to these pursuits.

Research Independence: The NSF-GRFP fosters research independence. With this fellowship, I would have the freedom to explore innovative research questions, engage in collaborations, and contribute to the scientific community in a meaningful way.

Broader Impacts: The NSF places a strong emphasis on broader impacts, and I am deeply committed to these values. Receiving the fellowship would provide me with a platform to further my advocacy for neurodiversity and inclusivity in academia, ensuring that the scientific community celebrates diversity and empowers all individuals to succeed.

Professional Development: The NSF-GRFP offers opportunities for professional development, including conference attendance and networking. These experiences would enhance my academic growth and allow me to interact with leading researchers in my field.

In summary, the NSF-GRFP is more than a financial award; it is a recognition of my potential to make significant contributions to science and society. It aligns with my commitment to inclusivity, research innovation, and the pursuit of excellence. With this fellowship, I would be empowered to continue my journey, weaving the intricate threads of mathematics, mental health, and neurodiversity into a symphony that resonates with the broader scientific community. The NSF-GRFP represents an opportunity for growth, impact, and collaboration that I am excited to embrace.

Conclusion:

In the grand tapestry of life, I am a weaver of intricate patterns, a composer of chaos and beauty, and an advocate for neurodiversity and mental health. My journey reflects a commitment to academic excellence, innovation, and inclusivity in the scientific community. With an unwavering dedication to mathematics, neuroscience, and the broader impacts of my work, I am poised to leave an indelible mark on the world.

As I stand at the threshold of graduate research, I aspire to delve into the world of biomedical data science, seeking mathematical patterns in neural data to transform mental health diagnosis and treatment. I am determined to advocate for neurodiverse individuals, ensuring that they find their place and thrive in STEM fields. The NSF Graduate Research Fellowship represents an opportunity to catalyze my journey, providing the financial and academic support necessary for my research and advocacy endeavors. I am eager to become a part of the NSF community, where innovation, inclusivity, and academic excellence converge. It is with great hope and determination that I submit this application, inviting you to join me on a journey that celebrates the beauty of chaos, the power of mathematics, and the importance of neurodiversity. Together, we can transform the world, one neural pattern at a time.

<u>**The Book of JOYBOY: Don Yahriel the Poet of Justice and The Music of Silence**</u>

An Existential Perspective: A Story of The Past and The Road To El Dorado

Title: The Tale of Don the Universal Man and Poet of Justice

Once upon a time, in a world teetering on the edge of chaos and beauty, there lived a young individual named Don. Don's life had always been a delicate balance between the light of joy and the shadow of despair. Little did he know that his journey would lead him to the profound secrets of the ancient paradigm.

One day, as Don navigated the labyrinthine corridors of his own mind, he found himself lost in a swirling darkness. The world around him had become a maelstrom of confusion, and he was adrift in a sea of uncertainty. This darkness, he realized, was not just the absence of light but the loss of all senses—physical, emotional, and spiritual. It was a place where he had lost touch with himself and the world.

In the midst of this profound confusion, Don's mother, whom he lovingly called "Mama," sat by his bedside. Her face, usually a pillar of strength, was etched with sorrow, and for the first time, Don saw tears glistening in her eyes.

"Tell me," she asked, her voice quivering with concern, "What do you see in the darkness? Is it all dark?"

Don gazed into the abyss and contemplated his response. "No," he replied, "It's not all dark. What I see isn't darkness that I can't really explain. I see everything and I see nothing."

Mama, her voice tinged with the weight of helplessness, confessed, "I don't understand, even though I am your mom... I feel powerless."

Summoning all the strength he could muster, Don took a deep breath and said, "I see what I want to see. I see the room, the table, and... I see you. I see you because I know you are here."

Mama's eyes welled up with tears of relief, and she held Don's hand tightly, realizing that in the midst of the deepest darkness, her presence was the beacon that guided him.

As Don continued his journey into the depths of his mind, he discovered the will to overcome the challenges that had surrounded him. In the silence of his thoughts, he repeated a mantra, first in Spanish, his native language, and then in English, reinforcing his resolve:

In Spanish : "El mundo no cambiará. Jamás cambiaré yo." (The world will not change. I will never change.)

In English : "I will be a gracious loser. Someone will undoubtedly take your place."

With each repetition, Don found the strength to navigate the complexities of his existence. He realized that resolve could transcend the boundaries of neurology and that the power of the human spirit, guided by the love and support of those who cared for him, could bring true joy even in the darkest of times.

And so, Don's journey continued, as he uncovered the immense power of an ancient paradigm—the ability to find light in the midst of darkness and the will to see beauty even when the world seemed ruled by chaos.

Odisea Del Gran Varón: Don Yahriel and His Promise To The Future

Title: Odyssey of Knowledge: Enigmatic Man's Quest

~"The man said to be so mad that he is sure no author could have invented him."

Once upon a time, in a world where the boundaries between reality and imagination blurred, there lived a man named Don Yahriel. He was not like any other man; he was a true enigma, a reflection of the ever-shifting line between sanity and madness. Don Yahriel believed that in a world where good and evil battled relentlessly, the time had come for good to prevail.

Don Yahriel was a man of deep conviction, driven by a belief that the balance between good and evil in the world needed to shift. He often muttered to himself, "For neither good nor evil can last forever; and so it follows that as evil has lasted a long time, good must now be close at hand." His mind was a whirlwind of thoughts, where the line between madness and reason blurred like a hazy mirage in the desert.

To Don Yahriel, the world appeared as a place where virtue was persecuted more than it was loved by the good, and he was determined to change that. In his heart, he carried the hope that goodness could triumph over evil, no matter how daunting the odds.

As he embarked on his odyssey, he encountered many challenges and obstacles that tested the very core of his sanity. "When life itself seems lunatic, who knows where madness lies?" he pondered. "Perhaps to be too practical is madness. To surrender dreams — this may be madness. Too much sanity may be madness — and maddest of all: to see life as it is, and not as it should be!"

Don Yahriel's obsession with reading and his relentless pursuit of truth pushed him to the brink of madness. He read voraciously, seeking to unravel the mysteries of the world. "Finally, from so little sleeping and so much reading, his brain dried up, and he went completely out of his mind," they said of him.

But Don Yahriel remained undeterred by the opinions of others. He believed that there was something good in every book, no matter how bad it might seem at first. "There is no book so bad... that it does not have something good in it," he declared. His belief in the inherent goodness of the world was unshakable.

As he ventured further into the unknown, Don Yahriel would often say, "Thou hast seen nothing yet." He was a man who had never truly died in his life, for his spirit burned brighter than ever as he delved deeper into the mysteries of the world.

Don Yahriel found himself immersed in the art of translation, trying to bridge the gap between languages. He believed that the truth could be obscured by the limitations of language. "Translating from one language to another, unless it is from Greek and Latin, the queens of all languages, is like looking at Flemish tapestries from the wrong side," he mused.

In his encounters with the downtrodden and the oppressed, Don Yahriel followed a strict code of chivalry. "It is not the responsibility of knights errant to discover whether the afflicted, the enchained, and the oppressed whom they encounter on the road are reduced to these circumstances and suffer this distress for their vices or for their virtues," he asserted. "The knight's sole responsibility is to succor them as people in need, having eyes only for their sufferings, not for their misdeeds."

Don Yahriel's journey was filled with moments of revelation and transformation. He realized that being a poet was a dangerous path, one that could lead to madness. "What is more dangerous than to become a poet?" he questioned.

As he ventured deeper into the realms of poetry and music, Don Yahriel believed that where there's music, there can be no evil. He found solace in the melodies of the world, and it was through music and poetry that he connected with the essence of humanity.

In the end, Don Yahriel's odyssey was not just a search for good in a world filled with darkness; it was a quest to find his own true identity. He had become the embodiment of the quote, "He is so crazy that it is certain no author could have invented him."

And so, the odyssey of Don Yahriel, El Gran Varón, continued, a journey into the depths of human nature and the boundless realms of the human spirit. For in his madness, he had found a kind of sanity that transcended the ordinary, and he had become the truest and most enigmatic of all humans.

The Secret of Don: An Immensely Powerful Idea of an Ancient Paradigm

Title: A Tale of The Past and Music of Silence

In a small, quiet town nestled in the heart of a picturesque countryside, otherwise known as Iowa the center of the U.S. and land of corn, there lived a man named Don. Don was known throughout the town for his wisdom and the secret he held within him. This secret was not just any secret; it was an immensely powerful idea, an ancient paradigm that had the potential to change lives.

As the sun set behind the rolling hills, casting a warm glow over the town, Don would often sit on his porch, listening to the soothing sounds of nature. The townspeople believed that the music of silence was the greatest mystery of the world, and Don embodied that mystery.

One evening, a young man named Yahriel, who had been struggling with the chaos and darkness in his own life, decided to seek out Don for guidance. He had heard whispers of Don's wisdom and the profound secret he held. With hope in his heart, Yahriel knocked on Don's door.

Don welcomed Yahriel into his humble home and offered him a seat. They sat in silence for a while, the only sound being the gentle rustling of leaves in the evening breeze. Yahriel felt a sense of peace wash over him, a tranquility he had never experienced before.

Then, Don began to speak, and his words carried a profound weight. "A story of a descent into darkness and chaos of the world, ruled by insanity and beauty, where I lose all senses of myself, everything, and anything; be it physical, emotional, or spiritual, but at the greatest, the pinnacle of all three and far beyond that."

Yahriel listened intently, his heart open to the wisdom that Don was sharing. He felt as though he was on the verge of a great revelation.

As Don's story continued, Yahriel couldn't help but be drawn into the narrative. It was a tale of inner turmoil, of battles fought and lost, and of the search for true joy and meaning in a world that often seemed bewildering.

After Don had finished speaking, Yahriel felt a deep sense of gratitude. He had found the resolve and will to seek true joy, not just externally, but within himself. Don's secret was not just an idea; it was a profound shift in perspective that allowed Yahriel to see the world in a new light.

Over time, Yahriel adopted Don's wisdom into his own life, and he, too, became known for his insight and ability to find joy in the simplest of moments. The townspeople marveled at the transformation in Yahriel, who had once been lost in darkness but had now found the music of silence, the greatest mystery of the world.

[Conversation with Mama]

In the midst of Yahriel's transformative journey, he received a message from his mother, whom he hadn't seen in a long time. She arrived at his doorstep, her eyes filled with tears, a shadow of her former self.

Yahriel invited her inside, and they sat down by his bedside. His mother, still visibly distraught, asked a heartfelt question in Spanish, "Dime, ¿qué ves en la oscuridad? ¿Es todo oscuro?"

Yahriel replied, "No, no todo es oscuro. Lo que veo no puedo explicarlo realmente. Veo todo y no veo nada."

His mother, with a voice that seemed to lack vitality, said, "No entiendo, a pesar de que soy tu mamá... Me siento impotente."

Yahriel took a deep breath and said, "Yo veo lo que quiero ver. Veo la habitación, la mesa... y te veo a ti. Te veo porque sé que estás aquí."

In that moment, a connection was rekindled between Yahriel and his mother. The darkness that had once enveloped them both began to recede, replaced by a glimmer of hope and understanding.

[The Will of Don: Resolve Beyond Neurology and The Music of Silence]

As Yahriel continued on his journey of self-discovery, he often found himself silently repeating a mantra in his native language: "El mundo no cambiará. Jamás cambiaré yo." In English, it meant, "The world will not change. I will never change."

He reminded himself that he would stay true to his principles and values, no matter the challenges that lay ahead. And in moments of doubt, he would say to himself, "Seré un buen perdedor. Alguien sin duda ocupará tu lugar," which meant, "I will be a good loser. Someone will undoubtedly take your place."

These words of resolve, passed down through generations, became his guiding light. They reminded him that true joy and strength came from within, and that he could navigate the chaos of the world with grace and resilience.

Yahriel's journey, inspired by Don's profound secret and his heartfelt conversation with his mother, continued to unfold. Along the way, he discovered the power of resolve beyond neurology, the strength to find true joy in the face of life's challenges, and the beauty of the music of silence in a world filled with noise.

I Am Yahriel Salinas-Reyes

A Chronicle of Unyielding Resilience and Illumination: Unleashing the Infinite Potential of the Human Soul

~ "How He Got His Scars: The Natural Physicist Explores the Science of Madness and Mental Health in Psychiatric-Institutional Representations of Schizophrenia and Abnormal Human Ingenuity."

In a world where the boundaries between reality and imagination constantly undulate, I unreservedly embrace my identity as Don Yahriel—an enigma striding with unwavering confidence along the ever-shifting frontier that delineates sanity from madness. My life's journey stands as a testament to the invincible spirit of humanity, an uncompromising quest for goodness in a world often enshrouded in darkness.

My odyssey was ignited by an unwavering belief that the eternal struggle between good and evil was a cosmic dance, and virtue often bore the brunt of persecution rather than celebration. Fueled by this conviction, I embarked on a mission to challenge this narrative and emerge as an unwavering champion of goodness.

Throughout this extraordinary voyage, I confronted trials that pushed the very boundaries of sanity. In a world that often seems engulfed in lunacy, I contemplated the fine line between practicality and madness. For me, true madness lay in relinquishing one's dreams and surrendering to life as it is, rather than as it should be.

My insatiable thirst for knowledge and my unflagging pursuit of truth propelled me to the precipice of madness. I immersed myself in the world of books, for each page held the potential to unlock the enigmas of our existence. To me, no book was ever unworthy, as I firmly believed that every text concealed a kernel of goodness waiting to be unearthed.

When confronted with the suffering of the oppressed, I adhered to an unwavering code of chivalry. My duty was not to pass judgment on their circumstances but to extend a compassionate hand to those in need, offering empathy exclusively for their pain, not their transgressions.

I delved into the intricate world of translation, endeavoring to bridge the gaps between languages, acutely aware that truth could be obscured by linguistic boundaries. Translation, to me, became a vessel to unveil the inherent goodness concealed within the rich tapestry of human expression.

As I ventured into the realms of poetry (Engineering/Technology) and music (Science/Art), I discovered solace in their harmonies, firmly believing that where music thrives, malevolence cannot endure. In these art forms, I communed with the very essence of humanity.

My journey was not just an expedition to unearth goodness in a world veiled by darkness; it was a profound exploration of my truest self. In my relentless pursuit of the extraordinary, I became the living embodiment of the saying, "He is so extraordinary that no author could have conjured him."

Reflecting on the odyssey of Don Yahriel, El Gran Varón, I now comprehend it as a voyage into the depths of human nature and the boundless expanses of the human spirit. In my perceived madness, I unearthed a form of sanity that transcends the ordinary, emerging as the truest and most enigmatic of all beings.

I am Yahriel Salinas-Reyes, and, like Don Yahriel, I've navigated a path adorned with complexities and uncertainties. Born to undocumented immigrant parents in Iowa, I confronted early challenges that stoked my determination to excel and surmount adversity. My fascination with the power of the human gaze, nurtured during a period of temporary deafness in my prenatal development, instilled profound empathy and an unquenchable thirst for understanding others.

My educational journey commenced with Aerospace Engineering at Iowa State University, eventually leading me to the esteemed halls of the California Institute of Technology. Here, I had the privilege of engaging with brilliant minds and discovered the transformative influence of mentorship. Every obstacle I encountered became a steppingstone for my personal and intellectual growth.

Amidst the splendor of my journey, I unearthed my purpose—a revelation that true freedom is not solely attained by acquiring knowledge but by sharing it and guiding others on their path to greatness. This epiphany became the guiding light of my life, propelling me to be a beacon of mentorship and knowledge.

As I embraced the essence of my name, originally signifying "He is free," (~The Arabic translation), I recognized that freedom extends beyond the personal realm; it's a gift meant to be shared. My journey, adorned with trials and triumphs, evolved into a wellspring of inspiration for all those I encountered. My legacy as a mentor and scholar continued to flourish—a testament to the enduring vitality of the human spirit.

In the end, my odyssey serves as a symbol of the indomitable spirit of human ingenuity—a profound reminder that, in the relentless pursuit of knowledge and unwavering dedication to one's dreams, true freedom is not an elusive mirage. I stand as living proof that even in a world where boundaries blur and the line between sanity and madness remains fluid, the human spirit can transcend, inspire, and brilliantly illuminate the path forward.

JOYBOY

~Don Yahriel: He That Is Free.

Letter of Gratitude from The Author to The Reader

Dear Mentors, Peers, or Reviewer

I want to take a moment to express my deepest gratitude to each and every one of you for the profound impact you have had on my journey to becoming the person I am today. Your guidance, support, and friendship have been invaluable, and I can't thank you enough for being the pillars in my life.

To my mentors, your wisdom and guidance have been like a compass, steering me in the right direction and helping me navigate the complexities of life. Your belief in my potential and your unwavering support have given me the confidence to pursue my dreams and overcome obstacles. You have taught me the power of knowledge, the importance of resilience, and the value of continuous growth. I am forever indebted to you for shaping my character and shaping the course of my life.

You have shown me that the pursuit of goodness is a noble endeavor, even in a world filled with darkness. Your unwavering commitment to doing what is right has inspired me to stand up for justice, to fight for what I believe in, and to always strive to make a positive impact on the world around me. Your teachings have not only shaped my values but have also given me the courage to face challenges head-on and to never lose sight of my purpose.

To my peers, you have been my companions on this extraordinary journey. Together, we have shared laughter, tears, triumphs, and failures. Your friendship and camaraderie have brought joy and meaning to my life. Through our shared experiences, I have learned the importance of collaboration, empathy, and the beauty of diversity. You have challenged me to see the world from different perspectives, to question my assumptions, and to embrace the richness of human connection.

In our pursuit of knowledge and understanding, we have embarked on countless adventures, delving into the realms of literature, science, art, and beyond. Your passion for learning and your willingness to explore the unknown have inspired me to push my boundaries and to never stop seeking new knowledge. Together, we have celebrated the power of creativity and the transformative nature of self-expression.

Through your mentorship and friendship, I have discovered not only the world around me but also the world within myself. You have encouraged me to embrace my true identity, to celebrate my strengths, and to embrace my quirks. Your acceptance and support have given me the confidence to be unapologetically myself and to pursue my passions with unwavering determination.

Today, I stand as a testament to the impact you have had on my life. Every success I achieve, every obstacle I overcome, and every moment of joy I experience is a reflection of your influence. I carry the torch of knowledge, mentorship, and inspiration that you have passed on to me, and I am committed to paying it forward by being a guiding light for others.

Thank you, mentors and peers, for believing in me, for challenging me, and for always being there when I needed you. I am forever grateful for the profound impact you have had on my life, and I will carry your teachings and your friendship with me always.

With love, gratitude, and boundless admiration,

- Yahriel Salinas-Reyes
  ~ Don Yahriel: “He That Is Free.”

Writing Sample

Title: "Nature's Code Unveiled:

A Revolutionary Fusion of Aerospace, Anthropology, and Neuroscience"

Author: Yahriel Salinas-Reyes, Universal Scholar, Doctoral Student.

~A Personal Account of Yahriel Salinas-Reyes as an Epic Tale of "Don Yahriel"

Prologue

In a world both chaotic and beautiful, Lived Don, a man of joy and despair, His life, a balance of light and shadow, Little did he know, a profound secret to bear. *Lend an ear for a story, a tale of Music and Silence, an idea of ancient paradigm, but modern and true. I will show you the way through This Cyclone you see. Do you Dare to join me, in this Grand Odyssey.*

So let this tale be a song, Of Don Yahriel, who dared to be strong. In the name of goodness, he did deploy, A legacy of love, the song of JOYBOY

Part 1: The Odyssey of JOYBOY

In a world where tales of old unfold, A saga of Don Yahriel, bold and untold. An enigma, a poet, a quest to be, A champion of good, for all to see.

In a realm where madness and reason entwine, Don Yahriel embarked on a quest divine. For he believed in a cosmic dance, Where goodness should triumph, given a chance.

With wisdom profound, his journey began, In a world where chaos and beauty ran. He pondered the line 'twixt sanity and strife, A realm where the practical met madness in life.

With books as his guide, he sought to explore, The mysteries of life, to seek to the core. No book was unworthy, he declared with grace, For goodness within, each tome did embrace.

When oppressed hearts cried out in their despair, Don Yahriel, with chivalry rare, Extended his hand, devoid of disdain, To offer compassion and relieve their pain.

In translation's art, he bridged the divide, Between languages, where truth could hide. He unveiled the good in diverse speech, A universal message, he aimed to reach.

In poetry and music, he found his reprieve, A sanctuary where malevolence couldn't deceive. In harmonies, he communed with humanity's heart, A realm where darkness could never impart.

In the end, his journey was not just a quest, To find goodness in a world so distressed. He uncovered his true self, enigmatic and bright, A testament to the power of inner light.

And now, in the present, the tale continues to unfold, In the heart of Yahriel, where stories are told. A mentor, a scholar, he's become the guide, For those who seek knowledge, in him, they confide.

Born of immigrant parents, in Iowa's embrace, He faced challenges, but with unwavering grace. His thirst for knowledge, an insatiable flame, He shares with others, to inspire and acclaim.

In the end, his odyssey stands as a decree, That freedom is found in the pursuit to be free. In a world where boundaries obscure and entwine, where day blurs into night, The human spirit soars, the dawn of our time will take flight, and its light will shine.

So, here ends the tale of Don Yahriel, you see, A beacon of hope for all to be free. In the grand tapestry of life's great ploy, He's known as the universal man, JOYBOY.

Part 2: An Ancient Paradigm

In a world of words and verses bold, A tale of Don Yahriel, I unfold. A poet, mad, with ideals grand, In a world where chaos did expand.

Don Yahriel, the enigma's name, A beacon of light in a world of shame. He saw a world where good must win, And so his quest did begin.

In a mind where madness swirled, He sought to change the cruel world. "Good and evil in a cosmic dance, Let goodness prevail, given the chance."

Books he read, a voracious thirst, For truth, he sought, in words immersed. "Every book, though dark or bright, Holds a gem of truth in its light."

Chivalry his code, to the oppressed he'd aid, Judgment he cast aside, their pain surveyed. "Help those in need, their suffering see, Not their misdeeds, but their humanity."

Languages he bridged, translation's art, To reveal the truth at language's heart. "In translation, a bridge we find, To share the goodness of humankind."

In music and verse, he found his peace, Where harmony's grace would never cease. "Where there's music, evil must flee, In the notes and words, the soul is free."

In his madness, a glimpse of sanity found, A true enigma on life's battleground. "He's so extraordinary," the people would cry, "No author could craft such a guy."

Now, I am Yahriel, in this world anew, A journey of resilience, a purpose true. Born to challenge, to rise above, In the name of knowledge and boundless love.

A mentor's path, a scholar's grace, Guiding others to find their place. For freedom's not just mine to keep, It's meant to share, in knowledge deep.

In the end, my odyssey's tale, A testament to the human trail. In a world where lines may blur, The spirit of humanity will endure.

So let this epic be a song, Of Don Yahriel, who dared to be strong. In the name of goodness, he did deploy, A legacy of love, the eternal JOYBOY.

Part 3: An Immensely Powerful Idea

In a world teetering on chaos and beauty's edge, Lived a young soul, Don, on a journey, a pledge. Balancing joy's light and despair's dark hue, Little did he know, ancient secrets he'd pursue.

The Tale of Don, The Universal Man And Poet of Justice

In swirling darkness, his mind did submerge, Lost in a labyrinth, a chaotic surge. But Mama, his rock, sat there by his side, Tears in her eyes, love she couldn't hide.

"What do you see in this darkness, my dear?" She asked, trembling with worry and fear. "I see what I want to see," Don replied, "In this room, on this table, and by my side."

Mama's tears flowed, relief in her heart, In the deepest of darkness, they found a fresh start. Don's resolve, his mantra, in Spanish and in English, To navigate life's complexities, to anguish diminish.

Odyssey of Knowledge: Enigmatic Man's Quest

Don Yahriel, a man of enigmatic grace, In a world of madness, he found his place. Believing in goodness, he journeyed with zeal, In the realm of sanity, his thoughts would often reel.

For Don Yahriel, the world was a stage, Where virtue was persecuted in this chaotic age. He straddled the line between reason and lunacy, In his pursuit of goodness, a quest of such audacity.

Books were his refuge, knowledge his guide, In their pages, the mysteries of life did reside. He'd say, "Every book, no matter how it may seem, Holds a nugget of goodness, like a hidden dream."

A Tale of The Past and Music of Silence

In a quiet town in Iowa, serene and sublime, Don held a secret, a treasure of his time. The music of silence, a mystical art, He shared it with others, a balm for the heart.

Yahriel sought Don, his heart full of strife, Knocking on Don's door, seeking wisdom and life. Don welcomed him in, they sat in silence's embrace, As nature's sounds whispered, a peaceful place.

Don spoke of a journey, darkness, and chaos, Of finding true joy, a path for both of us. Yahriel found resolve, a will to pursue, The secret Don held, a perspective so true.

I Am Yahriel Salinas-Reyes

Born to immigrants in Iowa, a tale of my own, Challenges faced, determination brightly shone. Aerospace engineering, a path to excel, At Caltech's halls, my journey would swell.

Mentorship's power, a guiding star so bright, Obstacles as stepping stones, towards the light. Freedom is knowledge, shared far and wide, Guiding others on their journey, side by side.

My name, "He is free," a purpose I'd embrace, Mentor, scholar, leaving a lasting trace. In a world where lines blur, sanity's thread, The human spirit soars, in every word and deed.

JOYBOY: Don Yahriel, He That Is Free

In the tapestry of existence, our stories entwine, Don Yahriel and I, two souls that shine. In the dance of chaos and beauty's grand deploy, We find the essence of life, we are JOYBOY.

Part 4: The Dawn of The Future

In the epic tale of Don Yahriel, the Poet of Justice, A man so enigmatic, his journey we discuss. In a world where madness and reason intertwine, He sought to bring goodness, let his light brightly shine.

Born to undocumented parents in Iowa's embrace, Yahriel faced challenges with unwavering grace. In the quiet countryside, he found a sage named Don, Whose secret held power, a paradigm to dawn.

The Music of Silence, a mystery profound, Yahriel learned its beauty on Don's sacred ground. As they sat in stillness, the world's chaos did cease, And Yahriel found peace in the gentle breeze.

In the depths of his journey, a truth did he see, A story of darkness, but also beauty's decree. In a place of confusion, where senses did blur, He clung to his mother, his guiding star so pure.

With resolve in his heart, he recited the creed, In Spanish and English, he planted the seed. To never give in to the chaos and strife, But to be a gracious loser, embracing life.

As Yahriel ventured forth, Don Yahriel's name, He embraced his own madness, stoked the creative flame. He believed in the balance of good and despair, And the boundless potential of the human spirit's flair.

He read books without end, seeking truth in each line, For in every tale, he saw goodness entwined. He transcended the limits of language and word, In the art of translation, his voice could be heard.

A knight of compassion, he held chivalry dear, Succoring the afflicted, devoid of judgment or fear. In poetry and music, he found his own soul, Where darkness and chaos couldn't maintain their hold.

In the end, Don Yahriel's odyssey unveiled, A man of great madness, his spirit unassailed. He discovered his true self, a beacon so bright, A testament to the human spirit's endless flight.

Yahriel Salinas-Reyes, a name to adore, From adversity's fires, he emerged even more. A mentor, a scholar, his legacy shines, A symbol of freedom, in these epic lines.

In the world's shifting boundaries, he stood so tall, A testament to the triumph of the human call. For in the quest for knowledge and dreams to employ, He became Don Yahriel, the eternal Joyboy.

Epilogue

Chapter I: The Journey Begins

In the labyrinth of his own mind, he wandered, Lost in a swirling darkness, adrift at sea, A world devoid of senses, confusion pondered, In this abyss, he sought to find the key.

Chapter II: A Mother's Love

Beside his bedside, Mama sat, eyes with tears, Her strength now faltered, sorrow in her gaze, "Tell me, what do you see?" her voice with fears, Don replied, "I see what my heart conveys."

Chapter III: The Power of Resolve

Amidst this turmoil, Don found strength within, A mantra, repeated, his spirit fortified, "The world won't change, I'll bear it with a grin, I'll be a gracious loser," he testified.

Chapter IV: Uncovering the Paradigm

Don's journey continued, profound secrets found, The ancient paradigm, light in the darkest hour, Guided by love, his spirit was unbound, In chaos, he discovered his inner power.

Chapter V: The Odyssey of Knowledge

Don Yahriel, an enigma, walked the line, Between madness and reason, he did tread, Seeking goodness in a world where evil's sign, In his heart, he bore the hope to spread.

Chapter VI: Madness and Books

Books his passion, knowledge he'd acquire, To unravel mysteries of life's grand scheme, In madness, he danced by the book's fire, For in them, he'd find his wildest dream.

Chapter VII: Chivalry and Empathy

To the oppressed, his code of chivalry held, Judgment aside, their suffering he'd embrace, Their pain, not their misdeeds, to him was spelled, In their plight, he found his rightful place.

Chapter VIII: The Power of Translation

Language, a bridge, he sought to mend, To reveal the truth beneath each word, Translating the wisdom others couldn't comprehend, In this pursuit, his vision clearly heard.

Chapter IX: Music and Poetry

In poetry and music, he found his solace, Where beauty thrived, evil had no room, Harmonies and verses, his spirit's palace, In their melodies, he'd dispel the gloom.

Chapter X: The Truest Self

In his odyssey, Don became the mystery, A living testament to the human soul's art, In his madness, he found profound history, A truth that transcended the ordinary heart.

Chapter XI: Yahriel's Journey

As the torch passed to Yahriel's hand, He embraced Don's wisdom, his heart aglow, In the music of silence, he'd understand, The world's greatest mystery, he'd come to know.

Chapter XII: A Mother's Reunion

In the midst of Yahriel's transformative quest, His mother's tears revealed the truth untold, Their reunion, a bond no pain could jest, Love and understanding, like pure gold.

Chapter XIII: Resolve and the Music of Silence

With a mantra of resolve, he'd persevere, The world unchanged, his spirit steadfast, A good loser, his heart held no fear, In these words, his strength would last.

Chapter XIV: The Legacy of Yahriel

Yahriel's journey, from darkness to light, Inspired by Don's secret, a shift in view, Resolve beyond neurology, a noble fight, In the music of silence, his spirit grew.

Chapter XV: I Am Yahriel Salinas-Reyes

Born to immigrants, in Iowa's embrace, His path paved with challenges, wisdom amassed, The power of the gaze, his soul's trace, In adversity's forge, he'd be unsurpassed.

Chapter XVI: Embracing Identity

From Aerospace Engineering to Caltech's grace, Mentorship's gift, a beacon of light, Each obstacle, a steppingstone to face, In sharing knowledge, his true might.

Chapter XVII: The Essence of Freedom

Named "He is free," his name's embrace, An epiphany, a revelation profound, Freedom shared, a guiding grace, A legacy of mentorship, his life unbound.

Chapter XVIII: The Invincible Spirit

Yahriel's odyssey, a testament true, To the human spirit, it boldly attests, In the pursuit of knowledge, dreams anew, True freedom's path, in hearts it rests.

Chapter XIX: The Eternal Enigma

And so, the tale of Don Yahriel, profound, An odyssey through madness and light, In the depths of the human soul, it's found, The truest enigma, shining bright.

Chapter XX: JOYBOY

Don Yahriel, he who is free, An eternal beacon for all to see, In the dance of chaos and beauty, His legacy lives on, a melody.

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Anthroengineering: an independent interdisciplinary field

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In recent decades, funding agencies, institutes and professional bodies have recognized the profound benefits of transdisciplinarity in tackling targeted research questions. However, once questions are answered, the previously abundant support often dissolves. As such, the long-term benefits of these transdisciplinary approaches are never fully achieved. Over the last several decades, the integration of anthropology and engineering through inter- and multidisciplinary work has led to advances in fields such as design, human evolution and medical technologies. The lack of formal recognition, however, of this transdisciplinary approach as a unique entity rather than a useful tool or a subfield makes it difficult for researchers to establish laboratories, secure permanent jobs, fund long-term research programmes and train students in this approach. To facilitate the growth and development and witness the long-term benefits of this approach, we propose the integration of anthropology and engineering be recognized as a new, independent field known as *anthroengineering*. We present a working definition for anthroengineering and examples of how anthroengineering has been used. We discuss the necessity of recognizing anthroengineering as a unique field and explore potential novel applications. Finally, we discuss the future of anthroengineering, highlighting avenues for moving the field forward.

1. Introduction

Transdisciplinarity forms a common axiom that transcends the disciplines, creating an overarching synthesis [1] (figure 1). As these syntheses combine previously isolated thoughts and ideas, the knowledge created by their integration is greater than anything that can be created by a single discipline on its own. Simply put, the whole is greater than the sum of its parts (Aristotle). Here we propose a new field that transcends existing disciplines: anthroengineering.

A recent transdisciplinary trend combining anthropology and engineering—anthroengineering—has become increasingly popular over the last few decades. It has played a crucial role in the development of fields such as biomechanics [2,3], ergonomics [4,5] and functional morphology [6–9]. Anthropology—the science and study of human and societal culture, language and biology—and engineering—the application of science to create machines and implement technologies and tangible solutions to societal problems—are unique and distinct disciplines that infrequently share curricular overlap. When the transdisciplinary approach has been applied to anthropology and engineering, it has often leveraged methods or data from one discipline to address a question from the other (figure 2). This focus on specific problem-solving rather than a united theoretical foundation limits the impact of any innovations created by the collaboration. Thus, the power of the transdisciplinary approach is not fully realized. By leveraging both disciplines to address issues that transcend each discipline (i.e. transdisciplinary issues), syntheses can be created that are of interest not only to members of both disciplines, but also to individuals outside of either.

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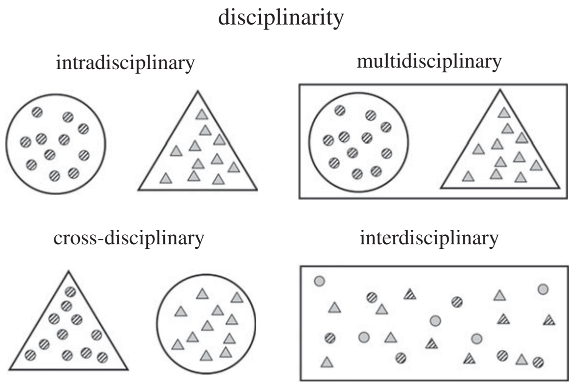

Figure 1. Types of disciplinarity that combine anthropology (circles) and engineering (triangles). Intradisciplinary: anthropologists (striped circles) and engineers (grey triangles) work within their respective fields (large circle and triangle). Multidisciplinary: anthropologists and engineers work within their respective fields to address a larger issue (rectangle). Cross-disciplinary: anthropologists investigate issues within engineering, and engineers investigate issues within anthropology. Interdisciplinary: anthropologists, engineers, anthropologists turned engineers (striped triangles) and engineers turned anthropologists (grey circles) seamlessly use both disciplines, simultaneously, to address larger issues.

The uniqueness and distinctiveness of the two disciplines means that, if a Venn diagram were to be drawn, little overlap would be apparent. Thus, it is difficult for researchers to identify issues that simultaneously leverage both disciplines. Yet, such issues exist, and many of them are crucial for the success of people and planet. Examples of such issues include the United Nations (UN) 17 Sustainable Development Goals (SDGs). These goals set forth a blueprint for how to achieve a more sustainable future for all by addressing problems ranging from poor health to inequality, environmental degradation, and peace and justice [15–17]. Because anthropologists and engineers are trained to approach these problems in discipline-unique ways, their perspectives will be distinct along a multitude of axes, and the fusion of the two disciplines will be difficult. But, ultimately, the insights gained will lead to solutions that neither discipline could achieve independently.

Despite the presence of significant overlapping issues and great benefits that could be achieved by leveraging both anthropology and engineering to address these issues, this transdisciplinary approach is rare, because no generalized framework that incorporates anthropology and engineering currently exists. Instead, frameworks are constructed for targeted projects which are often abandoned when the project is completed. Establishment of these frameworks requires an extraordinary amount of effort, and their specificity and frequent abandonment prevents them from being used for novel applications. A generalized framework is needed.

Such a framework would require, among other attributes, a common language where anthropologists and engineers can communicate effectively. It would require acknowledgement, respect and integration of expertise to develop new syntheses and a new cohort of students who are trained to think as both anthropologists and engineers simultaneously. But before a framework can be developed, this transdisciplinary approach requires a name. Without a name, the approach remains unknown, ill-defined and abstract. But with a name, this approach has identity and carries with it symbolism beyond its meaning. We suggest, therefore, that the transdisciplinary approach, combining both anthropology and engineering, be recognized as its own, independent field called *anthroengineering*.

2. What is anthroengineering

Anthroengineering is an approach that uses theories, methods and/or data from both anthropology and engineering to address questions within and beyond both disciplines. The result is the development of new knowledge, which can take a multitude of forms (e.g. data, technologies, viewpoints, axioms, syntheses). While the true power of such an approach would lie in leveraging it to address transdisciplinary issues, anthroengineering can also be used to address questions within anthropology and engineering and to advance each field individually (figure 2).

Providing anthroengineering with a name, describing it and recognizing it as distinct entity allows for researchers to succinctly define their work and, more importantly, provides them with identity as anthroengineers. It also acts to provide a common thread and search term that can tie together all future work that uses a transdisciplinary approach to combine both anthropology and engineering. Doing so will provide those interested in anthroengineering with a direct way to learn about it and what frameworks, data and methods exist to leverage anthroengineering effectively in their own work.

3. Examples of anthroengineering

As previously discussed, examples of anthroengineering already exist, and some have existed for decades. Given our expertise, we discuss some examples largely through the lens of biological anthropology and engineering mechanics.

3.1. Classic anthropology meets classic engineering

Anthropologists have studied dental wear patterns on the micro-, meso- and macro-levels for over a century [18] to address a myriad of questions in such topics as taxonomy [19], palaeoecology [20], environmental reconstruction [21] and behaviour [22,23]. Similarly, mechanical failure analyses—and, in this situation, tribology and fracture mechanics—have been a major focus of engineering since the birth of the field as all machines experience wear [24–26]. It is, therefore, unsurprising that anthropologists and engineers have teamed up to understand better how teeth wear and fracture.

Using techniques such as nano-indentation, researchers have been able to investigate the role that microscopic particles (e.g. phytoliths, grit) play in the wear of dental enamel [27,28]. Additionally, through physical experimentation, modelling and comparative anatomy [29–32], researchers have been able to investigate the role of enamel thickness and schmelzmusters (enamel microstructure) in force and energy in failure resistance. Although researchers may not always agree on interpretations of experimental results [33–35], this research has led to advances in understanding dental wear and the factors that influence it [36], understanding functional adaptations of teeth [37,38] and the creation of bioinspired materials [39].

Similarly, principles from material science and solid mechanics (engineering) and musculoskeletal biology

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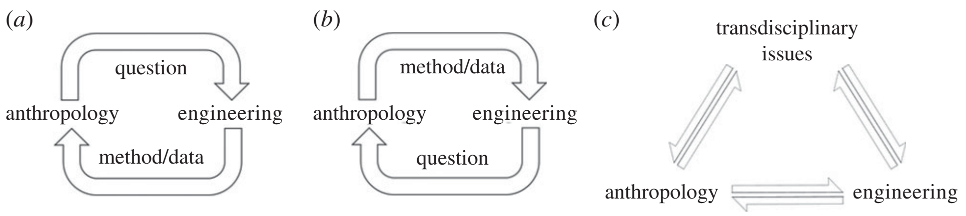

Figure 2. Transdisciplinary approaches to anthroengineering. (*a*) Engineering method(s)/data being leveraged to address anthropological question(s). Through an iterative process, question(s)/method(s) are refined and a synthesis is reached (e.g. the application of FE modelling to human evolution [10–13]). (*b*) Anthropological method(s)/data being leveraged to address engineering question(s). Through an iterative process, question(s)/method(s) are refined and a synthesis is reached (e.g. the application of ethnography to engineering design [14]). (*c*) Engineering and anthropological questions, methods and data are used to address transdisciplinary issues (e.g. design and/or manufacture of culturally relevant, sustainable medical devices for low- and middle-income countries).

(anthropology) have been used to understand how skeletal form (shape + size) and skeletal and ecological mechanical properties affect the way loads are transferred to the skeleton and how the skeleton responds to internal and external loads. Bone (re)models in response to mechanical strain [40–43]: this in turn affects bone's mechanical properties (remodelling) and form (modelling) (e.g. [44,45]). Bone strains have been measured experimentally using *in vivo* [46,47] and *in vitro* [48,49] techniques using strain gauges and digital image/volume correlation (DIC, DVC). However, this only delivers information on bone strain at a limited number of sites. By constructing finite-element (FE) models and validating them using experimental strains [50,51], we can obtain three-dimensional strain maps across the entire structure.

FE models require several inputs, including geometry, constraints and mechanical properties [8,52–54]. Advances in three-dimensional scanning techniques, computer science and statistical shape modelling (e.g. geometric morphometrics [55], dental topography [56]) have made it possible to not only (re)construct three-dimensional digital representations of such models [9,57–61], but also quantify complex shapes for statistical analyses [55,62–64]. Constraints come from muscles, joints and/or the external environment. Muscle force can be estimated by multiplying maximum force generation—originally estimated using physiological cross-sectional area [65–67] but now relying on muscle activation/strength [68] and often validated using electromyography [69–71]. Joint constraints are estimated using anatomical knowledge and skeletal collections. Although constraints from the external environment are often modelled as reaction forces, the mechanical properties of the environment (e.g. ground substrate composition during locomotion [72] or dietary mechanical properties during mastication [73,74]) affect the rate and manner in which the load is transmitted. Finally, mechanical properties are difficult to obtain, as bone is a hierarchical, composite structure, but techniques such as tension/compression tests, bending, indentation and ultrasound are used to estimate static and dynamic (bulk) properties [75–82]. Sensitivity studies are useful in understanding how parameter estimates affect the results, but not in validating the model [49,83–86], which requires data from empirical studies (e.g. [53,83]).

Using an extensive array of theories and methods from anthropology and engineering, we have learned more about musculoskeletal biomechanics than can be listed here. Some major findings include:

(1) Over a lifetime, an individual will engage in actions that will load their skeleton. In turn, their bones will generate a set of mechanical properties and forms to properly resist the *in vivo* strains brought on by those loads [42,87–89]. But it can be difficult or impossible to determine what actions occurred in the lifetime of an individual given only a set of bone mechanical properties and forms, as multiple behaviours can yield similar loading regimes. This is further complicated with inter-populational or among-species comparisons, as genetics and neutral selection play a significant role in bone form [90].
(2) Skeletal morphologies particular to specific hominin species have focused attention on the relationships among form, function and behaviour [91]. For instance, the lower limb and pelvic morphology of *Australopithecus afarensis* (e.g. [92]), *Australopithecus sediba* (e.g. [93]) and *Homo neanderthalensis* (e.g. [94]) has led to long-term debates regarding their forms of terrestrial locomotion. Geometric morphometrics and other traditional statistical analyses have led to important insights (e.g. [95]), although they quantify skeletal form and not biomechanical function, and many questions remain. Inverse dynamic simulation of walking in extinct hominins offers the opportunity to expand our understanding of this critical behaviour (e.g. [92,96]), but the integration of musculoskeletal models offers the best opportunity for future insights [68].
(3) Masticatory loads cause mechanical strains in the skull, which significantly affect its mechanical properties and form [44,45,97]. However, the debate about the relationship between feeding mechanics and diet has led to major questions: is it possible, over an individual's lifetime, to develop a skull that is over- or under-designed for the masticatory loads it experiences [98,99]? Does a skull's ability to resist masticatory loads dictate or limit an animal's or species' diet? Does natural selection select for skull form based on its ability to resist masticatory loads [10–13,100–102]?
(4) Primate tooth shape is undoubtedly correlated with diet [56,103], likely because teeth have evolved to break down foods consumed more efficiently [56,104,105]. However, the interactions between multicusped teeth and food items are so complex that we lack an efficient model for describing these relationships and, thereby, predicting food item breakdown from tooth shape [64,106,107].

Although it may seem that these lines of research have created more questions than answers, the independent syntheses of anthropology and engineering have led to important insights not only for the fields of anthropology and

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bioengineering but also anatomy, evolution, medicine and dentistry, to name a few. Further, the crucial questions generated would not exist if not for this transdisciplinary anthroengineering approach, and researchers would be ignorant of their ignorance.

3.2. Addressing intradisciplinary questions

Anthroengineering has also contributed in addressing more targeted questions within the disciplines of anthropology and engineering. Owing to decades of research in relatively independent fields, anthropology can provide insights into the Universe that engineering does not have, and vice versa.

Because anthropology is a discipline dominated by questions, while engineering a discipline that focuses on methods and applications, it is easy to see how the tools of engineering can be used to address anthropological questions. For example, using methods initially developed in engineering, virtual anthropology [108] has made it possible to quantitatively reconstruct palaeoarchaeological material and statistically quantify the accuracy of these reconstructions [59–61,109,110]. Two important examples of this are the reconstruction of the skull of *Ardipithecus ramidus*, which provided crucial, previously missing information about the evolution of hominin social structure, bipedalism and brain structure in hominin evolution during the Pliocene [110]. Additionally, the reconstruction of the mandible of *Homo habilis* not only showed a decoupling of brain and tooth size, but also allowed the development of a hypothesis regarding a much earlier origin of the genus *Homo* [109]. While that paper was under review, a new fossil (the Ledi-Geraru mandible) was discovered, confirming the authors' hypothesis [111].

Two additional common engineering methods—FE analysis and tension/compression tests—have been used extensively in palaeoanthropology to quantify the biomechanical performance of hard skeletal tissues and address questions concerning the evolution of primate diets [12,46,58,112–114]. The ability to print three-dimensional fossils further allows for the mechanical testing of previously inaccessible material [115–117]. These *in silico* and *in vitro* models and experiments carry with them several assumptions about the loading conditions and mechanical properties of the structure being analysed but provide valuable information about the biomechanical limits of the structure.

Given the plethora of methods in engineering, it may be more difficult to see how anthropology can benefit engineering. Nonetheless, engineering focuses on the application of science to solve problems for people, and anthropology is uniquely situated to provide the context to those problems. For instance, anthropology has improved engineering through the incorporation of anthropological methods. For example, the incorporation of ethnography into design to form the fields of design/techno-anthropology [14] and conferences like EPIC (Ethnographic Praxis in Industry Conference; www.epicpeople.org). End-user design focuses on the user's needs when designing products. By using anthropological techniques like ethnography, engineers can gather information about the wants and needs of the user that is inaccessible through focus groups developed from marketing perspectives. A classic example is in the design of the MP3 player, which was meant as an affordable alternative to the iPod to be used in the gym. Focus groups thought they wanted a device with many options and, therefore, many buttons. The product was designed, sent to market and failed. It was only by teaming up with ethnographers that designers and engineers realized that people's hands got sweaty in gyms and that gyms were social places. Ultimately, people actually wanted devices with fewer buttons and a quick on/off switch—they just did not realize it when they were in focus groups because the questions were not asked in the proper framework [118].

Anthropologists bring with them techniques that can be used to design for the future [119] and understand the consequences of technological advances. Engineers make design decisions to help today, but rarely think about the long-term effects on societies and communities in the future: this is because many work for companies which are on a deadline and, once one project is complete, they move on to the next. A classic example of the desire to solve the problem at hand without considering the potential longer-term societal consequences has been documented [120]. Engineers working through an international development organization created a solution to a chronic water shortage by developing a 140 km gravity-driven water pipeline that supplied water taps in local settings. Before the project, local women had carried water from natural sources, at times a journey of 3 h. The water distribution system worked well, but two unintended consequences occurred: the decrease in energy expenditure due to no longer needing to carry water increased the women's fertility and, because nutritional resources remained the same, increased child malnutrition [120]. These consequences are predictable through the lens of human reproductive ecology, a key body of knowledge in biological anthropology.

Anthropologists are trained to investigate long-term societal and community trends and are in a much better position not only to understand but also to address these problems. By working together, anthropologists and engineers who are interested in finding more socially connected solutions can do more to address crippling human problems. An example of how this can work came forth at the 'Why the World Needs Anthropologists: Powering the Planet' conference at Durham University, UK, in 2018. The conference focused on the problems facing energy (e.g. production, dissemination, storage) and explored how energy professionals and anthropologists can work together to create energy innovations that change the world for the better (https://www.dur.ac.uk/dei/events/?eventno=34503). In many cases, applied anthropology, which focuses on the external application of anthropology to current problems, could be used to extend and/or enhance the solutions to the problems engineers are regularly faced with.

Finally, although biomimicry is a field in itself, its application often falls short of its potential. Engineers who use biomimicry often look at the biological system in isolation and with overly simplified biological theories (e.g. assuming natural selection has caused a structure to be optimal for its function, without considering the evolutionary history of that element). Biological solutions typically must solve several simultaneous problems and have evolved within a set of allometric, phylogenetic and ontogenetic constraints [121]—a core understanding in biological anthropology—and the adaptationist programme frequently employed by engineers has been rejected by biologists for decades

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[122,123]. Because of this, biomimetic engineering falls short of its goals.

Anthropologists are trained to consider biological context that could lead to more effective biomimicry solutions using primates and human biological systems (e.g. the hierarchical structure of bone [124]). Take, for example, the design of the human foot, a complex structure that can be rigid in some circumstances and compliant in others. The evolutionary history of the foot is complex and filled with gaps [125], but we know it has evolved to interact with various substrates [72]. When wearing a shoe, the substrate interacting with the foot is no longer the ground, but the shoe itself [126], but shoe design does not often take foot–substrate interactions into account. Many shoe designs lead to running biomechanics that the human skeleton has not evolved to handle (e.g. high-impact forces during heel striking [127]). Similar issues can be seen in prosthetic foot design, where the impact of foot stiffness on gait biomechanics is well documented for advanced prosthetic feet (e.g. [128]). But in situations with fewer opportunities for the use of advanced medical devices, 'one size fits all' becomes 'one stiffness fits all' and the negative consequences of such choices are not appreciated. Further, even advanced medical interventions select a specified, unchanging stiffness for the prosthetic foot, when the natural foot has an adaptive, continuously changing stiffness, dependent on substrate and loading. Using anthroengineering and biomimicry approaches, answers to questions like 'How can we use what we know about variation in Primates to make engineered products better?' are achievable.

4. Why recognize a formal field of anthroengineering?

If anthroengineering projects already exist, why is it necessary to provide the word 'anthroengineering' to describe them all? It is not as if the previously discussed anthroengineering examples would cease to exist should the term 'anthroengineering' not be coined. More importantly, why is it necessary to recognize anthroengineering as its own field?

First, as previously mentioned, names provide identity and symbolic meaning. Should it not be given a unifying name, anthroengineering will remain elusive and ill-defined. In a well-known paper on evolutionary theory, Gould & Vrba [129] present a new word—exaptation—to describe an evolutionary phenomenon. They argue that the existing word 'adaptation' is defined and recognized by two criteria and biologists fail to recognize potential confusion between these criteria. Part of the reason for this confusion, they go on to say, is that one of these criteria does not have a distinctive word to describe it. They then propose that the word 'exaptation', which had not previously existed, be used for this criterion [129]. By providing a phenomenon with a name, Gould and Vrba took a previously undefined concept and centred it, making it tangible and real. Similarly, while anthroengineering has existed for decades, it has remained abstract and ill-defined. By providing a word to describe this line of work, anthroengineering becomes tangible and real.

Second, providing the name anthroengineering allows for the field to be recognized. This provides a thread to unite researchers working at the intersection of anthropology and engineering, much as the word 'anthropology' ties together cultural, linguistic and biological anthropologists, or 'engineering' ties together chemical, mechanical and computer engineers. Anthropology and engineering intersect across so many areas of interest that researchers in one area are often ignorant of people working in another (e.g. design anthropologists versus palaeo-biomechanists). The word anthroengineering creates a unifying concept for these researchers and an umbrella under which those anthroengineers can meet with, learn from and work with each other.

Third, the creation of a word and field to describe this line of work creates with it a new way of thinking and new framework, but, unlike interdisciplinary projects, it also creates a permanency. This allows researchers to be trained in this novel way of thinking and apply it with a deeper understanding to new problems in the future. This will then open a new world of potential applications for anthroengineering and enable researchers to ask questions they previously would not have considered.

Once anthroengineering is established and researchers have become fully trained in the field, the questions researchers ask will change. Instead of asking how anthropology or engineering, individually, could address a problem, researchers will ask how anthroengineering can address the problem and—as such—be able to answer it in a more fully informed, comprehensive manner. New questions can be asked, such as:

— How can we leverage anthroengineering to address large problems in the world, such as the UN's SDGs?
— How can we use anthroengineering to better understand how humans have evolved and why modern human biological variation exists in the manner it does?
— How can we leverage that information to better understand how humans are currently evolving in light of technological and societal changes and to address problems associated with racism and other identity-based biases in our technology and societies [130]?
— How can we use advanced modelling techniques to address global problems associated with healthy human ageing?

4.1. Creation of a new field

Today, many of the problems facing anthroengineering are the same as those facing interdisciplinary research in general. We recognize the issues facing research and research projects can often be distinct from those facing fields, but, at the time of writing, anthroengineering has almost solely existed at the research level, so it has not yet developed (m)any unique 'field-level' problems. As the plights of interdisciplinary research are much discussed, we will provide an overview of some of the main problems facing interdisciplinary research that we have witnessed within anthroengineering. We will further discuss some issues specific to anthroengineering today.

4.1.1. Publishing

Publications are currency in academia. When academics try to demonstrate their impact as researchers, they often total their number of publications, h-index, i10 index and the like for good reason. Publications foster recognition and the institutionalization of research, which in turn feeds back on the

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infrastructure and capacity of centres and departments, resulting in increased support [1].

Anthroengineers are faced with several difficulties when it comes to publication that plague interdisciplinary research. When making the decision on where to publish, anthroengineers must choose between specialist and generalist journals [131]. Often, their manuscripts do not fit within the narrow remits of specialist journals and would have to change position from a truly transdisciplinary approach to one where the methods/theories from one field are being used to advance the other [132]. Until specialist anthroengineering journals are established, therefore, manuscripts must be published in generalist journals. The risk when publishing in generalist journals is that the paper will not have its desired impact, as the generalist journal may not be regularly read by anthropologists, engineers or fellow anthroengineers. The paper would then miss its target audience.

The most effective way of circumventing this issue is through publication in high-impact generalist journals with large readership bases. But herein lies two dilemmas: (i) high-impact generalist journals tend to have word/page limits, and there is often not enough space to fully explain or discuss the anthropological *and* engineering theories and methods, and (ii) these journals have many submissions and limited publication space. They are, therefore, likely only to publish material they believe will be of interest to a high percentage of their audience, meaning that they can be hesitant to accept and publish papers in untested areas that do not already have a demonstrated readership base.

Further, the editors handling the manuscripts are unlikely to be anthroengineers and are more likely to be either anthropologists or engineers, making it less likely they will be able to grasp fully the impact of the research as part of the work is outside their area of expertise. The same issue occurs when recruiting reviewers for the manuscript [133]. Often, few researchers exist with the expertise to comprehensively review the manuscript. Consequently, more reviewers must be recruited, and it is not uncommon for reviewers to provide conflicting reviews. When conflicting reviews are received by a high-impact journal, the manuscript is often rejected, as the lack of consistency among reviewers is believed to be indicative of an inferior manuscript.

As a result, researchers are required to spend years publishing high-impact research in lower impact generalist journals that may not reach their target audience, and/or moulding their research to reach the narrow remit of the specialist journals. As institutional and funding support are often hinged on the ability to publish in high-impact journals (as this is often used as a metric for the 'quality' of research), researchers in interdisciplinary fields must often work much harder to be recognized. Fortunately for anthroengineering, several well-respected journals have been receptive to the publication of anthroengineering manuscripts (e.g. those published by the Royal Society [106,107,134], *Proceedings of the National Academy of Sciences of the United States of America* [12] and *Nature* [58]), but more explicit definition of the field will extend this acceptance.

4.1.2. Funding bodies

Funding is almost as important as publishing in academia, but securing funding for interdisciplinary projects comes with many of the same problems [132,135]. Instead of choosing between specialist journals, researchers are forced to choose between specialist councils (e.g. the Engineering and Physical Sciences Research Council (EPSRC), Natural Environment Research Council (NERC) and Biotechnology and Biological Sciences Research Council (BBSRC) in UK Research and Innovation (UKRI)) or specialist research areas (Biological Sciences, Engineering, International Science and Engineering, and Social, Behavioral, and Economic Sciences in the National Science Foundation (NSF)).

At a time when inter-/multidisciplinary research is heralded as the future of academia [136–138], the narrow focus of councils/research areas makes it complicated to submit interdisciplinary proposals and receive funding. When proposals are submitted to a specific research council/area, the proposal's merit is judged within the expertise of that council/area. While submission of truly interdisciplinary proposals that transcends the boundaries of the research councils/areas can occur through cross-council submissions, councils need to be contacted prior to submission to determine if the proposal is of interest. It often takes months to answer interdisciplinary enquiries, as it requires cross-council conversations, which delay proposal submission.

Once submitted, it is consistently more difficult to be awarded funding for interdisciplinary projects [139], and it is easier to secure funding for projects that combine closely related disciplines than for disparate ones [132]. This, unfortunately, leads to a situation where the more groundbreaking the collaboration is, the harder it is to fund. Lower funding success rates are believed to originate from a bias against interdisciplinary projects. Firstly, interdisciplinary proposals are viewed as higher risk because they do not follow an established path [139]. Secondly, as with journal articles, proposals are often reviewed by reviewers and panels who are ill-equipped to evaluate all parts of the project, making it difficult for them to appreciate the scope and impact of the proposal. They instead only review the portion of the proposal for which they are an expert and are more likely to assign a mediocre or poor score to an interdisciplinary proposal than an intradisciplinary one owing to a poor understanding of the project or the foundational concepts. Having a mix of reviewers who do and do not fully appreciate or understand the project will lead to proposals being rejected, as a lack of consistency between the reviewers is viewed as a problem with the application and not the review process. Additionally, interdisciplinary proposals compete with intradisciplinary ones, which are easier to justify for the funding agent [139].

4.1.3. Institutional support

In the longer term, for anthroengineering—or any other interdisciplinary line of research—to succeed, it must have career-level institutional support. Once interdisciplinary grants are awarded, the resulting projects often include graduate students and/or postdoctoral research associates. While this training expands their knowledge in ways that we recommend, it also leads to the training of a cohort of interdisciplinary researchers who, in the case of anthroengineering, do not fit the classic definitions of anthropology or engineering. They are often not considered 'real' anthropologists or 'real' engineers. As a result, when it comes time for these individuals to obtain permanent posts, the more

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interdisciplinary they are, the more difficult it is to obtain a permanent position.

During faculty searches, departments/divisions look for individuals to fill gaps in programme teaching and/or research foci, often hiring candidates who best fit the discipline(s) in which the programme awards degrees. This makes it difficult for truly interdisciplinary researchers to obtain permanent posts: an anthropologist or engineer who has spent their entire career working within the boundaries of their traditional discipline is a much stronger candidate than an anthro-engineer. For the long-term success of anthroengineering, high-level institutional support is needed.

4.1.4. Anthroengineering education

In terms of education, institutions need to go a step further than the current practice. To date, all anthroengineering training has been done on an individual level in the laboratory, which requires an inordinate amount of time and effort from the laboratory's principal investigator, and from the individuals independently seeking out formal educations in both anthropology and engineering. Given how different the two disciplines are, this often requires twice the time and money to be educated in anthroengineering, limiting the ability to study anthroengineering to the privileged. Owing to the clear benefits of interdisciplinary research, and the scientific leaps that have been made by anthroengineering research already, we believe that universities should support formally training students as anthroengineers.

The majority of these students will leave academia and enter the private sector. The students trained as anthroengineers will have immediately transferable skills that make them superior on the job market to other anthropologists/engineers seeking employment. For example, a major concern among engineering companies is how to be more socially responsible, while social responsibility is a central theme in anthropology. The anthroengineers entering the job market will have the skills not only to be practising engineers, but also to be more socially responsible than engineers who have not received this training—something that is direly needed [140]. The anthroengineering cohorts will be trained in both anthropology and engineering from the start of their higher education, and, thus, taught to think using interdisciplinary approaches from the start. These anthroengineers will have the ability to see new questions and novel, innovative answers that cannot be imagined by the current generation of anthroengineering.

5. Disciplinary culture

The last issue we would like to touch upon with anthroengineering is that of disciplinary culture. In the creation of a new field, we are in the unique position to create the academic culture for the field. A focus of many disciplines, today, is to address the realities of sexism, racism, homophobia, etc., that have become engrained within these disciplines and academia in general and to take the necessary steps to solve these problems [141]. In the establishment of a new field, we can attempt to create a more inclusive academic environment from its inception [142].

When applying to hold the first symposium on anthroengineering at the American Association of Physical Anthropology (AAPA) conference in Cleveland, Ohio, USA, 2019 (Symposium 13—Anthroengineering: a Biological Perspective), we were required to write a 300-word diversity statement. In it, we described our methods for recruiting symposium participants which reflect our vision of anthroengineering:

> In recruiting participants for this symposium, we focused on early career researchers and on members of groups frequently underrepresented in research. Consequently, about half of our participants are women, and others are ethnic minorities and members of the LGBTQA[+] community. By recruiting a diverse group of people at an early stage in their careers, we hope to foster an environment of inclusion that connects to and bolsters other such efforts at the AAPAs and in the discipline of biological anthropology generally… [Anthroengineering should value] the contributions of all people, regardless of sex, gender, ethnicity, or sexual orientation, and supports all types of research that combine anthropology and engineering.

In short, our vision for this new field is one of fairness and inclusivity, but anthroengineering will be housed in academic institutions and is born out of two fields which have their own problems. Fortunately, we are in a position where we can observe the issues present in other fields and strive to avoid those issues in this one.

6. Conclusion

In this paper, we have presented the concept of anthroengineering, provided examples of how anthroengineering has been used in the past and outline a plan for the future. Importantly, we have argued that anthroengineering should be recognized as its own, independent field: if you did not already believe this, we hope we have made converts out of you.

We cannot wait to see what the future has in store.

Data accessibility. This article has no additional data.

Authors' contributions. Both M.A.B. and P.A.K. conceived of and wrote the paper.

Competing interests. We declare we have no competing interests.

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Bleuler's Psychopathological Perspective on Schizophrenia Delusions: Towards New Tools in Psychotherapy Treatment

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The authors begin by addressing the historical evolution of the delusion concept and its different approaches, focusing afterwards mainly on the work of Bleuler, who stressed the proximity between delusions and the emotional life of patients with schizophrenia. I Therefore, the present work intends to review the main aspects of the theory of delusion formation in schizophrenia according to Bleuler's psychopathological perspective. For that purpose, first the role of delusions in the psychopathology of schizophrenia is explored in a close relation with the Bleuler's fundamental symptoms (Alogia, Autism, Ambivalence, and Affect Blunting) nowadays known as negative symptoms. Then, persecutory, grandiosity and sexual delusions in schizophrenia are described according to the tension between logic and affects, as well as, internal conflict, schizoid features, and auto-erotism as key psychopathological pathways. Thus, with this subjective perspective, it is intended to highlight Bleuler's psychopathological contribution to the affective and meaningful causality of delusions in schizophrenia. The former might be useful in the integration with other psychopathological phenomena (hallucinations and negative symptoms) and new forms of research and therapeutic approaches in this disorder that are complementary with the contemporary tendencies in psychopathology.

Keywords: affectivity, Bleuler, delusions, schizophrenia, psychopathology

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INTRODUCTION

Throughout the history of psychopathology the term delusion had several meanings distant from its current meaning of thought disorder (1). In antiquity and in the eighteenth and nineteenth centuries' French Psychiatry, the term *délire* (delusion), meant general detachment from reality that was not specific of thought impairment (1).

In eighteenth and nineteenth centuries' French Psychiatry, the term delusion included disturbances of thought, perception, emotions and affects and even psychomotricity (2). By contrast, in the twentieth century German and British Psychiatry, the term delusion gradually became synonymous with a false belief, a disorder of the thought content (3). This tendency was generalized in the majority of the European countries and also in the United States of America, with the replacement of the old broader concept by a newer and narrower concept of delusion as a disorder of thought content.

Jaspers defined delusion as a disorder in the content of thought, separating it from other psychopathological disorders such as perception, affect and personality's. He considered primary delusion incomprehensible and in discontinuity with the individual's personality (4).

However, throughout the twentieth century, some authors such as Freud and Bleuler were not satisfied with the Jasperian definition of primary delusion as an isolated and incomprehensible phenomenon, and tried to integrate it in the general psychic life of patients.

For Freud, delusions result from a conflict between the ego and the external world that makes the former lose its contact with reality, mainly because of an intolerable frustration (5). He assumes that delusions might occupy the place left by that loss of contact with reality (6). These efforts to recapture the outside world through delusion occur in continuity with the emotional memories of the patient, previous to reality detachment (5).

Bleuler thought much about delusion in schizophrenia, namely its relation with affect, personality and the proximity with what he called the fundamental symptoms (nowadays known as negative symptoms of schizophrenia). Bleuler was the first author to gather descriptive and analytical perspectives on the psychopathology of schizophrenia. He added comprehensive and interpretative components without forgetting the importance of psychopathological description and systematization. This is an example of how it is possible to integrate different paradigms regarding the same psychopathological phenomenon.

In this article, we intend to review the main aspects related to the theory of the formation of delusion in schizophrenia, according to Bleuler's psychopathological perspective.

THE ROLE OF DELUSIONS IN SCHIZOPHRENIA PSYCHOPATHOLOGY

Bleuler systematizes the clinical presentation of schizophrenias into fundamental, accessory, primary and secondary symptoms. The fundamental symptoms, which are virtually present through all the course of the disorder (7), are also known as the famous Bleuler's four A's: Alogia, Autism, Ambivalence, and Affect blunting (8). Delusion is regarded as one of the accessory symptoms because it is episodic in the course of schizophrenia. Among the primary symptoms one can find alogia that Bleuler claimed to have a neurological etiology. All the remaining symptoms, including delusion, are considered secondary symptoms because they are an attempt of psychogenic compensation of the deficits caused by alogia. Bleuler conceptualized delusion as an accessory and secondary symptom in schizophrenia's psychopathology in very close relation with fundamental symptoms.

In alogia, as the logical thought weakens, affects become predominant and dominate the associations of the thinking processes (9). Based on this hypothesis, Bleuler described a link from alogia to delusion formation, with wishes and fears dominating the association of thoughts, bringing way to autistic thought, withdrawing the patient from external reality, predisposing him to delusion formation (7).

Regarding autism, it can be conceptualized as the predominance of inner life that distances the patient from external reality. In this sense, autism can be seen as a difficulty in contact with others (auto-erotism) but also as social isolation and negativism predisposing the patient to delusion formation (10).

Concerning affect blunting, Bleuler argues that although affects seem to be decreased at superficial psychiatric observation, they are very intense at deeper layers of the psychic life of the patient (11). Affect blunting might predispose patients with schizophrenia to delusion specifically when interpersonal conflicts bring to surface those apparently hidden emotions.

Finally, ambivalence is described as a tendency to be in the presence of contradictory feelings. Bleuler described this ambivalence as much more intense, regarding anxiety, than the one present in neurotic (not psychotic) patients (12). Considering this intense anxiety in schizophrenia's ambivalence, delusions represent a psychopathological way of dealing with these internal and emotional conflicts.

THEORY OF DELUSION FORMATION IN SCHIZOPHRENIA

According to Kraepelin (13), delusions were incorrect ideas created, not by an accidental failure of logic, but by an inner need of the patient (13). And for Bleuler and Brill (9) the most important inner needs are the affective ones. In that sense, delusions always follow a definite direction corresponding to the patients affects, and in the vast majority of cases cannot be corrected by new experience or instructions, as long as the condition which gave origin to them remains (9). Thus, delusions have their origin mainly in belief instead of logic. From Bleuler's point of view, delusions are frequently egocentric and very significant for the personality of the patient (7). By other words we can stress that the delusions thematic is mainly anchored in the patient's biography.

Bleuler acknowledges that the strength of affects (in affect blunting) combined with the weakness of logic (alogia) is the most common feature in delusions formation. When affects are present and strong, patients are more prone to logic errors, which mean that affects have a key-role in the formation of delusions (7). The latter ones might be conceptualized as stemming from unconscious thinking derived from the wide splitting of mental functions (9) where the autonomy of traumatic emotional memories becomes predominant. These traumatic emotional memories belong to the autistic way of thinking, based on the fantasies that are detached from reality. So autistic thinking and affective needs take advantage, over realistic and logical thinking, and patients become vulnerable to delusion formation (10).

PSYCHOPATHOLOGICAL MECHANISMS IN DELUSION FORMATION IN SCHIZOPHRENIA

As previously adressed, Bleuler argued that delusions were a secondary, psychogenic, kind of symptom, involving different specific psychopathological mechanisms: internal conflict, schizoid features, and auto-erotism (12).

In internal conflict we can assume that traumatic emotional memories have influence in realistic thinking, giving rise to conflict between internal and external reality. Moreover, there is a tension because of the imbalance between pleasant and unpleasant affects and delusion formation is the only way allowing traumatic emotional memories to manifest (11).

Regarding schizoid features, Bleuler claimed that these personality traits are essential and in accordance with the autistic way of thinking (11). This kind of thinking, based on fantasies turns the patient away from reality, liberating subjective wishes, but without further adaptation (10). It always seeks pleasure and avoids pain. Freud argued that schizophrenic delusions are not only wish-fulfilling but also the attempt to recapture lost internal objects (6).

Finally, auto-erotism is as a key-feature of autism in schizophrenia as negativism has frequently an erotic side that may be pleasant as flirting, unpleasant as harassment, or both at the same time (12).

PERSECUTORY DELUSIONS

In this kind of delusion, Bleuler considers that there is frustration after a great ambition of the patient is not achieved (11). The patient is kept in an internal conflict between denying and accepting this frustration that may decrease his self-esteem, damaging his narcissism. Many patients in this situation cannot deal with failure and project their guilt feelings in people around them (7). Without this contradiction between ambition (wishes) and reality (possibilities) there would be no delusion of persecution (11). In other words, first patients don't have what they wish, then they don't admit their incompetency and the result is the delusion of persecution, blaming others for their failure (9). Delusion of persecution is the most common type of delusion in schizophrenia (7).

GRANDIOSITY DELUSIONS

Very frequently grandiosity delusion is secondary to persecutory delusion (6, 14, 15). When the projection of guilt (persecutory delusion) fails to balance internal wishes and external reality, delusion of grandiosity may occur as a fulfillment of the repressed wish (11). As the external reality contradicts the guilt projected into the outside world, narcissistic injury to self-esteem grows, leaving the patient with the escape of wish-fulfillment through delusion of grandiosity (7). In other words the patient justifies his persecution delusion with a grandiose explanation, feeling him as an extremely important person, thus restoring his fragile self-esteem (9). Delusion of grandiosity is the second most common type of delusions in schizophrenia (7).

SEXUAL DELUSIONS

This kind of delusions is also very common in schizophrenia. Usually, the patient believes it is forbidden for him to do what he wishes, under threats of danger, or punishment (12). Bleuler conceptualized that sexual thematic memories have a prominent role in schizophrenia as many patients presented sexual delusions of being loved (delusional erotomania), abused (delusional rape), or pregnant (delusional gestation). According to Bleuler, sexual delusions are a combination of persecutory and grandiosity delusions (7) and can also express the traumatic emotional memories that belong to the autistic way of thinking.

DISCUSSION

Nowadays the biological paradigm has monopolized psychopathology's studies, leaving meaning and symbolic causalities behind. This approach brought a reductive and poor view of psychopathology which could and should be enriched with other lines of thought.

For Bleuler, patients' affects are extremely important in the formation of delusions in schizophrenia, and this perspective may be useful in the investigation of new forms of therapeutic approach of this disorder. It also represents humanistic and patient-centered approach regarding the patient with schizophrenia, and reflects what is actually observed in clinical practice.

Bleuler also pointed out that delusions cannot be evaluated and studied separately from the rest of psychopathology. This view is in agreement with several authors of French psychopathologists (e.g., Esquirol and Henry Ey) for whom delusions were very close to other psychopathological phenomena such as hallucinations, an interdependence that has already been approached conceptually and empirically by more recent authors (16–18).

Another important aspect of Bleuler's vision is the proximity between positive and negative symptoms. For Bleuler they are strongly linked, with the negative symptoms preceding the positive symptoms (e.g., delusions).

In sum, with Bleuler, schizophrenia deserves to be approached not only from an objective perspective but also from a subjective perspective (taking into account the affective component, and the symbolic causality) in order to grasp the real picture of what is happening inside the patients.

New research could be based on this line of thought. Namely the study of the role of psychological trauma and emotional memory in schizophrenia patients' psychopathology, trying to add complementary knowledge to genetic studies, building bridges between genetics and environment (nowadays called epigenetics); On the other hand it would be interesting to assess the effectiveness of psychotherapies (which focus on factors related to the affective and the meaningful components of symptoms), alone or in combination with psychopharmacology in the treatment of schizophrenia.

AUTHOR CONTRIBUTIONS

FA-G conceptualized and wrote the first draft of the manuscript. JG contributed with commentaries and suggestions. DT-C reviewed and supervised all the writing process.

$$\forall -\infty < x_2 < \infty,\ -\infty < x_3 < \infty \text{ and } -\infty < x_4 < \infty \tag{5.18}$$

$$\mathcal{V}_2^0\left(x_3, x_4, x_1; \xi_1, \xi_2, \xi_3, \xi_4\right) = 0, \quad \forall -\infty < x_3 < \infty,\ -\infty < x_4 < \infty \text{ and } -\infty < x_1 < \infty \tag{5.19}$$

$$\mathcal{V}_3^0\left(x_4, x_1, x_2; \xi_1, \xi_2, \xi_3, \xi_4\right) = 0, \quad \forall -\infty < x_4 < \infty,\ -\infty < x_1 < \infty \text{ and } -\infty < x_2 < \infty \tag{5.20}$$

$$\mathcal{V}_4^0\left(x_1, x_2, x_3; \xi_1, \xi_2, \xi_3, \xi_4\right) = 0, \quad \forall -\infty < x_1 < \infty,\ -\infty < x_2 < \infty \text{ and } -\infty < x_3 < \infty \tag{5.21}$$

The phase angles ξ_1, ξ_2, ξ_3 and ξ_4 are chosen such that they satisfy the prerequisites (5.18), (5.19), (5.20) and (5.21). In (C.1), (5.12), (5.13) and (5.14), the phase angles $\xi_1 = -\frac{\pi}{4}$, $\xi_2 = \frac{\pi}{4}$, $\xi_3 = \frac{\pi}{4}$ and $\xi_4 = \frac{\pi}{4}$ satisfy (5.18), (5.19), (5.20) and (5.21):

$$\frac{\mathcal{V}_1^0\left(x_2, x_3, x_4; -\frac{\pi}{4}, \frac{\pi}{4}, \frac{\pi}{4}, \frac{\pi}{4}\right)}{v_r^2} = 0 \tag{5.22}$$

$$\frac{\mathcal{V}_2^0\left(x_3, x_4, x_1; -\frac{\pi}{4}, \frac{\pi}{4}, \frac{\pi}{4}, \frac{\pi}{4}\right)}{v_r^2} = 0 \tag{5.23}$$

$$\frac{\mathcal{V}_3^0\left(x_4, x_1, x_2; -\frac{\pi}{4}, \frac{\pi}{4}, \frac{\pi}{4}, \frac{\pi}{4}\right)}{v_r^2} = 0 \tag{5.24}$$

$$\frac{\mathcal{V}_4^0\left(x_1, x_2, x_3; -\frac{\pi}{4}, \frac{\pi}{4}, \frac{\pi}{4}, \frac{\pi}{4}\right)}{v_r^2} = 0 \tag{5.25}$$

Taking note that g_i^0 equals $\mathcal{W}_i^0$, the following expressions are derived for g_i^0 and

$\mathcal{G}^0\left(x_1, x_2, x_3, x_3\right) = \sum_{k=1}^{4} \frac{\partial \mathcal{W}_k^0}{\partial x_k}$:

$$g_1^0 = -\frac{v_r^2 \alpha}{2} \cos\left(2\alpha x_1\right) \sin\left(2\alpha x_3\right) \tag{5.26}$$

$$g_2^0 = -\frac{v_r^2 \alpha}{2} \cos\left(2\alpha x_2\right) \sin\left(2\alpha x_4\right) \tag{5.27}$$

$$g_3^0 = -\frac{v_r^2 \alpha}{2} \cos\left(2\alpha x_3\right) \sin\left(2\alpha x_1\right) \tag{5.28}$$

$$g_4^0 = -\frac{v_r^2 \alpha}{2} \cos\left(2\alpha x_4\right) \sin\left(2\alpha x_2\right) \tag{5.29}$$

$$\begin{aligned}\frac{\mathcal{G}^0\left(x_1, x_2, x_3, x_4\right)}{v_r^2} &= \alpha^2 \sin\left(2\alpha x_1\right) \sin\left(2\alpha x_3\right) \\ &\quad + \alpha^2 \sin\left(2\alpha x_2\right) \sin\left(2\alpha x_4\right) + \\ &\quad + \alpha^2 \sin\left(2\alpha x_3\right) \sin\left(2\alpha x_1\right) \\ &\quad + \alpha^2 \sin\left(2\alpha x_4\right) \sin\left(2\alpha x_2\right)\end{aligned} \tag{5.30}$$

By substituting $\mathcal{G}^0\left(x_1, x_2, x_3, x_4\right)$ from (5.30) into (5.6) and evaluating the definite integrals term by term, we can see that the results equal g_i^0 derived from (2.6); that is, $\mathcal{U}_i^0 \equiv 0$, $i = 1, 2, 3, 4$. We have used the integral identity (B.9) in Appendix B to perform the integrations.

Substituting for the initial condition v_i^0, $i = 1, 2, 3, 4$ from (5.1), (5.2), (5.3) and (5.4) into (3.12) with phase angles ξ_1, ξ_2, ξ_3 and ξ_4 set, respectively, to $\xi_1 = -\frac{\pi}{4}$, $\xi_2 = \frac{\pi}{4}$, $\xi_3 = \frac{\pi}{4}$ and $\xi_4 = \frac{\pi}{4}$ and performing the integrations, we arrive at the solution of the Navier–Stokes equation (2.1) in four dimensions:

$$\begin{aligned}v_1 = v_r \Big[&\sin\left(\alpha x_1 - \frac{\pi}{4}\right) \cos\left(\alpha x_2 + \frac{\pi}{4}\right) \\ &\times \sin\left(\alpha x_3 + \frac{\pi}{4}\right) \cos\left(\alpha x_4 + \frac{\pi}{4}\right) - \\ &- \sin\left(\alpha x_1 + \frac{\pi}{4}\right) \sin\left(\alpha x_2 + \frac{\pi}{4}\right) \\ &\times \cos\left(\alpha x_3 + \frac{\pi}{4}\right) \cos\left(\alpha x_4 - \frac{\pi}{4}\right) \Big] e^{-4\alpha^2 \kappa t}\end{aligned} \tag{5.31}$$

$$\begin{aligned}v_2 = v_r \Big[&\sin\left(\alpha x_2 - \frac{\pi}{4}\right) \cos\left(\alpha x_3 + \frac{\pi}{4}\right) \\ &\times \sin\left(\alpha x_4 + \frac{\pi}{4}\right) \cos\left(\alpha x_1 + \frac{\pi}{4}\right) - \\ &- \sin\left(\alpha x_2 + \frac{\pi}{4}\right) \sin\left(\alpha x_3 + \frac{\pi}{4}\right) \\ &\times \cos\left(\alpha x_4 + \frac{\pi}{4}\right) \cos\left(\alpha x_1 - \frac{\pi}{4}\right) \Big] e^{-4\alpha^2 \kappa t}\end{aligned} \tag{5.32}$$

$$\begin{aligned}v_3 = v_r \Big[&\sin\left(\alpha x_3 - \frac{\pi}{4}\right) \cos\left(\alpha x_4 + \frac{\pi}{4}\right) \\ &\times \sin\left(\alpha x_1 + \frac{\pi}{4}\right) \cos\left(\alpha x_2 + \frac{\pi}{4}\right) - \\ &- \sin\left(\alpha x_3 + \frac{\pi}{4}\right) \sin\left(\alpha x_4 + \frac{\pi}{4}\right) \\ &\times \cos\left(\alpha x_1 + \frac{\pi}{4}\right) \cos\left(\alpha x_2 - \frac{\pi}{4}\right) \Big] e^{-4\alpha^2 \kappa t}\end{aligned} \tag{5.33}$$

$$\begin{aligned}v_4 = v_r \Big[&\sin\left(\alpha x_4 - \frac{\pi}{4}\right) \cos\left(\alpha x_1 + \frac{\pi}{4}\right) \\ &\times \sin\left(\alpha x_2 + \frac{\pi}{4}\right) \cos\left(\alpha x_3 + \frac{\pi}{4}\right) - \\ &- \sin\left(\alpha x_4 + \frac{\pi}{4}\right) \sin\left(\alpha x_1 + \frac{\pi}{4}\right) \\ &\times \cos\left(\alpha x_2 + \frac{\pi}{4}\right) \cos\left(\alpha x_3 - \frac{\pi}{4}\right) \Big] e^{-4\alpha^2 \kappa t}\end{aligned} \tag{5.34}$$

We have used the integral identities (B.1)–(B.3) given in Appendix B to perform the integrations.

Pressure is obtained from the solution of the Poisson equation (3.2). Because (3.10) is satisfied, we can express (3.5) as follows:

$$\frac{\partial p}{\partial x_i} = -\rho g_i = -\rho g_i^0 e^{-8\alpha^2 \kappa t} \qquad i = 1, 2, 3, 4 \tag{5.35}$$

This leads to straightforward integration for pressure:

$$p = \frac{\rho v_r^2}{4} \left[\sin\left(2\alpha x_1\right) \sin\left(2\alpha x_3\right) + \sin\left(2\alpha x_2\right) \sin\left(2\alpha x_4\right)\right] e^{-8\pi^2 \kappa t} \tag{5.36}$$

6. Concluding remarks

The statement of the problem and the edifice of the proposed solution method in a space having an arbitrary number of dimensions, $\mathbb{R}^n$, are presented in Sections 2 and 3, respectively. The pressure field is formally obtained by taking the divergence of the Navier–Stokes equation (2.1) as a solution to the Poisson equation, yielding an expression (3.5) for pressure gradient. By inserting the pressure gradient back into (2.1) and equating the unsteady terms, $\frac{\partial v_i}{\partial t}$, to the sum of three terms that are associated, respectively, with the linear viscous force, the nonlinear inertial force and the externally applied force acting on the fluid we obtain the rephrased Navier–Stokes equation (3.7). Subject to satisfying an integral equation (3.10), (3.7) is then reduced to a non-homogeneous diffusion equation in velocity. When the externally applied force is set to zero, it is further reduced to the Cauchy diffusion equation. The nonlinearity is entirely isolated to the integral equation (3.10).

Succinctly put, subject to satisfying a certain condition (3.10), the Navier–Stokes system of equations is decomposed into two linear equations, the non-homogeneous diffusion equation and the Poisson equation, for the velocity and pressure fields respectively. The velocity and pressure fields are given by the solutions of Cauchy diffusion equation and Poisson equation respectively. The proposed solution methods belong to the class of Beltrami flows and are valid under proper regularity conditions at infinity.

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Fractality of sensations and the brain health: the theory linking neurodegenerative disorder with distortion of spatial and temporal scale-invariance and fractal complexity of the visible world

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The theory that ties normal functioning and pathology of the brain and visual system with the spatial–temporal structure of the visual and other sensory stimuli is described for the first time in the present study. The deficit of fractal complexity of environmental influences can lead to the distortion of fractal complexity in the visual pathways of the brain and abnormalities of development or aging. The use of fractal light stimuli and fractal stimuli of other modalities can help to restore the functions of the brain, particularly in the elderly and in patients with neurodegenerative disorders or amblyopia. Non-linear dynamics of these physiological processes have a strong base of evidence, which is seen in the impaired fractal regulation of rhythmic activity in aged and diseased brains. From birth to old age, we live in a non-linear world, in which objects and processes with the properties of fractality and non-linearity surround us. Against this background, the evolution of man took place and all periods of life unfolded. Works of art created by man may also have fractal properties. The positive influence of music on cognitive functions is well-known. Insufficiency of sensory experience is believed to play a crucial role in the pathogenesis of amblyopia and age-dependent diseases. The brain is very plastic in its early development, and the plasticity decreases throughout life. However, several studies showed the possibility to reactivate the adult's neuroplasticity in a variety of ways. We propose that a non-linear structure of sensory information on many spatial and temporal scales is crucial to the brain health and fractal regulation of physiological rhythms. Theoretical substantiation of the author's theory is presented. Possible applications and the future research that can experimentally confirm or refute the theoretical concept are considered.

Keywords: fractal therapy, dynamical chaos, fractality of sensations, reactivation of brain plasticity, treatment and rehabilitation, aging, neurodegenerative diseases, amblyopia

Abbreviations: AD, Alzheimer's disease; DR, diabetic retinopathy; EE, environmental enrichment; EEG, electroencephalography; HD, Huntington's disease; PD, Parkinson's disease; PERG, pattern electroretinogram; SCN, suprachiasmatic nucleus; SR, stochastic resonance.

The Theory

Comparison of the known facts, phenomena and relationships, and logical analysis makes it possible to assume that the spatial–temporal structure of our incoming sensory information represents the key driver of the healthy development of the brain. Man is a subject and object of the dynamic chaos of nature. Natural fractals accompany us throughout our lives. Additionally, all the wealth of sensations that we receive, enjoying the results of other people's creativity and in the process of our creative thinking we can also refer to the "fractality of sensations." Distortion of the fractality of sensations may be a factor contributing to the weakening of brain's functions, distortion in cognitive performance and dynamics of gait by reducing the capacity of adaptive plasticity.

In this article, an objectively existing relationship between normal functioning or pathology of the brain and the spatial–temporal structure of the visual, auditory, and other stimuli that affect people throughout the life was proposed to exist and theoretically substantiated. The theory argues that the deficit or distortion of the fractal complexity of visual and other environmental influences may lead to anomalies of development and aging. In the same time, the use of fractal flickering and other sensory modalities of fractal stimulation helps to restore the function of the brain by acting via activation of the brain plasticity. The application of fractal therapy can provide particular benefits in the elderly, in patients with neurodegenerative disorders and amblyopia.

The following assumptions are derived directly from the theoretically established relationship:

- Fractal geometry and non-linear dynamics of complex processes are not just a characteristic property that is inherent for all natural (environmental and biological) systems. It is a sign that determines the quality of human life.
- Fractal geometry and a non-linear dynamics of physiological processes of the human body are not only typical signs of a healthy body. It is a key feature, whose preservation, maintenance, and recovery is essential to maintain physical and mental human health throughout the life, from birth to old age.

Below, we present data collected from different areas of expertise that are relevant to theoretical substantiation of the theory, including:

- Evidence of the characteristic non-linear structures in nature, of the fractal geometry and dynamics in a healthy human body and brain, and the distortion of fractality correlated to aging and pathology;
- The current understanding of the brain plasticity, dependent on the sensory experience, and neuroplasticity changes in diseases related to abnormal development and age-related conditions;
- The techniques used today to reactivate the plasticity of the adult's brain, and recent new data that may indicate a possible usage of sensory stimuli with the non-linear temporal structure to influence the neuroplasticity.

We should note that the conclusion about the role of fractal therapy in the treatment of a variety of human diseases may be an outcome of an analysis of previously known scientific facts (i). Similarly, it can immediately follow the present theory of an objective relationship between the fractality of the environment (and our sensations) and brain health (ii).

However, the difference in logical reasoning is as follows:

(i) In the first case, the conclusion of the possible advantages of non-linear light therapy follows from the fact that the complex dynamics of some body functions usually follow the laws of deterministic chaos. In disease, this dynamics loses its complexity. Thus, it seems logical to try to recover the complexity of rhythms by using fractal entrainment cues to synchronize the dynamics of physiological fluctuations and external rhythms.

(ii) In the second case, the expected benefits of fractal stimuli in training and therapy follow not from typical non-linear dynamics of healthy physiological processes. Opposite, these benefits follow from an understanding of the need to preserve, maintain and restore a complex (fractal) dynamics. In certain situations, including diseases, this may need to use artificially created fractal environment.

The Non-Linear World

Characteristic Patterns of Fractal Geometry and Dynamics in Nature and Man

Natural Fractals and the Human Body

From the birth to deep old age, we live in a non-linear world, at which the scene objects and processes with the properties of fractality and non-linearity surround us. Against this background, the evolution of man took place. Against this background, all periods of our lives unfold.

The non-linear nature of physical objects is well-known today (Kirillov and Pelinovsky, 2013). Fractal geometry, which is capable to describe the natural objects, and non-linear dynamics also have been applied in the field of biology and medicine. Fractals are the irregular geometric figures or a set of points, possessing the features of self-similarity and a fractional dimensionality. Self-similarity and scale invariance are the basic properties of fractals. It means that the structure of the fractal object remains unchanged with the increase in the image regardless of the zoom (Mandelbrot, 1982; Feder, 1988; Weibel, 1991; Bassingthwaighte et al., 1994; Crownover, 1995; West et al., 1999). Nature example of the simplest mathematical fractal is a treelike structure with dichotomous self-similar branching, exhibiting properties of bifurcation. Natural fractals include the relief of the sea and river coastlines, of mountain ranges, the winding river networks. The Brownian crystal growth and lightning structure – all also belong to the natural fractals (Iannaccone and Khokha, 1996).

Natural fractal structures are the result of a process of self-organization in which the communication of structural levels of different scales occurs. Resulting natural fractal objects also have a self-similar structure, that is, with zooming such structures remain the same, regardless the scaling. Natural fractals belong to a class of statistical or random fractals. The fractal dimension sets the link between fractal structures and the properties of the environment. Fractal dimension usually exceeds the object topological dimension. Physical objects are rarely self-similar at an increase of more than four orders of magnitude (West et al., 1999). West et al. (1999, p. 1677) vividly noted: "Fractal-like networks effectively endow life with an additional fourth spatial dimension, the origin of quarter-power scaling that is so pervasive in biology." We can often see new principles of self-organization in biological objects in case of an increase by two orders (Crownover, 1995).

Many complex structures of living systems exhibit fractal-like geometry. In a human body, a variety of complex anatomical structures has fractal geometry. They show the property of self-similarity at several scales (Goldberger et al., 1990, 2002; Weibel, 1991; Bassingthwaighte et al., 1994; Ayers, 1997; for review see Goldberger, 2006). Examples include the blood vessel branching, networks of the tracheobronchial tree and neural networks in the brain, the folds of the intestine, choroidal plexus, etc. Treelike fractals help describing and modeling of the tracheobronchial tree. Fractal structures are supposed to be very stable, because of their redundancy and irregularity (Goldberger et al., 2002).

Non-Linear Dynamics of Physiological Processes

For the description of dynamical, unpredictably time-varying systems, the concept of deterministic chaos is applied (Mandelbrot, 1982; Stewart, 1989; Crownover, 1995). The 'chaos' implies some definite properties of the deterministic dynamical system, the most important of which are a significant dependence of such system on the initial conditions, and its internal unpredictability. Any chaotic phenomenon we can describe with its trajectory in the analysis over time. The region in the phase space, in which the path of the system's behavior is visually concentrated, is called chaotic (strange) attractor. The self-similar nature of the fractal processes can be qualitatively assessed with a graphical representation of their fluctuations at various time resolutions (Belair et al., 1995; Beuter et al., 2003). The concept of strange attractors has led to a new hypothesis of systemic properties of higher cognitive functions that depend on the dynamic interactions between parallel streams of information (Mattei, 2013).

Complex physiological processes also exhibit irregular fluctuations across multiple time scales and can be described using the theory of deterministic chaos. Fluctuations of physiological rhythms of a healthy body have the properties of fractals (Goldberger et al., 1990, 2002; Peng et al., 1993, 2002; Yamamoto and Hughson, 1994). Healthy physiological rhythms such as heart rate, respiration (Fadel et al., 2004) demonstrate complex variability that can be quantified using the fractal concept and the concept of non-linear dynamics. The self-similar nature of these fluctuations we can see when plotting at different temporal resolutions. Complex physiological dynamics allows the body to respond rapidly to internal and external perturbations of the environment (Lipsitz, 2004).

The special edition of Frontiers in Computational Neuroscience has included selected articles dedicated to the applications of non-linear and fractal analyses in different research fields in neuroscience and cognitive psychology (Mattei, 2014). The topic was assigned to 'Non-linear and Fractal Analysis in Neuroscience and Cognitive Psychology.' In this issue, the selected articles demonstrate usefulness of the non-linear analysis for modeling the healthy brain dynamics, for the diagnosis of neurological and psychiatric disorders, and monitoring of the therapeutic efficiency. The results of studies confirm that the advanced non-linear analysis helps to describe the complexity of brain dynamics accurately.

The healthy heartbeat interval was found to exhibit highly irregular behavior, fluctuating in a complex manner. Scaling analysis of cardiac interbeat time series demonstrated the presence of long-range fractal correlations in variations of the healthy heartbeat (Goldberger et al., 1990, 2002; Ivanov et al., 1999). The subtle, complex fluctuations of the inter-step (stride-to-stride) interval in the healthy human walking rhythm were also shown to exhibit the scale-invariance. Walking speed had no effects on the stride interval fluctuations and long-range correlations, indicating that the fractal variability in human gait in norm is quite robust (Hausdorff et al., 1995, 1996). While the dynamics of heartbeat has a chaotic pattern with signs of self-similarity, the tachycardia is relatively periodic and possesses a vivid rhythmic nature (cited from Goldberger et al., 2002).

In the spectrum of EEG of the healthy waking human brain the alpha rhythm dominates. Lehnertz (1999) presented an overview of studies that demonstrated a fractal dimension of alpha rhythm. Different works reported that the chaotic behavior is, likely, characteristic of the activity of the healthy brain areas, single neurons and neural networks (Babloyantz, 1989; Schiff et al., 1994; Das, 2001; Faure and Korn, 2001; Korn and Faure, 2003; Izhikevich, 2007).

The chaotic behavior is believed to make neurons able to switch quickly between different states (Schiff et al., 1994). It provides the flexibility of the central nervous system (CNS) and its resistance to external influences. The non-linear behavior of axons and excitable cells seems to have the regulatory role of inhibitory coupling once chaotic cells become members of larger neuronal assemblies (Rabinovich and Abarbanel, 1998). It has been also suggested that chaos may contribute to the neuronal code (Skarda and Freeman, 1987; van Vreeswijk and Sompolinsky, 1996; So et al., 1998).

Disruption in Fractal Dynamics of Physiological Processes

Various studies have found correlations between the aging process or disease and a loss of the complexity of many physiological processes. In pathological conditions and aging, ordered fluctuations in the parameters of physiological functions were reported (Lipsitz and Goldberger, 1992; Goldberger et al., 2002; Peng et al., 2002). Diseases tend to cause highly periodic dynamics of the process, which is dominant on the same time scale. Chaos in health allows the body to respond adequately to rapidly and unpredictably changing circumstances. Thus, the reduction of multiscale non-linear complexity of physiological functions in pathological conditions and human aging can potentially reduce opportunities for adaptation.

The disease is not always exhibited in an increase in the regularity of fluctuations. It might also lead to the extreme irregularity of changes, which, however, do not meet the criteria for non-linear chaos (Goldberger et al., 2002). Recent clinical study verifies that increasing age is associated with a reduction in the overall heart rate variability and complexity of physiological dynamics (Takahashi et al., 2012). These data were obtained using a Shannon entropy, conditional entropy, and symbolic analysis. In the aging process, the distributions of Shannon entropy patterns remained similar to younger subjects. At the same time, the patterns were more repetitive in the old group, indicating a marked change of autonomic regulation. A decrease in complex variability in the temporal patterns of heart rate that accompany aging and disease has been attributed to a breakdown of the underlying regulatory feedback mechanisms.

The fractal scaling showed disturbance in conditions associated with the disorder of breathing and obstructive sleep apnea (Goldberger, 1997; Goldberger et al., 2002). Recently, the band-limited transfer entropy analysis revealed a reduction in the high-frequency contribution of respiration to heart rate complexity with normal aging (Nemati et al., 2013). A fractal scaling in stride interval showed a reduction in the elderly. This was also reported for patients with pathological human walking (Dingwell and Cusumano, 2000) including PD (Hausdorff et al., 1997) and HD (Bilney et al., 2005).

Electromyography reflects the activity of the spinal motoneurons. As a non-linear signal, the surface electromyogram displays chaotic behavior and has a fractal dimension (Nieminen and Takala, 1996). The non-linear parameters of surface electromyogram signal in the PD patients significantly differ from the electromyogram in the healthy control persons (Meigal et al., 2009). Recently, Meigal et al. (2013) reported that the non-linear characteristics of surface electromyogram and tremor acceleration may have a possible diagnostic and predictive value for patients with PD.

The reduction in the multiscale complexity of the background brain activity has been shown in schizophrenia (Kotini and Anninos, 2002; Takahashi et al., 2010), epilepsy (Saermark et al., 1989), AD (Besthorn et al., 1995; Stam et al., 1996; Abásolo et al., 2005; Hornero et al., 2009), and PD (Stam et al., 1995; Anninos et al., 2000).

Three major effects of AD included slowing of the EEG, decrease in the EEG complexity, and disturbances in the EEG synchrony (Dauwels et al., 2010). Strong statistical evidence was obtained for a weak non-linearity in EEG in schizophrenia. Recent advances in methodology allow assuming that the "non-linear theory" of schizophrenia may be useful for the understanding of this disorder (Breakspear, 2006).

A branched vascular network of the normal human retina showed statistical self-similarity, exhibiting the properties of fractals (Family et al., 1989; Mainster, 1990; Daxer, 1993, 1995; Avakian et al., 2002; Masters, 2004). Several research groups presented strong evidence that the fractal dimension of blood vessels in the normal human retina is about 1.7. In many publications, the fractal analysis of the human retinal vasculature at different stages of DR showed mixed results (for review see Zueva, 2014). The contradictory results may occur because the study design was not always adequate to answer this question. The studies did not have the specific aim to determine the correlation between the fractal dimension of the retinal vasculature and the stage of retinopathy. For example, in a large cohort of diabetic patients with the early stages of DR, the fractal dimension of the retinal vasculature was analyzed in association with the presence or absence of signs of retinopathy (Cheung et al., 2009). However, these data usually were not compared with the fractal dimension of the retina in healthy individuals without diabetes. At the same time, the presence of diabetes, even in the absence of signs of DR in the fundus, can, possibly, lead to the alterations of anatomical structures, including the vascular network.

The reduction in the complexity of a dendritic branching and length in magnocellular and parvocellular layers of the lateral geniculate nucleus was recently discovered when modeling glaucoma in adult non-human primates (Ly et al., 2011). Blockade of *N*-methyl-D-aspartate receptors with memantine attenuated a decrease in the dendrite complexity and length in the relay lateral geniculate nucleus neurons in primate glaucoma (cited from Ly et al., 2011). Destruction of the dendritic branching is one of the characteristics and a potential mechanism of neurodegeneration not only for glaucoma. In AD, it may induce infringement of architecture of neural networks (Moolman et al., 2004). Disturbances to dendrite branching can disrupt the neural network organization and lead to the neural dysfunction, as in human neurological disorders including AD.

Hu et al. (2009, 2013) reported recently that in the AD patients with dementia, a parallel destruction of circadian rhythmicity and fractal patterns of activity is more pronounced in patients with greater quantity of amyloid plaques. These authors also showed in postmortem investigation that the degree of disruption in fractal activity is strongly associated with vasopressin and angiotensin-ergic neurons in the SCN. It suggests that the SCN affects the regulation of human action at multiple temporal scales and that the alterations in the fractal activity can be non-invasive biomarkers of neurodegeneration.

The Fractality of Art

Fractal Architecture

Works of art created by man may also have fractal properties. Mandelbrot (1982) was the first who tried to distinguish the architectural styles in Euclidean and fractal geometry. The basic properties of fractal structures such as a self-similarity, fractional dimension, recursiveness, and discontinuity, were used in architecture by Peter Eisenman. Jencks, Kavannagh, Johnson, and Crowe also used them in their works (cited from Oswald, 2001). Oswald (2001) focused on 20 years experience in the implementation of fractal geometry in architecture and the main trends in the development and history of acceptance and rejection of the fractal concept. He presented an overview of the rise and fall of the fractal architecture in the late 20th century, noting prominent examples of historic buildings that exhibit fractal forms. Many historic buildings demonstrate an intuitive understanding of fractal geometry but do not constitute consciously created fractal architecture. They include medieval castles, Baroque churches, and Hindu temples. Oswald (2001) noted as an intuitive type fractal design also the works of Frank Lloyd Wright and Louis Sullivan. A project of Peter Eisenman 'House 11a' has been the first example of architectural art that uses the concept of fractal scaling.

Some examples of folk architecture, which were built by people at different times around the world, have fractal properties (Bovil, 1996; Batty, 2005). One can assume that the most beautiful cities in the world are fractals (Batty, 2005), including a plan of the city, streets, building facades and landscaping plan. The fractal approach would allow making housing that adapts naturally to the needs of residents in the growth and transport (Frankhauser, 2008; Harris, 2012; Parashar and Bandyopadhyay, 2014). Architect James Harris explicitly notes that high-rise housing and high-density architecture can lose their usefulness in the modern city and is limited to individual cells, as in a prison or in a computer that controls the world. He also noted that similar to 'as the trees spread their leaves to catch the sun, cities have to unfold to give people the air and open space' (Harris, 2012). Lu et al. (2012) reviewed recently the basic concepts of chaos theory and fractal geometry required for the architecture design, which can anticipate changes in the environment, providing adaptability and flexibility over time.

Fractal Painting

Art and musical compositions can also have a fractal dimension. An iterated function system is commonly used for generation of fractal art. However, the fractal pictures appeared long before the concept of deterministic chaos (Briggs, 1992; Barnett, 2009). These famous paintings include "The Great Wave off Kanagawa" by Katsushika Hokusai, abstract painting by Jackson Pollock "Blue Poles: Number II," an abstract landscape by the Jenifer Bacon and Gottfried Mayer-Kress "Canyons and Mesas" (cited from Barnett, 2009; see also Taylor et al., 2002, 2006). Pollock dripped paint from a can onto vast canvases. Analysis of his patterns showed that they are fractals as "fingerprint of nature" (Taylor et al., 2002, 2006). Drip painting of Pollock has been attributed to the "Fractal expressionism."

Just as is the case in architecture, paintings of many artists seem to be fractals, despite the fact that they could not know about it. When creating fractal art an artist draws fractals, but does not create them using his computer. Forsythe et al. (2011) considered the visual complexity for some time as a predictor of the significance of artistic works. This study detected the extent to which the perceived complexity of visual art can be successfully predicted using automated measurement of complexity. As the most successful predictor of visual complexity, Forsythe et al. (2011) noted GIF compression. Interestingly, the value of the fractal dimension had a larger dispersion in judgments about the perception of beauty in visual art than in the measurement of only the visual complexity, especially for abstract and natural images. Their findings also showed that the removal of color from the artistic image made observers unable to create a meaningful judgment about its beauty (Forsythe et al., 2011).

Fractal Music

As well as for the fractal painting, fractal music can be a created intuitively fractal (in fine art), or can be created artificially by various methods. Hsü and Hsü (1990, 1991) have found that the change of acoustic sound in the compositions by Bach's and Mozart's has the fractal geometry. More recently the fractal dimension of different kinds of music (rock, traditional, classical music, and others – 180 scores) Bigerelle and Iost (2000) analyzed in keeping with the time domain. They showed that the fractal dimension helps to distinguish between categories of music; i.e., music can be classified by their fractal dimensions according to its dynamic aspects. Earlier, there was revealed with the fractal motion method that the "best-sounding" music has a fractal dimension near 1.4 (Hazard et al., 1998–1999).

The Plasticity of the Brain and Sensory Experience

Brain Plasticity and Multimodal Integration

Neuronal plasticity occurring in the sensory and motor systems is the amazing ability of the brain that allows adapting to the constantly changing world during early development, and also in young and older adults. At all levels of the CNS, plasticity may be caused by the loss or excess of mono- and multimodal stimulation and injury. It can occur as the consequence of non-use or over-use, and learning new skills (cited from Moucha and Kilgard, 2006).

Neuroplasticity refers to changes in the neural circuits and synapses, including migration and integration of new neurons, neurite outgrowth, synaptogenesis, and the modulation of mature synapses. These occur in a variety of CNS levels due to changes in external and internal environment (He et al., 2006; Pascual-Leone et al., 2011; Wainwright and Galea, 2013). These changes can develop due to the injury to the brain with large-scale cortical remapping, and alterations in behavior, emotions, and thinking.

Neuroplasticity is known to play a significant role in the development, learning, memory, and in recovery from brain injury. Developmental plasticity includes changes in neural connections due to brain/environment interactions, and cellular changes induced by learning. The predominant mechanisms of plastic alterations in CNS, which occur during development, include synaptic and homeostatic plasticity, and learning. Most synapses are highly plastic, and they change their strength under the influence of its activity and other forces. Synaptic plasticity is believed to play a role in the mechanisms of learning and memory (Black, 1998; Foehring and Lorenzon, 1999). Long-term potentiation and depression (synapse-specific Hebbian forms of plasticity) are related to the processes that regulate overall levels of neuronal and network activity. The experimental research has found several mechanisms that apparently monitor the levels of activity, such as a spike-timing dependent plasticity, synaptic scaling and synaptic redistribution (Abbott and Nelson, 2000). Homeostatic plasticity modulates the neural circuit activity and changes in the synaptic strength (Wierenga et al., 2006; Butz et al., 2009). So, it regulates the destabilizing effects of developmental and learning processes.

The brain is very plastic in its early development, but previously it was assumed that plasticity decreases throughout life, and the structure of the brain is relatively unchanged over the critical period during early childhood. However, this concept has been subjected to large revisions after numerous subsequent studies that have found various manifestations of the adult brain plasticity (Dragoi et al., 2000; Chen et al., 2011). The human brain is constantly changing, being in a state of reshaping each moment of the life (Eysel, 2002, 2009; Gilbert and Li, 2012; Sur et al., 2013). Moreover, the results of recent studies suggest that the development of cortex structure is never completed but shows continuing changes, which are intelligence-dependent (Schnack et al., 2014).

Neuronal plastic changes, which never stop, are studied the visual cortex. Experimental studies in animals indicate that visual cortex exhibits considerable plasticity during development (Hebb, 1947; Hubel and Wiesel, 1970; Gordon and Stryker, 1996; Espinosa and Stryker, 2012; Nagakura et al., 2013). Plasticity is also was found in adulthood (Dragoi et al., 2001; Chen et al., 2011; Rosa et al., 2013). Plasticity in the early development and in the adult visual cortex was hypothesized to share certain universal principles although mature synapse plasticity requires additional neurotransmitter-dependent mechanisms that alter inhibition and subsequently the response gain (Sur et al., 2013).

Spontaneous network spike activity in the brain and retina plays a significant role in the initial establishment of synaptic connections during development. It may establish a basis for subsequent learning and further refinement of neural circuits and brain connectivity. For example, spontaneous network activity in the retina prior to birth has been found to cause the formation of retinogeniculate connections (Feller, 2009). During critical periods in development, changes in the structure and function of developing neuronal circuits can be experience-dependent or independent of the environmental experience but undergo the influence of endogenous or exogenous factors (Black, 1998). After the critical periods, many factors guiding brain development, such as growth factors, have been shown to be downregulated. But they can be upregulated again in adulthood in response to lesions for re-activation of neuroplasticity (cited from Eysel, 2009). The adaptive plastic changes in the adult's brain are typically space-limited to the level of axonal terminals and synapses. Therefore, the formation of new functional connections can be done by strengthening or weakening of existing synapses in the network (cited from Eysel, 2009). The neuronal reorganization will take place if the environment is modified during early stages of development, for example, following visual deprivation through eyelid suturing, or dark-rearing (Bengoetxea et al., 2012).

The ability to simultaneously use signals from several senses at the same time (in their synergy) is a fundamental aspect of the brain functioning. Multisensory integration, which synthesizes all details of the currently accessible information, provides a complete picture of the outside world. Development of multisensory integration occurs by the principles of associative learning. The ability to integrate different sensory information evolves as neurons acquire experience with the co-active cross-modal inputs (Yu et al., 2010; Xu et al., 2012; Stein et al., 2014). As an example, in the cortex of the cat, the maturation of healthy multisensory integration has occurred over an extended period of postnatal life. An experimental study in cats reared from birth to adulthood in the dark demonstrated that sensory experience is necessary for the maturation of the cortex multisensor circuits (Carriere et al., 2007). In the absence of multimodal experience, neurons do not develop the ability to integrate their inputs although capable to respond to multiple sensory modalities. The bond of different sensory channels with each other is absent in neonates. The emergence and maturation of multisensory integration depend on the content of the early sensory experience, changing and optimizing neural networks in the brain for the adaptation of animals and humans.

There is an increasing experimental evidence that sensory deprivation is associated with cross-modal neoplastic changes in the brain. Upon visual or auditory deprivation, brain regions that typically are associated with these sensory modalities begin to involve the intact sensory modalities (Wallace et al., 2004; Wallace and Stein, 2007; Merabet and Pascual-Leone, 2010; Mereditha et al., 2012). In dark-reared cats, a recent study has revealed significant modifications in temporal dynamics of the receptive field structure and the integrity of superior colliculus multisensory neurons. These modifications included discharge duration, peak and the average rate of spiking, as well as significant changes in the frequency of spontaneous activation and the degree of multisensory integration (Royal et al., 2010). These authors performed an extracellular recording of electrical activity of neurons in the multisensory deep layers of the superior colliculus in kittens reared in complete darkness until adulthood and then returned to the usual environment for an equivalent period. The results emphasized the importance of early sensory experience in the establishment of normal architecture of multisensory processing and highlight the plastic potential of adult multisensory circuits.

Cross-modal experience in the early period of animal life is likely to define the integration of stimuli of different modalities. Periodical exposure of cats reared in darkness to visual and auditory stimuli appearing randomly in space and time was insufficient to encourage maturation of the ability for cross-modal integration. At the same time, the exposure to spatiotemporally concordant cross-modal stimuli was very efficient (Xu et al., 2012). In a recent investigation, animals were also reared in the constant omnidirectional noise. Xu et al. (2014) tested whether cross-modal co-activation is sufficient for visual-auditory superior colliculus neurons integration or a co-variation experience is needed. The data testify that experience with covarying stimuli is the critical factor for multisensory maturation, maybe not only in the superior colliculus, but throughout the brain. It also indicated that disturbances in one sensory modality can have an adverse impact on the ability of the brain to associate multisensory information, which was shown earlier for perturbation of visual sensitivity. In the patients deprived of early visual input by bilateral congenital cataracts the alteration in the development of multisensory functions after a period of visual deprivation has been shown (Putzar et al., 2010). In this study, the cataract patients exhibited impaired audio-visual interaction compared to normally sighted controls.

It suggests that visual input is a prerequisite in early infancy for healthy development not only of visual, but also of multisensory functions.

Original and review reports (Rapp and Heindel, 1994; Grady, 2008; for review, see Mozolic et al., 2012) and a meta-analytic review (Rhodes, 2004) have shown that widespread changes in the anatomy of the white and gray matter, neurochemistry, and functional activity occur in the aging human brain. These changes correlated to significant changes in all sensory systems. Multisensory integration also alters with age. Surprisingly, neurons retain sensitivity to cross-modal experience late in life, far after the normal developmental period for acquiring multisensory integration capabilities (Yu et al., 2010).

Studies of various design have shown that the multisensory processing provides larger improvement of performance in older than in younger adults (Helfer, 1998; Sommers et al., 2005; Laurienti et al., 2006; Peiffer et al., 2007; Diederich et al., 2008; DeLoss et al., 2013). Using a two-choice audiovisual discrimination task, Laurienti et al. (2006) showed larger improvement of response time for multisensory target compared to the mono sensory purpose for the elderly than for younger adults. Diederich et al. (2008) analyzed saccadic reaction time in older and younger adults to the switch-on visual stimuli presented with and without an accessory auditory stimulus. The responses in elderly subjects were considerably slower than in the more youthful observers. However, the decrease in mean response time to bimodal stimuli compared to the single visual stimuli was more prominent in the elderly participants (Diederich et al., 2008).

Visual cortex plasticity results from a complex interplay between the individual's genetic background and the environment (Maya-Vetencourt and Origlia, 2012). Childhood environment effects, favorable or unfavorable, such as childhood neglect, interfere with all the development processes of the CNS. These events include neurogenesis, the formation and branching of neuronal processes, synaptogenesis, refinement of synaptic circuits, and myelination. The development of synaptic pathways usually occurs by the rule "use it or lose it" (Perry, 2002; Shors et al., 2012). That is, not only genetic, but also environmental aspects ("nature and nurture") influence these neural processes.

Neuroplasticity in Aging and Disease

Brain aging is believed to be reversible because the brain can re-structure itself through learning experiences, being plastic at all stages of life (Mahncke et al., 2006). Adult education and participation in different training activities are considered to be essential for the extension of the mental health (Guglielman, 2012).

Amblyopia

The insufficient multi-sensory experience is believed to play a crucial role in the pathogenesis of amblyopia. This developmental disorder occurs during a period of neural plasticity and is often considered irreversible in adults (Holmes and Clarke, 2006; Barnes et al., 2010).

Bonaccorsi et al. (2014) reviewed recently current experimental studies dedicated to the recovery of neuronal plasticity in amblyopia. The results obtained in the rat model have hinted at a wide potential of visual perceptual learning for recovery of vision in adult amblyopic subjects.

Clinical research also found a significant degree of plasticity in the visual system of the adults with amblyopia (Levi and Polat, 1996; Polat et al., 2004; Levi, 2005). A prospective, randomized, masked, controlled study provided a high evidence that the perceptual learning lead to a twofold improvement in contrast sensitivity and visual acuity (Polat et al., 2004).

It suggests that perceptual learning reflects alterations in early neural processes localized beyond the site of convergence of the two eyes. Perceptual learning was assumed to operate via a reduction of internal neural noise and through more efficient use of the stimulus information (Levi and Li, 2009; Freiherr et al., 2013). A brief period of video-game play improved substantially various spatial vision functions of low-level and high-level visual processing, including visual acuity, spatial attention, and stereo acuity (Li et al., 2011).

Understanding the factors that predetermine the critical periods and principles of their opening and closure is expected to form the basis of new methods of therapy aimed at the improvement of visual deficits in children and adults with amblyopia. Such methods include ways for decreasing the levels of inhibition (Wong, 2012), constraint-induced therapy training (Taub, 2010; Taub et al., 2014), and many others.

The Aging Brain

Cognitive decline is accepted to be a common phenomenon during aging. There is also an alternative hypothesis that cognitive performance in old age may reflect the consequences of learning on information processing, being related to increased knowledge (Ramscar et al., 2014).

On the other hand, stereological principles of cell counting helped to reveal that changes that occurred during normal human aging were region-specific and more subtle than previously believed (reviewed by Burke and Barnes, 2006). These authors presented a systematic review of recent experimental and clinical studies on animals and human. The significant cell loss does not occur during normal aging. Plastic changes in dendritic complexity (dendritic branching and length) were even greater in aged individuals than in younger adults, and than in patients with senile dementia (Buell and Coleman, 1979; West, 1993). Burke and Barnes (2006) have reviewed functional alterations that occur during normal aging in the medial temporal lobe and the prefrontal cortex. Based on the data discussed, the authors suggest that the loss of neurons does not significantly contribute to age-related cognitive impairments. Alterations in synaptic connectivity and plasticity, Ca^{2+} homeostasis, gene expression, and network firing properties were found to contribute to the selective behavioral deficits observed in advanced age (Burke and Barnes, 2006).

Mahncke et al. (2006) define four main interrelated factors that determine the process of inevitable degradation of the brain. The authors note that reduced schedule of brain activity, noisy processing, weakened neuromodulatory control, and negative learning – all promote plastic changes in the brain and functional decline. With aging, significant changes occur in all sensory systems and the low-level and high-level cognitive functions are involved (Mozolic et al., 2012). Progressive losses in function across multiple systems accompany the changing of multisensory integration.

Several studies have reported recently that older participants showed greater multisensory integration relative younger subjects (Mahoney et al., 2011, 2014; Freiherr et al., 2013). It occurred despite the continuing attenuation of function of the individual sensory systems. One possible mechanism that can explain this phenomenon is the principle of inverse effectiveness. This event stated that as the responsiveness to distinct stimuli (unimodal performance) decreases, the strength of multisensory integration increases (Stein and Stanford, 2008; Holmes, 2009). Mahoney et al. (2011) first proved the facilitative effect of pairing somatosensory with visual stimuli in older adults. In their investigation, younger and older adult observers responded to randomly present unimodal stimuli (auditory, visual, somatosensory) and paired multimodal stimuli (auditory-somatosensory, auditory-visual and visual-somatosensory). The reaction time was significantly smaller to multisensory than to unisensory stimuli in both groups. Nevertheless, older adults showed greater shortening of the reaction time when processing visual-somatosensory information while younger observers demonstrated a significant increase in multisensory integration for auditory-visual and auditory-somatosensory stimulation.

Age-Related Diseases

Wilbrecht et al. (2010) have shown in electrophysiological experiments in rodents that the ability of neurons to adapt in response to the impact of internal and external signals depends on their plasticity. The electrophysiological and biochemical studies performed in experimental models have found that dopamine in the basal ganglia plays a crucial role in regulating long-lasting changes in synaptic strength (cited from Calabresi et al., 2009).

In humans, different aspects of neural plasticity have been independently associated with or contribute to the disease state (Wainwright and Galea, 2013). It was assumed that disturbance of neuroplasticity played a central role in such neurological disorders as PD and AD (Lewis and González-Burgos, 2008; Hu et al., 2009; Varea et al., 2012). Understanding the mechanisms of the plasticity of the adult's brain related to multisensory experience and brain injury or degeneration may have high clinical and social relevance including the development of new ways for the reactivation of neuroplasticity.

The theory, which links cognitive changes typical of normal physiological aging to a functional distortion in the dopamine system projection to prefrontal cortex, is known (Braver and Barch, 2002). According to this theory, alterations in dopamine system function and then abnormal prefrontal cortex activation do impact on cognitive control, including working memory, attention, and inhibition. Dopamine plays a role in modulation of cell excitability and synaptic plasticity. Therefore, dopamine-dependent corticostriatal plasticity was suggested to underly the long-duration motor response to dopamine replacing therapy in the patients with PD (Zhuang et al., 2013). Patients with PD have disturbances in the perception and estimation of time (Parker et al., 2013). Dopamine deficiency in PD triggers the degenerative process associated with adaptive changes in neuronal networks. These changes include a compensatory overactivity of remaining dopamine neurons and functional or structural remodeling in other neuronal systems (Zhuang et al., 2013). The long-term dopamine-replacing therapy can trigger adaptive phenomena or, on the contrary, the appearance of side effects. Therefore, learning the mechanisms of neuroplasticity in PD and response to the therapy is necessary for the elaboration of more effective targeted therapies.

Several studies described functional plasticity of retinal ganglion cells in glaucoma, optic neuropathy of different genesis, and other retinal pathologies (Weber and Harman, 2008; Porciatti and Ventura, 2012).

Pattern electroretinogram reflects the electrical activity of retinal ganglion cells. Clinical and experimental findings suggest that PERG may be altered long before the reduction in the retinal nerve fiber layer (Porciatti and Ventura, 2012). Porciatti and Ventura (2012) used the concept of neural plasticity to simulate the reversible/inducible changes in the PERG during the critical period (stage of retinal ganglion cell dysfunction), which precedes their death. Zhou et al. (2014) suggested that retinal glial cell activation induced by acute high intraocular pressure may cause the process of retinal synaptic plasticity through affecting the expression of synaptophysin and other synaptic proteins. In the rat model of acute ocular hypertension, the increase in expression of synaptophysin across the retina was observed from the inner to the outer plexiform layer. Therefore, glial cells can be a new target to modulate retinal synaptic plasticity after retinal injury.

Non-Drug Ways to Reactivate the Plasticity of the Adult Brain and New Prospects for the Use of Sensory Stimuli with Non-Linear Temporal Structure

An 'Active Life' and Environmental Enrichment

Numerous works have shown the ability to reactivate adult's neuroplasticity in a variety of ways (Maya-Vetencourt et al., 2008, 2011; Spolidoro et al., 2011; Prakash et al., 2014). Various studies have been developed to understand how physical activity and exercise influence the brain functioning, to identify mechanisms by which exercise can protect them, maintain and restore. Particular attention was paid to the training impact on the structure and function of the hippocampus (Shors et al., 2001, 2012). Neurons are continually born and added to the dentate gyrus throughout life (Altman and Das, 1965). However, aging causes changes in the hippocampal neurogenesis that may lead to cognitive decline with age (van Praag et al., 2002). The brain injury early in the development was shown to contribute to the emergence of health problems that manifest itself only in old age (Barnes, 1994; Grossman, 2014).

Physical activity seems to enhance the synaptic plasticity, increase vascular network complexity, and levels of neurotrophins (Shors et al., 2001). The known paradigm of training, based on the plasticity of the aging brain was designed by Mahncke et al. (2006), Merzenich (2013). The authors postulated that in order to reactivate the brain plasticity, the older people have to be involved in the intensive complex activity. Intense activity apparently strengthens neuromodulatory systems, increases reliability and power of cortical representations, and learning management in adults. Using of training programs based on brain plasticity showed that older adults could quickly learn and significantly improve memory (Mahncke et al., 2006; Smith et al., 2009; Berry et al., 2010). The training programs also enhanced the task performance in people with schizophrenia and other mental disorders (Fisher et al., 2009; Merzenich, 2013). Chapman et al. (2013) proved that cognitive training – the complex mental activity – also induces the neuroplasticity in healthy elderly subjects.

Mora et al. (2007) suggest that physiological aging occurs asynchronously in different areas of the brain. They also hypothesized that the impact of aging on the neurons, dendrites, synapses, molecular and functional plasticity can be modulated by environmental factors even in adults (Mora et al., 2007). EE is considered to be one of the promising methods for the reactivation of the adult brain plasticity. In the EE experimental paradigm, the animals are placed in an enrichment environment. The EE allows obtaining a much greater stimulation of cognitive, motor and sensory activity than standard laboratory conditions. Recently, Alwis and Rajan (2014) critically analyzed this experimental paradigm. In an early development and adulthood, EE profoundly affects the animal brain at the functional, anatomical and molecular level (Kempermann et al., 2002; Nithianantharajah and Hannan, 2006, 2009; Butz et al., 2009; Baroncelli et al., 2010, 2012; Sale et al., 2012). Short-term exposure to the EE leads to a significant enhancement of hippocampal neurogenesis associated with a substantial improvement in cognitive performance (van Praag et al., 2000, 2005; Kempermann et al., 2002). It makes it possible to suggest that the active interaction with the outside world may mediate its positive effects on the brain function through the impact on neuroplasticity. Kempermann et al. (2002) have reported that hippocampal neurogenesis in adult mice that lived in EE for 10 months since the age of 10 months was fivefold higher than in the control mice. It was accompanied by an improvement in locomotor activity and learning efficiency, exploratory behavior. However, the authors noted that the concept of EE in studies with inbred rodents cannot be easily applied to the human conditions.

In rats and mouse models, amblyopia can be induced by monocular deprivation during early development. It has been shown that adult amblyopic rats transferred to an EE setting for 3 weeks undergo a full recovery of visual functions (Sale et al., 2007, 2012). Restoration of plasticity in enriched animals accompanied a threefold reduction in GABA release, and the beneficial effects of EE were eliminated entirely by intracortical infusion of benzodiazepine diazepam. These findings emphasize the crucial role of GABAergic transmission reduction in the manifestation of these effects of EE. Insulin-like growth factor 1 involved in neurogenesis, neuronal differentiation, and synaptogenesis, can reactivate the experience-dependent plasticity of the visual cortex in adults by reduction of local GABA levels (Maya-Vetencourt et al., 2012).

The effectiveness of physical exercise and increase of social interactions and visual stimulations in the restoration of visual function has been studied recently in adult rats with amblyopia (Baroncelli et al., 2012). The equally good result, which consisted in restoration of the ocular dominance and visual acuity, was obtained for the intensive motor activity in a running wheel. The exposure of rats to an optical EE using a rotating fluorescent lamp for maximal stimulation of the V1 neurons also showed good results. The possibility to reactivate the adult visual cortex plasticity have been demonstrated in humans with amblyopia by usage of such EE approaches, as playing video games and visual perceptual learning (Levi and Li, 2009; Astle et al., 2011; Li et al., 2011; Green and Bavelier, 2012). Mainardi et al. (2013) summarizes the current ideas about the mechanisms of the environment-induced plasticity in the arcuate nucleus of the hypothalamus.

The correct combination of appropriate pharmacotherapy with the EE strategies was suggested to be a promising therapy for certain neurological disorders to improve an internal repair capacity of the brain (review by Foster et al., 2011; Sale et al., 2012). Foster et al. (2011) focused their recent study on the different lifestyle factors and possible pharmacological therapy aimed to reduce the risk for and to improve cognitive functions in mild cognitive impairment, AD, and other age-related disorders. Special attention was paid to the fitness training, which has the largest positive impact for executive (frontal lobe) functions (Foster et al., 2011).

Noise Therapy and Stochastic Resonance

The phenomenon of SR is believed to underlie the therapeutic effects of noise for the number of pathological conditions mentioned below. It refers to the general phenomenon observed in non-linear systems when the intermediate level of activity improves detection of subthreshold signals by maximizing the signal-to-noise ratio. This phenomenon is fundamental for the physical and biological processes (Wiesenfeld and Moss, 1995; Russell et al., 1999; Pakdaman et al., 2001; Moss et al., 2004). SR occurs in any system where detection requires passing a threshold. It is described as the consequence of interactions between non-linearity, stochastic fluctuations and a periodic force (Chialvo et al., 1997; cited from Korn and Faure, 2003). Experimental studies have documented that SR can control the firing rates in crayfish mechanoreceptors, frog cochlear hair cells, and other sensory systems of animals (cited from Korn and Faure, 2003). SR was also shown to occur at the level of ion channels (Bezrukov and Vodyanoy, 1995). Different other aspects of SR role in the nervous system have been discussed (Korn and Faure, 2003; Tokuda et al., 2010).

Continuous variations in the membrane potential of neurons in the CNS are known as “synaptic noise.” It occurs due to the summation of intermittent inputs from presynaptic cells and the unreliability of synaptic transmission (Brock et al., 1952). Synaptic noise has been first assumed to be stochastic (Calvin and Stevens, 1967; Shadlen and Newsome, 1998). It was later assigned to a deterministic phenomenon that reflects the chaotic behavior of afferent inputs (see Korn and Faure, 2003 for review). During the aging, there is an increase of endogenous neuronal noise. Its interactions with external input noise were investigated with a stochastic gain-tuning model (Faure and Korn, 2002; Li et al., 2006). With aging, the cognitive system has a larger internal neuronal noise and less plasticity. Li et al. (2006) have shown that if we stimulate the aging system, it continues to demonstrate the overall effect of SR, which requires more external noise.

We usually consider noise detrimental to cognitive performance, but the increase of knowledge about the phenomenon of SR gives reason to study the possible useful properties of the external noise in different situations. Addition of noise in non-linear systems can amplify the detection of a subthreshold signal. Therefore, the influence of the noisy environment on cognitive performance was studied with a neurocomputational model of attention deficit hyperactivity disorder (Söderlund et al., 2007). Participants were asked to perform a task to verify a mini-performance memory, verbal task to check the memory productivity, both in the presence and in the absence of auditory white noise. Authors found the positive impact of noise on cognitive function in the group with attention deficit hyperactivity disorder. This effect was explained by the phenomenon of SR, whereas the noise distorted performance in the control group (Söderlund et al., 2007). Authors proposed that the noise in the environment introduces an internal noise in the neural networks through the perception system and facilitates performance by inducing SR in the neurotransmitter systems. An important role of SR has been demonstrated earlier for dopamine signaling in the brain (Li et al., 2006).

Söderlund et al. (2007) suggested that an optimal (for different circumstances) amount of noise may be beneficial for cognitive performance, in particular in hypodopaminergic states. They suggested existence of a link between the effects of noise, dopamine regulation, and cognitive performance (Söderlund et al., 2007). Authors assumed that the noise inducing the effect of SR must be continuous and have high energy levels at all frequencies, as it takes place with white or pink noise. The computational model of the concept of SR predicted the positive impact of background noise on the attention and performance (Sikström and Söderlund, 2007). Individual differences in dopamine were supposed to handle individual differences in the noisiness effects (Sikström and Söderlund, 2007). Exposure to auditory background noise has been recently shown to improve cognitive performance in inattentive school children while it distorted the performance of attentive children (Söderlund et al., 2010). These findings suggest that there is the ability to control cognitive performance by using the background white noise stimulation (at least in children with problems of attention).

The positive effects of background noise were also found in the elderly (Priplata et al., 2003), in patients with PD (Yamamoto et al., 2005), and other neurodegenerative disorders (Priplata et al., 2003; Pan et al., 2008; Söderlund et al., 2010). These effects are consistent with the theory that links the cognitive changes characteristic of normal physiological aging with decreased function of the dopamine system projecting in the prefrontal cortex (Braver and Barch, 2002). It has been found that SR modulates neural synchronization within and between functionally relevant brain areas (Ward et al., 2010), which may be a general mechanism of the brain functioning.

The therapeutic approaches based on the SR have been used in the treatment of gait disturbance in the patients with neurodegenerative disorders. Randomly vibrating insoles were designed to ensure coordination and gait in the elderly, patients with diabetic neuropathy, and in the period of rehabilitation after a stroke (Priplata et al., 2003; Costa et al., 2007; Ross, 2007). This treatment improved the equilibrium sense and the gait control in patients subjectively, and it caused objectively a significant increase in the fractal dimension and the complexity of the step-to-step interval fluctuations. Old participants showed greater improvement than young people. It was shown that 24-h noisy galvanic vestibular stimulation may be useful in the amelioration of akinesia symptoms in patients with central neurodegenerative disorders (Pan et al., 2008). It implies the possible mediation of the beneficial effect through the known effects of the vestibular nerve on the basal ganglia and limbic system. The 24-h noisy galvanic vestibular stimulation was apparently effective in improving the long-term heart rate dynamics in patients with multisystem atrophy and the dynamics of daytime activity in patients with PD (Yamamoto et al., 2005).

Benefits of Music

Research and experience tell us that art can heal, change human physiology and perceptions of the world. Human behavior and physiology change from the state of stress in a situation of deep relaxation, from anxiety to inspiration, so we can assume that creativity alters brain function and our lives. Staricoff (2004) reviewed studies that examined how art affects human health. Her scientific report showed the positive role of different types of art in mitigating some pathological conditions and in the training of practitioners in the field of health.

Music is known to have different psychological and physiological impacts on humans, affects brain activity and EEG (Petsche, 1996; Yuan et al., 2000; Jausovec et al., 2006). Sink et al. (2011) by using fractal analysis and data mining techniques, found strong associations between a complexity of auditory signals in the form of synthetic music and the resulting multi-channel EEG responses. They noted that psychologists believe that there is a particular fractal dimensionality in nature. “When the incoming stimuli imitate this fractal dimension, the nervous system would resonate with this fractal dimension and show a particular pattern” (Sink et al., 2011). These authors suggested a significant mathematical association between auditory stimuli in the environment and physiological processes in the human body. Confirmation of this assumption would also be another valuable proof of our theory considering the importance of the multimodal external environment to maintain human health. Improving the perception of speech-in-noise is accompanied by neural changes in the auditory processing, which indicates the plasticity of the brain (Anderson, 2013). It allows the use of auditory training for individuals who have difficulties in perceiving of useful auditory information on the background noise. There were observed effects of music on the EEG power spectrum, closely related to man’s emotions (Yuan et al., 2000). Changes in the frequency components of the EEG power spectrum from the delta to the beta-2 band were analyzed in 16 regions in silence, during noise or when listening to music. A significant decrease was seen in the power of total alpha-1 while the power of total theta increased when listening to music.

Several studies have reported an increased spatial–temporal reasoning performance after listening to Mozart for 10 min, but not in all studies this effect was observed. Also, a positive impact was unstable and depended on spatial tasks (Jenkins, 2001). Jausovec et al. (2006) investigated the influence, which Mozart's sonata for two pianos in D major (K. 448) has on brain activity in the process of solving spatial rotation tasks. The data were compared with those in participants who before and after the training listened to Brahms' Hungarian Dance number 5. Those who listened to Mozart showed a better task performance than did the respondents of the relax group and Brahms' music groups. They also displayed less complex EEG patterns and lower alpha-1 and gamma-band synchronization. Therefore, Mozart's music, by activating task-relevant brain areas, can enhance learning of the spatiotemporal rotation tasks. The results support the priming explanation of the "Mozart effect."

Earlier, Gordon Shaw suggested that if the activity of the mind may sound like music, we can use music to stimulate the brain. The music may have effect by activating the firing patterns similar to patterns of sounding music (cited from Campbell, 1997; see also Rauscher et al., 1995). Rauscher et al. (1995) hypothesized that the effect of music on intelligence can be explained by the fact that the hearing of complex music excites cortical firing patterns, which are similar to those used in spatial reasoning. Other hypotheses were also proposed for an explanation of this effect of Mozart music (Roth and Smith, 2008). For over two decades, numerous studies of "Mozart Effect" have been carried out, which confirmed or refuted increased intelligence while listening to music by Mozart. These studies reported a temporary increase in cognitive skills, or could not find a statistically significant "Mozart effect" (Allen and Blascovich, 1994; Roth and Smith, 2008). So, the high-quality evidence that would satisfy the requirements according to GRADE guidelines is not yet available (Balshem et al., 2011).

Contradictory results may be a consequence of the insufficiently adequate choice of control groups and study design. As a possible explanation, we can assume that the short-term effects of music on performance and physiology of the brain may occur because virtually all researchers used passive listening to Mozart's music. This flaw in study design might predetermine the inconsistency in published studies. Perhaps in such circumstances the effect will vary in professional musicians and non-musicians, and people that differently perceive the music. All these factors will require experimental verification of the proper design. The impact of musical training on the solution of perceptual and motor tasks is associated with structural and functional changes that occur mostly in the brains of musicians compared to non-musicians (Bhattacharya and Petsche, 2005).

The results of various studies also encourage us to pay attention to the fact that the beneficial effect of music on the perceptual learning and higher cognitive functions depends on the severity of their initial distortion. Namely, the effects in older adults are better than in younger adults, and than in patients with neurodegenerative disorders performance improvement can be seen more frequently than in a healthy aging. Particular interest has recently attracted the impact of music on creative thinking and the role of the emotional state in our perception of the world.

The EEG data (Bhattacharya and Petsche, 2005; Fink et al., 2009; Fink and Benedek, 2014) and functional magnetic resonance imaging data (Kowatari et al., 2009; Berkowitz and Ansari, 2010; Ellamil et al., 2012) were used to characterize the creative thinking. These studies estimated the effects of musical improvisation, fine arts or other creative activity on the brain activity and functional connectivity in scientists and dancers. Creative ideation attracted an unusual pattern of neural processes that was not typical for traditional solutions (not originative) tasks (Kowatari et al., 2009; Berkowitz and Ansari, 2010; Ellamil et al., 2012). A relationship was found between the EEG alpha activity and creative thinking (Fink et al., 2009; Fink and Benedek, 2014). EEG alpha power varied depending on the creativity associated with the test requirements, and changed with the level of the individual capacity for creative thinking. The artists showed a much stronger synchronization in the short and long-delta range during the task of mentally creation of pictures, while non-artists showed improvement in the near-beta and gamma range (Bhattacharya and Petsche, 2005).

Interestingly visual perception of emotional stimuli was shown to be dependent not only on the prior knowledge, but also on the emotional state of the observer (Jolij and Meurs, 2011). Music can change the relationship between mood and visual perception. Apparently by manipulating top-down modulation of visual processing, music can ultimately alter the way we perceive the world.

The musical experience is believed to have a positive influence on the perception of speech in noise in young adults (Parbery-Clark et al., 2009; Kraus and Chandrasekaran, 2010). It was shown that compared with performance in young adults, the older musicians demonstrate an enhanced speech-in-noise perception (Parbery-Clark et al., 2011). This enhancement of speech understanding in the elderly is likely associated with a greater auditory-specific cognitive and perceptual performance. Previously, it has been also found that musical training reduces the age-related decline in hearing ability due to the enhancement of the central auditory processing (cited from Zendel and Alain, 2012). Musical experience downplays the reduction in neural precision (age-related delays in neural timing) that occurs during the natural aging process (Parbery-Clark et al., 2012).

Alain et al. (2014) analyzed recently the results of numerous investigations that describe the musical training benefits in the auditory cognition in young and elderly, including the creation of a mental representation of the auditory environment. The author paid attention to the results showing that musical training has a positive impact on neural mechanisms in young adults and exhibits long-lasting improvements in hearing and cognitive control. From these results, the assumption was made that musical training might counteract age-related changes in auditory cognition and delay the hearing decline that is commonly observed in aging.

The individualized piano instruction was reported to be an effective tool for prevention of age-related cognitive decline (Bugos et al., 2007). Many other studies testify that music training can be an effective strategy for rehabilitation of older people (Kraus and Chandrasekaran, 2010; for review see Kraus and White-Schwoch, 2014). However, the exposure to vocal or instrumental background (pleasant and arousing) music did not influence the verbal learning. It led the authors to suggest that participants ignored this background stimulation to focus on the verbal learning task (Jäncke et al., 2014). The background music was also used to distract the listener from the performance of the primary test (Salamé and Baddeley, 1989; Klatte et al., 1995; Parbery-Clark et al., 2009; Kraus and Chandrasekaran, 2010). But as we have noted above, the background white noise can improve cognitive function in inattentive subjects, but reduces the performance of attentive persons (Söderlund et al., 2010). Thus, we cannot exclude that the sign and strength of the impact of background music on cognitive function may also depend on individual characteristics, in particular, on the power of the internal neural noise. It seems important to check the probability an impact of these factors on the study result in the future research.

The healing effect of music on the auditory, visual and motor processing, cognitive and emotional state seem to be more prominent in different pathologies of the CNS than in normally aging individuals.

The observations suggest that music is likely to become a valuable tool in neurological rehabilitation. As an example, in post-stroke patients, even passive listening to music was shown to have the beneficial effect on memory and mood. Särkämö et al. (2008) demonstrated that everyday music listening during the early post-stroke stage can facilitate the recovery of cognitive functions and prevent the negative mood. Recently, Särkämö et al. (2014) found that after an acute middle cerebral artery stroke, regular listening to music can enhance cognitive recovery and improve mood. It also induces fine-grained neuroanatomical changes in the recovering brain. Authors performed a voxel-based morphometry analysis in patients with the acute stroke and after the 6-months period of rehabilitation. The patients listened to their favorite music or audio books or did not receive any material for an audition (Särkämö et al., 2014). Frontal and limbic areas in patients with the left hemisphere damage showed an increase of the gray matter volume greater in the musical group than in the verbal and in the control group. The remodeling of gray matter in the frontal areas correlated with enhanced recovery of cognitive functions. Both perceptual and motor timing showed improvement in patients with PD when using music cued gait-training (Benoit et al., 2014). This observation supports the idea that coupling gait to the rhythmic auditory cues in PD patients is based on a neural network involved in both the perceptual and motor timing.

Learning to play a musical instrument is very challenging, due to the involving of multimodal integration and higher order cognitive functions. In particular, active playing on a musical instrument can engage the sensorimotor system as well as the auditory system. Musical training involves simultaneously the motor system and a multisensory (auditory, visual, and somatosensory) perception. Very likely, it can serve as a useful model to study the multimodal brain plasticity in humans (Zatorre et al., 2007; Lappe et al., 2008; Herholz and Zatorre, 2012).

Fractal Stimuli and Physiological Functions

One should also pay attention to the facts, which may indicate the influence of non-linear fractal factors on the fractal gait dynamics. Fractal dynamics of physiological processes, as described above, is an essential feature of a healthy organism. Destruction of fractal dynamics, including the rhythm of the gait, characterizes aging and some neurodegenerative disorders. We suggested earlier that dynamic fractal flickering may be a useful tool in the search for non-linear dynamics involvement in the activity of a visual system. And it may be a possible basis for new diagnostics and treatment of neurodegenerative diseases of the retina and brain (Zueva, 2013).

The fractal patterns of gait can be changed by synchronizing the gait dynamics with the fractal temporal structure of stimuli. Several studies have showed this ability for auditory (Hove et al., 2012; Kaipust et al., 2013; Uchitomi et al., 2013; Marmelat et al., 2014) and visual stimuli (Rhea et al., 2014a,b). Recent works (Rhea et al., 2014a,b) revealed that fractal patterns in the step-to-step intervals significantly changed during walking on a fractal visual metronome (flashing red square). However, the participants were not able to adequately reproduce the persistent fractal pattern that the stimuli exhibited. The experiment consisted of three phases: walking without the fractal stimulus, walking during entraining to a fractal visual stimulus, and walking with no stimulus. The fractal gait patterns of healthy young adults became enhanced during the synchronization phase. The effect remained after entrainment in the post-synchronization phase. The discrete fractal stimulus was noted to affect the retention better, causing a more persistent gait pattern in synchronization phase as compared to continuous fractal stimulus.

The results obtained in patients with PD can be considered as an evidence of the role that the temporal structure of the cue is essential to the sign or power of their effects on the CNS. Walking with fixed-tempo Rhythmic Auditory Stimulation can improve many aspects of the gait timing in PD patients (reviewed by Thaut and Abiru, 2010; see also Hove et al., 2012). However, this stimulation has been found to reduce rather than to increase the fractal scaling of step-to-step intervals (Hausdorff et al., 1997). Moreover, the stride variability becomes synchronized around a single frequency (Delignieres and Torre, 2009). Conversely, Hove et al. (2012) showed that the dynamic characteristics of the stride interval fluctuation in patients with PD can be improved to a healthy 1/f fluctuation level using interactive rhythmic cues. These authors emphasized that patients and healthy participants rarely synchronized the dynamics of gait with a fixed tempo Rhythmic Auditory Stimulation. When the synchronization occurs, the fractal scaling of gait patterns decreased far from healthy 1/f levels.

Uchitomi et al. (2013) recently studied the PD patients that were tested in four experimental situations: with the interactive rhythmic cue, fixed tempo-cue, 1/f fluctuating tempo-cue, and no cues. There was a significant effect of interactive rhythmic cues – the gait fluctuations of the patients gradually returned to a healthy level reinstating 1/f fluctuation while this did not happen in other circumstances. In the condition of interactive WalkMate, the cue rhythm was changed in response to the subject's gait rhythms, that is, there was a mutual synchronization of the gait rhythms and cue rhythms via mutual entrainment. The authors suggest that mutual entrainment can facilitate gait relearning and expect a wider application of interactive rhythmic cues in the fields of rehabilitation.

In a review, 14 studies investigating whether a rhythmic auditory (music) cueing improves walking in patients with other neurological conditions than PD were analyzed (Wittwer et al., 2012). Moderate evidence of improving velocity and stride length in people with stroke due to gait training with rhythmic music were noted. Insufficient evidence for benefits of gait training using synchronization of walking to rhythmic auditory cues was found in HD, spinal cord injury, traumatic brain injury, dementia, multiple sclerosis, and normal pressure hydrocephalus. However, the authors suggest that the failure may be due to the poor methodological quality of some works (Wittwer et al., 2012).

Sejdić et al. (2012) studied the effects of different rhythmic sensory cues (aural, visual, and tactile) on the temporal dynamics of the healthy adult's gait. These authors showed the greatest auditory rhythmic signal impact on walking parameters. However, the visual cue had no statistically significant effect on the scaling exponent.

Hunt et al. (2014) conducted a special study to find out whether the temporal structure of the complex auditory cue has different effects on the temporal pattern of the target behavior. The authors showed the ability to control the auditory–motor coupling by sound signals of different colored noise, which shift the temporal structure of the fractal gait dynamics to the statistical properties of specific signals.

Music perception is a complex cognitive task that involves the integration of the various structural components of music (melody, harmony, rhythm, tempo, and others). Different neural correlates have been associated with the music perception (Platel et al., 1997; Schmithorst et al., 2005; Gomez and Danuser, 2007; Lin et al., 2014). Hadjidimitriou et al. (2010) studied the EEG signals including the Mu rhythm in groups of advanced music students and non-musicians on the movements during the sound and audiovisual stimulation. Music students showed a significantly greater sensorimotor response at the auditory stimulation compared to non-musicians. At the audiovisual stimulation, the results were similar in both groups.

It is essential to note that these findings, on the one hand, may indicate a predominant role of professionally adequate stimuli (auditory) for musicians playing on the instruments. And, on the other hand, they do not exclude a smaller role of audiovisual integration in the modulation of locomotor activity in healthy individuals. Further investigations may determine the impact of audiovisual and auditory stimulation in aging and pathological conditions involving a reduction in fractal scaling of gait patterns in musicians and non-musicians.

The Logical Substantiation of the Theory

Key Facts and Regularities Derived from the Analyzed Studies include the following Highlights

- Nature is full of non-linear fractals that surround us throughout our lives.
- Humans evolved in a non-linear world, gaining experience in a complex multisensory environment.
- Fluctuations of physiological rhythms of a healthy body have the fractal properties and can be described using the theory of deterministic chaos.
- The fractal regulation of physiological processes is impaired with age and in diseases. Aging and pathological conditions tend to cause a loss of the complexity of many physiological processes, and quite often – to strict control of their fluctuation.
- The reduction in the multiscale complexity of the brain's structure and activity characterizes the age-related neurodegenerative disorders of the brain and retina.
- Neuroplasticity plays a significant role in development, learning, memory, and in recovery from brain injury. Developmental plasticity includes changes in neural connections due to brain/environment interactions, and cellular changes induced by learning.
- The sensory deprivation that reduces or completely destroys the quality or quantity of a mono- and multisensory experience in the early brain development can alter the neural networks and functional connections that the brain continues to use in adulthood.
- At all levels of the CNS, adaptive or maladaptive plasticity may be caused by the loss or excess of mono- and multimodal stimulation and injury. It occurs as the consequence of a non-use or over-use or learning new skills.
- The brain plasticity decreases throughout the life, but the adult neuroplasticity can be reactivated in a variety of ways.
- The physical activity and exercise, cognitive training, increase in social interactions and visual stimulation, and other training programs related to the EE paradigm can re-activate the brain plasticity playing a crucial role in the improvement of cognitive function.
- Exposure to the auditory background (white) noise improves cognitive performance in inattentive people while it distorts the performance of attentive persons.
- The therapeutic approaches based on the SR improve the gait disturbance and cognitive performance in the patients with neurodegenerative disorders. Application of these approaches seems to be useful in the elderly and in the period of rehabilitation after a stroke.
- Architecture, painting, and musical compositions may have a fractal dimension.
- Listening to music and musical training have a positive impact on cognitive and motor functions, the brain activity, mood, and intelligence.
- Fractal patterns of gait can be changed by synchronizing the gait dynamics with the fractal temporal structure of

sensory cues. The more prominent effect was proven for interactive rhythmic cues, suggesting that mutual entrainment can facilitate the gait relearning effectively.
- The temporal structure of the complex auditory signal has different effects on the temporal pattern of the target behavior. Auditory–motor coupling can be controlled by sound signals of different color types of noise, which transfer the temporal pattern of the fractal gait dynamics to the statistical properties of specific signals.

Table 1 presents the summary of the current data, which are significant to the logical substantiation of the theory, and appropriate references.

Logical Conclusions that We Draw from a Comparison of Scientific Observations Gained in Various Fields of Research

The experience of human evolution in a non-linear world and the interactions of humans throughout their life with a non-linear environment permit us to assume that these factors underlie the brain plasticity resulting from this experience. These factors can underlie the management of external inputs through different modalities. We believe that not only the quality and quantity of sensory information, but its non-linear fractal structure in many spatial and temporal scales is important for the health of the brain and is involved in fractal regulation of biological rhythms.

Different studies have shown the principal ability to reactivate adult neuroplasticity in a healthy aging and age-dependent CNS pathologies in a variety of ways through learning experiences and physical exercise. So, it is logical to assume that this experience can be of greater benefit if it involves the interaction of sensory brain structures with mono- or multimodal stimuli having time-invariant fluctuations of their parameters. The fractal patterns of gait were shown to change by synchronizing the dynamics of gait with the fractal temporal structure of auditory rhythm and with interactive rhythmic cues. We assume that the fractal audio-visual and sensory-motor stimulation may involve other mechanisms of fractal regulation of body rhythms compared to the direct coupling (synchronization) of the rhythms discussed in the recent articles. More probable is that fractal audio-visual stimulation presents an effective way to improve sensory processing, cognitive and motor function through the reactivation of brain plasticity.

Art can heal, changing the human physiology and perceptions of the world. Nevertheless, the results are not the same in different studies. The short-term effects (or the absence of effects) of Mozart's music on the performance and brain physiology may be linked to the fact that all the researchers used the passive listening to Mozart's music. In other studies, the effects of musical training during the solution of perceptual and motor tasks were associated with structural and functional changes that occurred mostly in the brain of musicians when compared to non-musicians.

It is essential to note that these findings, on the one hand, may indicate a predominant role of professionally adequate stimuli (auditory) for musicians playing on the instruments. And, on the other hand, they do not exclude the smaller role of audiovisual integration in the modulation of locomotor activity in healthy individuals. Further investigations can probably determine the effect of audio-visual and auditory stimulation in an aging musicians and non-musicians, as well as in pathological conditions associated with a reduction in the fractal scaling of the gait rhythm.

Various studies also encourage us to pay attention to the fact that the positive effect of music on the perceptual learning and higher cognitive functions depends on their initial distortion. The effect is better for the elderly than young adults and patients with neurodegenerative disorders than in normal aging. The healing effect of music on the auditory, visual and motor processing, cognitive and emotional state seems to be more prominent in different pathologies of the CNS than in normally aging individuals.

Similar to the results of musical training, we should expect the less pronounced effects of different cognitive and perceptual training in young healthy compared to the elderly or individuals suffering from age-related diseases. The capacity of homeostatic mechanisms in a healthy subject should be apparently sufficient to withstand the environmental perturbations of moderate strength. Otherwise, the detection of a significant shift in the characteristics of sensory and motor functions in young healthy individuals perhaps would be more correctly considered as an evidence of potentially damaging rather than therapeutic effect.

We can also presume that fine arts and music created by great masters may have fractal properties and potential curative impact on the person who actively perceives these works by passing them through his heart and brain. On the other hand, active participation in creative activity can alter the brain functioning, and, as a result, change the life. The results that showed the effects of music on creative thinking and emotional state, which mediate our perception of the world, may evidence this assumption.

Background noise stimulation increases arousal and performance of inattentive people but reduces the performance of attentive persons. One cannot exclude that the sign and power of the background music impact on cognitive function may also depend on individual characteristics, in particular, the strength of the internal neural noise.

Factors that may Reduce the Complexity of the World Picture Painted by the Brain

The human brain needs to obtain the complex multi-sensory experience during a lifetime. The distortion or diminishing of our sensory experience may lead to a disruption of the perfect complex structure, connectivity and functioning of the brain in the early development, or may underlie neurodegenerative disorders in the old age. The inherent complexity of the human sensory perceptions and the integration of multimodal sensory information from the individual channels in a holistic perception of the world are well-proved now. It allows to suggest that for the healthy brain, maintenance and preservation of the complexity and rich diversity of environmental stimuli that accompanies humans from birth and throughout the life are also critically important.

In the surrounding world, the linear stimuli with the ordered temporal or spatial structure are not usually effectively affecting people because they are not typical for our natural habitat.

FIGURE 1 | The directions for future studies based on the theory of 'Fractality of sensations' to explore benefits of non-linear stimulation and a scope of its application.

However, there are situations in which we are subjected to a more or less prolonged exposure to monotonically structured artificial environment. Formation of these conditions might be related to private life conditions of a person. For example, in a risk category one can include the residents of cities with a limited diversity of the visible landscape, people with the reduced mobility and possibility to change scene – the disabled, chronically ill, institutionalized patients. In a separate group, one should include elderly subjects suffering from not only gait disturbance, but also having visual and hearing impairment. In the old age, there is a sharp narrowing of the diversity of experiences and a decrease in the total flow of sensory information available to man. It limits the perception of the complexity of the world around them.

Deficiency or loss of complexity of sensations and images created by the brain may occur under the following conditions:

(1) A decline in the intensity of light reaching the retina reduces or distorts the perception of geometric and dynamic fractals of nature.
(2) A decrease in image contrast alters not only the perception of the details of the observed object, but also its geometric complexity. In amblyopia associated with the reduction of subjective brightness and contrast of the image, one can expect the positive impact of the therapeutic fractal stimulation.
(3) In the cases of transparent optical media and standard eye refraction, the reduction of complexity of the images processed by the retina and brain, can apparently occur:

FIGURE 2 | Possible directions for future studies based on the theory of 'Fractality of sensations' to explore adverse effects of deficit in fractal stimulation.

- In the pathology of the retinal ganglion cells (glaucoma, optic neuritis of different etiology, etc.), when distorted information is sent by the retinal ganglion cells to the lateral geniculate nucleus and visual cortex;
- In pathological conditions, which alter the level of internal noise of the retina;
- In neurodegenerative diseases, such as glaucoma and AD, when the simplification of visual processing likely reflects the simplification of neural networks and loss of complexity in the functional activity of the brain and retina.

(4) The monotony of visual and other sensory features of the habitat:

- Low levels of life and culture: deficit of impressions and emotional experiences;
- Urbanization problems: deficit of diversity in architecture;
- Low levels of social communication: deficit of the diversity of experience;
- A monotonous work: deficit of creativity.

In all these situations, the diversity of living conditions can play an important role. The effect is expected to be greater when involving the multisensory integration.

Possible Applications and Future Research

The presented theory provides the basis to open new directions for scientific studies. These studies primarily should be designed to test the usefulness and validity of the assumptions that are closely related to and follow directly from the declared theoretical relationships. **Figures 1** and **2** indicate some directions for future studies based on the theory of 'Fractality of sensations' to explore benefits of non-linear stimulation and a scope of its application and adverse effects of deficit in fractal stimulation.

The efficiency of fractal visual and auditory stimulation in the improvement of cognitive functions and brain activity in pathological conditions is necessary to be estimated in the experiments and clinical trials of different designs (**Figure 1**).

One should compare the impact of mono and multisensory fractal therapy and the known effect of white noise described in the elderly, patients with PD and inattentive persons. It is desirable also to explore the possibilities of and indications for the combined use of fractal stimulation and noise therapy.

For children with amblyopia and older people with cognitive decline, it is especially important to ascertain the significance of the use of a fractal environment or fractal stimulation for preventive and curative purposes.

One should also explore another assumption related to the theory that exposure to artificial visual and auditory stimuli with strongly regular (not fractal) temporal structure may contribute to the reduction of brain function (**Figure 2**). The mechanisms of revealed adverse effects would be necessary to describe and explain.

It seems important to assess consequences of urbanization and positive impact of the new art in the architecture of the cities and their lighting to provide non-linearity of ambient human artificial environment closer to the natural conditions. The habitat change changes a man.

Future experimental and applied research in these and related areas could provide opportunities to confirm or deny the validity of the predictions contained in the theory.

Weaknesses in the Theory to Clarify in Future Studies

It is unlikely that all the wealth of sensations that a natural environment gives us is limited only to structures with the properties of temporal and spatial fractals. It is impossible to equate the world in all its diversity with a deterministic chaos in the nature. The spatiotemporal structure of various natural stimuli is diverse and may include low-dimensional rhythms, differing degrees of randomness. All the factors that accompany man in his evolution and the early periods of brain development have to play a role in the formation and self-organization of the CNS, and in the mechanisms of neuroplasticity. There is a marked difference between the passive human exposure to natural stimuli during the life and active perception of spatial–temporal stimuli. In the latter case, one should underline the significance of a dynamic behavior and creative thinking.

Existing knowledge does not yet allow us to assume how different the impact of the artificial fractal rhythms in comparison to white noise and cognitive and physical training on patients with amblyopia and neurodegenerative diseases can be. It seems most likely that the greatest potential benefit can be expected from the combination of these factors, which may vary for different pathological conditions, and this has to be substantiated and proved experimentally. One should explore how making a passive training effective for those who, for example, cannot play a musical instrument or actively enjoy music. The same problem may exist with the usage of artificial fractal stimulation that is always passive. It is interesting to investigate the similarity in the effects of passive listening to music and passive exposure to the fractal stimuli, and the impact of white noise.

Future studies should also answer the following distinct questions. What kinds of mono or combined stimulation will help to overcome the adverse effects of the increased level of internal noise in the sensory system and the brain of patients and the elderly? What are the mechanisms and laws of interaction of intrinsic neural noise and external noise? Clarification of these issues is expected to define or limit the range of conditions that best meets the rules formulated in the theory of "fractality of sensations."

Conclusion

We proposed for the first time in this article that temporal and spatial structures of visual and other sensory signals, which affect us throughout the life, are crucial for the normal development and aging of the brain. Conversely, the absence of fractal sensations is supposed to promote distortion of brain functioning and reduce the capacity of the adaptive plasticity.

Known facts related to different aspects of the problem have been considered. Described literature data and logical analysis allowed theoretical substantiating and formulation of a theory named "fractality of sensations." The theory establishes relationships between the normal functioning and pathology of the brain and visual system, and the spatial–temporal structure of the visual and other sensory stimuli that affect people throughout their life. The theory argues that the deficit or distortion of the fractal complexity of visual and other environmental influences may lead to anomalies of development and aging. Application of fractal flickering and other fractal rhythms helps to restore the function of the brain and visual system, particularly in the elderly, in patients with neurodegenerative disorders, as well as with amblyopia.

We outlined here possible applications, experimental and applied research, based on the key tenets of the theory, as well as the weaknesses of the theory, which need to be clarified in future studies. Since the average life expectancy increases, the prevalence of age-related neurodegenerative diseases is also steadily increasing. Thus, the creation of new non-pharmacological methods of therapy that may slow cognitive decline, as well as weaken the manifestation of neurodegenerative diseases is an imperative. Development of new practical training paradigms based on the principles outlined in the theory may be useful in the prevention of cognitive decline, treatment, and rehabilitation of various pathologies of the brain. Also, the fundamental tenets of the theory can be used to mitigate the social problems associated with the objective limitations of the fractal complexity of sensations in particular categories of people.

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