

Original Article

Correlations between U.S. county annual cancer incidence and population density

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Received October 10, 2015; Accepted October 14, 2015; Epub October 15, 2015; Published November 1, 2015

Abstract: Population density implicitly involves specific distances between living individuals who exhibit biophysical forces and energies. Objective was to investigate major data bases of cancer incidence and population data to help understand the emergent properties of diseases that become apparent only when large populations and areas are considered. Correlation analyses of the annual incidence (years 2007 to 2011) of cancer in counties (2,885) of the U.S. and population densities were convergent with these quantitative predictions and suggested an inflection threshold around 50 people per square mile. The potential role of subtle or even “non-local” factors coupled to averaged population density in the viability and mortality of the human species may serve as alternative explanations to the attribution of malignancy to “chance” factors. Calculations indicated average distances between the electric force dipole of the brains or bodies of human beings generate forces known to affect DNA extension and when distributed over the Compton wavelength of the electron could produce energies sufficient to affect the binding of base nucleotides. An inclusive science of human ecology might benefit from considering subtle forces and energies associated with the individual members within the habitat that could determine the probability of cellular anomalies.

Keywords: Cancer incidence, population density, coulomb forces, dna extension energy, public health

Introduction

The emergence of Human Ecology as exemplified by Bressler's [1] seminal text of that name altered the perspective of the contributions from the interactions between large populations and subtle environmental stimuli upon adaptation and biological viability. Although the effects of population density upon the development of disease and pathology have been documented since the time of Calhoun's [2] famous “galaxy” studies and there is a rich history of both correlation and experimental work involved with the contributory effects of different spatial proximities to a plethora of medical conditions [3], the relationship between one of the most enigmatic anomalous conditions, cancer, and human population density has been explored [4, 5], but not thoroughly beyond select regions [6].

The importance of population density for both morbidity and mortality was examined experi-

mentally in *Drosophila* decades ago by Milkman [7]. Flies maintained in population cages displayed higher proportion of mortality than was facilitated if empty spaces were provided. If placed in uncrowded conditions the flies were fertile and lived for several weeks. He found that this interesting phenomenon was dependent upon neither light nor age of the flies and that crowding was clearly the most important predictor. Here we present a potential contribution and the quantitative support to the variation in cancer incidence that could reflect recondite variables mediated by basic physical forces.

Cancer is often considered to be a disorder evoked by myriad stimuli that affect the DNA sequence of the cell's genome during replication or disrupts the active transcriptions to RNA equivalences that ultimately affect the protein structure and enzymatic function of the cell [8]. DNA damage can even occur during reversal apoptosis [9]. At the level of the molecular

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structure of double helical DNA the energy involved with the sequential addition of a base nucleotide is in the order of about 10^{-20} J. Gu, Xie and Schaeffer [10], reported that nucleobases have small electron affinities of 0.1 eV ($\sim 10^{-20}$ J) for thymine and cytosine. The vertical electron attachment energy for 2'-deoxycytidine-3',5-diphosphate, an important contributor to electron-capturing ability of single strand DNA, is 0.02 eV, or in the order of 10^{-21} J [10]. According to Avila, Gomez-Ramos and Soriano [11] insertion of a single base into a newly synthesized strand of replicating glia cells which does not match the antecedent ("parent") strand generates a mutation. Glia cells, particularly astroglia, constitute the greatest proportion of intrinsic brain tumors.

The quantities of energy associated with second shell hydrogen bonds that mediate the proton movement between hydronium ions, the action potential of the neuron, and the resting membrane potential of the cell are located within a narrow range of coefficients within the 10^{-20} J order of magnitude [12]. This quantity is associated with the sequestering of many ligands to receptors [13]. The emergence of the importance of 10^{-20} J as a fundamental increment of energy essential for living systems and its potential derivation from cosmological sources, derived from its emergence when the total force within the universe per volume of Planck's Length is multiplied over the distance of the neutral hydrogen line (21 cm), has been calculated [14].

More than 20 years ago Smith, Finzi and Bustamante [15] and later [16] it was demonstrated that the DNA molecule was extensible. The former researchers found that a force of only 2 to 3 pN (10^{-12} N) could stretch the DNA to 90% of its rest contour length. Previous estimates had indicated that DNA elasticity can sustain stretch forces of about 500 pN. A force of 2 to 3 pN applied across the width of a plasma cell membrane (10^{-8} m) would be approximately 2 to $3 \cdot 10^{-20}$ J. Applied across the somewhat thicker nuclear membrane, the energy would be increased by a factor of ~ 2 . In principle forces that could initiate such "distension" could affect transcription. There would be no requirement for protracted or permanent application of the force. Durations in the order of 1 or 2 kiloseconds, the critical periods during cell cycle, could be sufficient.

Excess correlations from "non-local" processes between distal clusters of malignancies have been demonstrated by recent experiments [17]. To accommodate any excess correlation between non-traditional distances between human beings that could affect these energies involved with the DNA components that contribute to anomalous divisions and ultimately to malignancy, we hypothesized that some variant of de Broglie's matter-waves [18] might exist that allows the interconversion between the width of the classical electron particle ($r = 2.8 \cdot 10^{-15}$ m) and its energetic waveform, the Compton wavelength of $2.4 \cdot 10^{-12}$ m. If a specific range of quantities of weak forces were applied over the latter distance the resultant energy of about 10^{-20} J would have the potential to affect DNA stacking or the serial quantifications of energy mediated through signaling pathways [19] that influence DNA activity.

According to the classic measurement of electric force between two sources, the relationship can be described as: $F = (q \cdot q) / (4\pi\epsilon)r^2$. Here q is the functional charge in A-s (Coulombs), ϵ = the permittivity of free space ($8.85 \cdot 10^{-12}$ F·m⁻¹) and r is the distance between loci, in this instance brains. For the human cerebral electroencephalographic activity, the typical variation involved with cognition is within the range of 40 ± 1 Hz [20]. Given about $1 \mu\text{V} \cdot \text{Hz}^{-1}$ [21] the functional value would be $3 \mu\text{V}$. The extracellular fluid within which the cells are immersed, the resistivity is $\sim 2 \Omega \cdot \text{m}$ [22] which results in 10^{-6} V·m⁻¹. When applied across the average linear distance of the human cerebrum (~ 11 cm), the net current would be $1.1 \cdot 10^{-7}$ A. Assuming this is the more or less constant current across one second, the value would be $1.7 \cdot 10^{-7}$ A·s.

Materials and methods

In our preliminary analyses, annual new cancer rates per 100,000 people for all races, sexes, and ages for approximately one-fourth (831) of the counties within the U.S.A. (12 states and one district) were obtained from the State Cancer Registry and the Centers for Disease Control and Prevention (CDC) National Program of Cancer Registries Cancer Surveillance System (NPCR-CSS) for the period 2007 to 2011. The five year trend in cancer incidence rates was age adjusted to the 2000 U.S. standard population. The average incidence rate in the U.S. for the period 2007 to 2011 was 459.8

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cases per 100,000 per year. The U.S. Census Bureau was queried for Counties Database (CenStats) 2010 archived information. The average population for the U.S. was 87.4 per square mile.

Results

Because we expected a non-linearity (in order for the force and energies to overlap with the properties of DNA activity) between population density and incidence rates per 100,000, Spearman rho as well as Pearson r values were calculated for successive decreases of population density in this order (total numbers of counties in parentheses): < 1000 (795), < 500 (766), < 400 (746), < 300 (721), < 200 (678), < 100 (575), < 80 (517), < 60 (441), < 40 (329) and < 20 (130). We found that the correlation (Spearman rho) between all cancer incidence rates per 100,000 people and the population density of the county peaked ($\rho = 0.40$, $P < .001$) for only those counties with population densities of less than 100 people per square mile, or, when the average distance between people was ~160 m. The average force between human brains for this average distance is $0.96 \cdot 10^{-8}$ N. When applied across the Compton wavelength ($2.4 \cdot 10^{-12}$ m), the energy for potential translocation of any two loci would be $2.3 \cdot 10^{-20}$ J. This is certainly within the range of the stacking energies associated with base nucleotides in DNA [10] and RNA [12] sequences or within the second shell energies strongly associated with the movement of protons from the hydronium ion [23].

However there are fluctuations in potential differences across the hemispheres that occur per 40 Hz. Consequently the product of $1.7 \cdot 10^{-7}$ A ($2.5 \cdot 10^{-2}$ s) would be $4.25 \cdot 10^{-9}$ A·s per brain. As a result the force per 20 to 25 ms, the time required to add a base nucleotide to a DNA sequence, for that distance between brains would be $\sim 6.3 \cdot 10^{-12}$ N or about 6 pN. This value is within the range, for both coefficient and order of magnitude discussed [16] to stretch the DNA molecule *in vitro*. However the functional potential difference could be $> 10 \mu\text{V} \cdot \text{Hz}^{-1}$ if the contribution from the relative permittivity (dielectric constant) associated with water (the primary component of cells in the human body) within the range of 25 to 40 degrees C were considered. Accommodation of this value (about 74 for water at this temperature), when

the appropriate frequency is considered, would result in comparable values of force.

Consequently for both steady state and frequency-dependent averaged voltages, the optimal distance between human beings within these counties that displayed the strongest correlation between population density and the incidence of cancer per 100,000 people resulted in equivalent energies. They would satisfy the involvement of applying a force across the Compton wavelength to obtain the stacking energy and the intrinsic force involved with stretching the DNA molecule when applied at a frequency whose duration matched the time required to add one nucleotide.

The human brain is an organ within which representations from other organs and cells are localized and hence could contribute indirectly to the probability of proliferation of malignancy within the remainder of the volume of the body. "Stress" which is an over-inclusive metaphor for large numbers of biochemical changes, many of which are dependent upon the perception of the experiment, has been correlated with development of cancers through presumably suppression of the complex reactions of the "immune system" [24]. However there should be quantitative convergence between the dipole potential difference of the entire human organism and intrinsic resistance and that of the brain.

Over 35 years ago, in the tradition of Leonard Ravitz [25] and Robert Becker [26] and while pursuing the frequently reported altered states by 19th century physiologists [27] when weak polarized steady-state (d.c.) currents were applied across the rostral-caudal axis of the skull we measured steady state potentials (with μV meters) between the cephalic or cervical regions and the distal portions of the four appendages of several dozens of supine human volunteers. As reported by Becker and his colleagues [26], the typical voltage between the rostral or caudal location in the center of the skull and appendages is about 30 mV. This was not a fixed value but could vary over the month and with the "state" of the participant to between 10 and 100 mV as initially reported by Ravitz [25].

Traditional estimates of internal resistance, which occupy a range of at least 10, exhibit a

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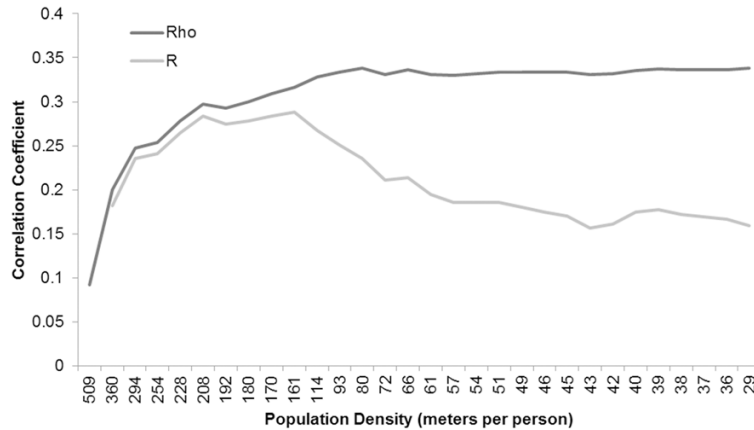


Figure 1. Significant ($P < .001$) Pearson R and Spearman's Rho correlation coefficients between United States County Incidence Rates of Cancer (per 100,000) and U.S. County Population Density (per square mile). To illustrate the relation of density, the x-axis square mileage has been converted to meters per person.

z-score transformations comparison, the $r = 0.288$ at 100 people per square mile was significantly ($P < .05$) stronger ($z = 2.6$) than the $r < 0.182$ values at population densities less than 20 per square mile or the r values < 0.180 for densities greater than 1100 per square mile. The inflection is not noted in the Spearman rho data. Rather the asymptote for no greater increase in correlation between annual incidence of cancers and population density occurs with distances less than 160 m (population density > 100 people per square mile).

median value of about 1000Ω . Consequently the current would be about $3 \cdot 10^{-5}$ A. Assuming the 40 Hz intrinsic vibration of muscle as the denominator, this equivalence would be about $7.5 \cdot 10^{-7}$ A.s. Assuming the more typical rest median frequency of 10 Hz for whole body muscle vibration, the order of magnitude would be the same. This is within the range of values sufficient, given the average distance between people where the correlation with population density and prevalence per 100,000 people was maximum, to be associated with 10^{-20} J if the Compton wavelength of the electron was involved.

To discern if the relationship was evident with the population density (adjusted to year 2000) and annual incidence of all cancers, the total numbers for all counties (2,885) were obtained from the NCI CDC data base. Successive correlations (Spearman Rho and Pearson r) were completed for serial 100 person per square mile decrease from 3000 to 100 and then 10 persons per square mile decreases from 100 to 10 persons per square mile. The correlations between the mean population density and annual incidence rates of all cancers as a function of the average distance (in meters) between people for those densities are shown (**Figure 1**).

For Pearson r values the maximum is about 90 to 100 people per square mile or an average of 160 to 170 m between people. According to the

If the range of the peak containing the correlation coefficients were significantly higher statistically ($P < .05$) than the coefficients below or above that range was considered, the effective population density would reflect average inter-person distances between 360 m to 57 m (20 to 800 people per sq mile).

This range does not change the order of magnitude of the force or energy levels. Considering the multiple degrees of freedom involved with the actual dynamic frequencies of the cerebral cortices the "critical" values required to produce the criterion forces and energy could be achieved frequently but not constantly.

Closer inspection of the scatter for population densities of less than 100 persons per square mile (**Figure 2**), revealed a conspicuous anisotropic distribution of residuals around the regression line in the range of 50 persons per square mile or an average distance of about 228 m between individuals. Given the above parameters, the inter-cerebral electric force would be approximately $3.1 \cdot 10^{-12}$ N. The electric force between body dipole strengths would be $9.7 \cdot 10^{-8}$ N. If the force were applied over the Compton wavelength the energy would be in the order of $2 \cdot 10^{-19}$ J which is within the near infrared range. If only 3 mV constituted the potential difference between the head and appendages and the A.s equivalents were obtained, the value would be within the $2 \cdot 10^{-20}$ J range that is significant for stacking of base

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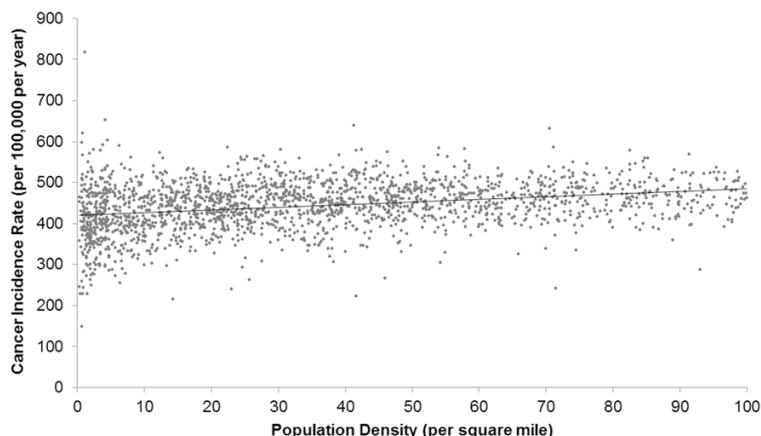


Figure 2. Scatter plot of Cancer Incidence Rates (per 100,000 per year) and counties whose Population Density is less than 100 (per square mile) with linear best fit shown.

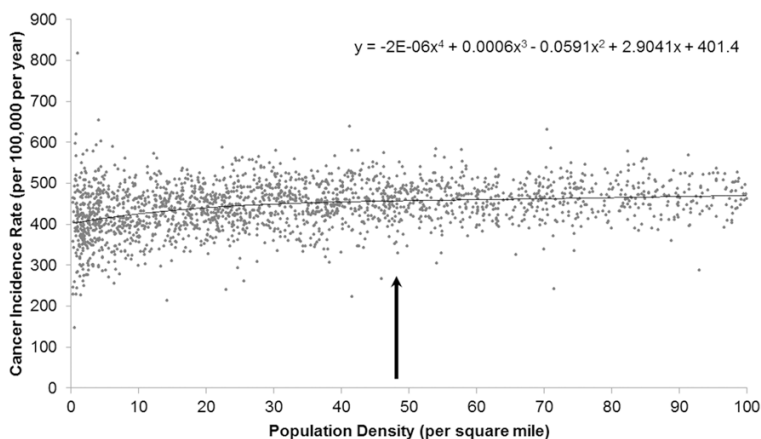


Figure 3. Scatter plot of Cancer Incidence Rates (per 100,000 per year) and counties whose Population Density is less than 100 (per square mile) with a polynomial of degree four (4) best fit shown. The inflection point (arrow) solved for population density of 48.54 (per square mile) or 230.99 meters per person.

nucleotides, action potentials, resting membrane potentials, and many ligand-receptor sequestering energies.

To pursue greater precision of the characteristics of these non-linearities for the increase in cancer incidence within narrow bands of population density, iterative polynomials were completed using MatLab curve fitting software. A four degree polynomial revealed the “best” fit equation with coefficient within a 95% confidence boundary (**Figure 3**). The inflection point of the regression polynomial was computed to be 48.54 people per square mile (inter-person distance of 230.99 m).

Discussion

The results of these analyses were within the range we predicted by Coulomb forces between individuals who can be modeled as electric dipoles either across the cerebrum, with or without time-variations, and between the cephalic regions and distal appendages. We appreciate there is a likelihood that the marked convergence between the predicted values and the ones derived from actual average distances between people from which the forces were obtained could be fortuitous. However the different solutions all occurred within the predictable ranges and one might argue reduces that probability. Application of basic biophysics to ecologically relevant contexts has been shown to be revealing and to open innovative possibilities by Cameron, Skofronick and Grant [28]. The forces and energies at which essential biochemical processes occur are extraordinarily small and within the range that could be created by these subtle forces.

There are several implications that emerge from this convergence between the predicted

distances between human beings, the incidence of cancer rates per 100,000 people, and the energies and forces derived from simple Coulomb processes. First, the results indicate that very subtle forces based upon the average Euclidean distances between individuals of our species may be more influential upon the processes that control the population than previously assumed. Mortality by aberrant cell proliferation, although there are many other equally viable explanations, may be considered an adaptive process by which population growth is modified or selected. The significance of the development of malignant cell clusters within human beings and death from cancer has

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become more apparent as the average life span of the human being has increased. Before this extension of viability other factors, such as disease or nutritional limitations, controlled the longevity and selectivity of the members of the species.

Second, the non-linear relationship between the population density and the increased annual incidence of cancer rates would be consistent with a potential intrinsic process for modulation of population selection. During the expansion phase of a group the average distance would be significant for potentially influencing which expressions of DNA occurred or which RNA transformations were manifested. The convergence between the actual intensity of the force for the intermediate population density and that required to affect the expansion of the DNA molecule (at least *in vitro*) would be consistent with that interpretation. At larger population densities this mechanism would be less effective because the “fluidity” to adapt to the particular biological niche had been reduced and the configuration of gene expression is more “stabilized”.

Third, the Compton wavelength for the electron in the production of 10^{-20} J permits the possibility for matter-wave interactions that could involve non-local processes. Excess correlation, where by the change in one system is correlated with the change in another system at distances where local or serial causal mechanisms are not obvious, has been shown for separated reactions involving photons [29] and shifts in pH [30] in water with physiological characteristics. Recently Karbowski, Murugan and Persinger [31] demonstrated that pairs of dishes containing melanoma cells demonstrated excess correlation for toxicity-induced necrosis if both shared the same circularly rotating magnetic fields with a specific rate of change. In their experiments the injection of hydrogen peroxide into the local dish of melanoma cells that was sufficient to produce about 50% mortality was associated with a comparable mortality in the non-local cells at a distance of either 3 m or approximately 1.3 km within 24 hr. The duration of the shared exposure was only 12 min. The effect required the viability of at least some cells in the local plates; necrosis of all of the cells in the local dish did not result in the non-local mortality.

That these experimental conditions could be simulated within the human being by natural processes is very likely. There is a recurrent rostral-to-caudal integrating wave of potential changes over large areas of the cerebral cortical manifold every 20 to 25 ms or ~40 Hz [32]. Our recent measurements [33] employing LORETA (Low Resolution Electromagnetic Tomography) and QEEG (Quantitative Electroencephalography) indicate that the well documented “default mode network” involved with “resting cognition” in a relatively external stimulus-free environment, may move in the (opposite) caudal to rostral direction, thus completing the quasi-circular pathway or “circuit”. If the precise physical parameters for one person whose body contained malignant cells were shared by another within the normal distribution of all people for places with optimal population density, then theoretically non-local induction or cancellation could occur. If this interpretation is valid, then the transfer of the condition for malignant cells would be a novel form of “contagion” mediated by an unanticipated type of vector.

The role of relative permittivity (dielectric constant) of essential substances that could influence the solutions for interpersonal force and energy is important. If water is the medium through which the interpersonal forces occurs then less intense dipoles would be required to result in the optimal force or energy levels to affect the DNA and RNA within the cell. On the other hand the potentially impeding effects from culture-related electric fields, such as power frequency gradients from transformers or sources of 50 Hz or 60 Hz line transmission, would be expected to be strong modulators of this phenomenon. According to our model, extraneous fields that alter the forces at specific population densities could increase that population’s refractory response to the formation of malignancies. We suggest that the increased odd-ratios for brain tumors, for example, for individuals within the electronics professions may not be due totally to the effects of the extraneous man-made power frequency fields but to the fact they shift the intra-organismic parameters to values that produce the forces and energies we have calculated to be effective.

Clearly the limiting application of this approach is that the position of a person in his or her life

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time is not fixed. The average distance between people within a county is likely to display a standard deviation (depending upon time of day and the occupation of the person) that is equal to the mean distance between persons. Assuming that only about 1 ksec is required (during a typical replication or transcription) to produce an altered gene sequence, one would expect the relatively weak correlation measured here. From this perspective the development of cancer would not be due to “bad luck” as recently suggested [34]. If the specifics of the person’s time line and location were known for every second per day, of every day, the specific probability could be estimated within practical levels of precision.

The small but quantifiable forces and energies that contribute to significant changes in the molecular structure or sequencing of DNA or RNA may be responsive to basic electric forces due to average distances between organisms. Assuming realistic quantitative values for “electric dipoles” between human beings as a function of population density per county, the range of interpersonal distance that would produce energies and forces that could affect intermolecular activity was associated with increased incidence of new cases of cancer per 100,000 people. The convergence of the predicted forces and the greater cancer incidence per 100,000 people in counties that might display these interpersonal distances indicates there may be very basic physical forces that might contribute to aberrant cell formation or function.

Acknowledgements

The authors thank Dr. W. E. Bosarge, Jr. CEO of Capital Technologies for his support of novel technology and ideas.

Disclosure of conflict of interest

None.

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