

Focused Feature: NPC epidemiology and genetics

On the trails of markers and proxies: the socio-cognitive technologies of human movement, knowledge assemblage, and their relevance to the etiology of nasopharyngeal carcinoma

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Abstract

Bacteria, pigs, rats, pots, plants, words, bones, stones, earrings, diseases, and genetic indicators of all varieties are markers and proxies for the complexity of interweaving trails and stories integral to understanding human movement and knowledge assemblage in Southeast Asia and around the world. Understanding human movement and knowledge assemblage is central to comprehending the genetic basis of disease, especially of a cancer like nasopharyngeal carcinoma. The problem is that the markers and trails, taken in isolation, do not all tell the same story. Human movement and knowledge assemblage are in constant interaction in an adaptive process of co-production with genes, terrain, climate, sea level changes, kinship relations, diet, materials, food and transport technologies, social and cognitive technologies, and knowledge strategies and transmission. Nasopharyngeal carcinoma is the outcome of an adaptive process involving physical, social, and genetic components.

Key words Human movement, knowledge assemblage, socio-cognitive technologies and networks, genetic narrative, prehistory, nasopharyngeal neoplasm, archeo-haplomics

Nasopharyngeal carcinoma (NPC) is a disease with a complex mix of viral, genetic, and environmental components and is considered enigmatic; however, when understood in all its dimensions, NPC could be a model for all such complex diseases^[1]. The etiology and developmental pathways of NPC were opened up by Wee *et al.*'s stimulating and ground breaking hypothesis^[2]. Wee *et al.* showed that the key to understanding the disease is maritime mobility. Following its submergence, the original inhabitants of Sundaland went to sea and spread out into Southeast China and Borneo, eventually creating links with the Austronesian Malayo-Polynesians of Southeast Asia, Inuit of Greenland, and Polynesians of Oceania, and groups in the Mediterranean and East Africa^[2]. This paper puts Wee *et al.*'s claim in the broadest possible context by looking at how people move and how, in that movement, knowledge is moved, assembled, and transmitted.

Movement tends to be downplayed or even ignored in many accounts of the place of humans in the world and the ways to understand it^[3]. Indeed, fixity in space and place has become the foundation of western rationality and epistemology. In this view, movement is equated with wandering, irrationality, and primitiveness, something that needs to be controlled and set in logical, linear order; whereas sedentism is taken to be the touchstone and precondition for civilization and modernity^[4]. This privileges the "Neolithic Revolution" in Europe as the origin of all that counts as regularized and legitimate forms of moving and knowing. There is, however, another narrative; there were no revolutions, and humans and their ancestors were members of continuously interacting diaspora around the world. Furthermore, in this view, the social, technical, and cognitive capacities that enabled such movements were developed not in Europe, but in Africa and in Southeast and Southwest Asia^[5,6].

Here, a series of claims are advanced: (1) movement itself often goes unexamined in accounts of human change and development; (2) understanding human movement requires the inclusion of a socio-cognitive dimension to the usual genetic, archeological, linguistic complex; (3) the genetic account

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is incomplete without continuous genetic information using haplomic technology^[7]; (4) there are inevitably differing forms of genetic modeling, such as phylogenetic arborescent on the one hand and reticulate rhizomatic models on the other; (5) the totality of interacting components can be conceived, either as a complex adaptive system in action, or as being unifiable in a grand archeo-genetic synthesis; and (6) these two differing approaches should be held in creative tension with one another. It is concluded that the orthodox archeo-genetic narrative of human movements around the world is overly simplistic in its assumptions and can now be usefully challenged by an alternative model that can be called “archeo-haplomics.”

Migration into the Pacific

This article starts by looking at the colonization of the Pacific because of the incidence of NPC amongst Pacific islanders and their genetic links to South China^[8,9]. In theory, Pacific migration ought to be an ideal model of human migration. As Rogers *et al.*^[10] pointed out, it is relatively recent, occurring within the last 3000 to 4000 years, with clearly defined time boundaries, and is largely free of external influences. However, Pacific migration has proved to be remarkably complex. Indeed, investigators from many disciplines, including genetics, archeology, linguistics, anthropology, paleoecology, sociology, history, zoology, botany, history of technology, architecture, mythology, indigenous knowledge, computer simulation, experimental voyaging, and so on, have encountered difficulties in understanding this diaspora. Pacific migration exemplifies the challenges of working backwards from a given demographic and linguistic state, such as the colonization of the vast expanse of Pacific Ocean islands by Melanesians, Micronesians, and Polynesians and the wide geographical spread of the Austronesian languages. The movement of people out of Southeast Asia has left a plethora of trails, markers, and proxies, which range from bacteria^[11] to rats^[12] and from breadfruit^[13] to canoe design^[14], but they do not tell the same story, instead pointing to differing origin points and routes of transmission. Thus, these diverse trails, markers, and proxies do not necessarily form a coherent, unified narrative. Rather, as Keith Dobney^[15], who has followed the genetic trails of pigs kept by Pacific colonizers and who participated in a replica canoe voyage into the remote Pacific, said,

“Many archaeologists have assumed that the combined package of domestic animals and cultural artifacts associated with the first Pacific colonizers originated in the same place and was then transported with people as a single unit...Our study shows that this

assumption may be too simplistic, and that different elements of the package, including pigs, probably took different routes through Island South East Asia, before being transported into the Pacific.”^[16]

There are four reasons for the difficulties in reconciling these differing route markers. As humans move in a given environment, they are not simply moving through it; they shape and affect it just as the environment shapes them. This co-evolutionary adaptive process, or co-production, is historical, time-dependent, and, hence, irreversible. However, the process of movement is much more than an ecological niche construction or a gene/habitat interaction. As the anthropologist Gamble^[17] argues, “what characterizes social life in humans rather than hominids is our ability to extend social relations across space and time.” Humans extend themselves in the world cognitively, socially, and linguistically, and in the process, they come to know the world and to alter it^[18,19]. Humans also deploy tools, materials, artifacts, and knowledge in complex systems of trade and exchange, thereby establishing “chains of connection”^[20] in social networks^[17]. In tracing these chains of connection, and in following the trails of languages, bacteria, or rats, humans are simultaneously creating cognitive trails that deploy the ontologies, epistemologies, and methodologies of their own disciplines. Many researchers dream of a grand synthesis, a consilience of inductions, and a convergence of all disciplinary data under one of the many banners that have been proposed, including archeogenetics, phylogeography, and genomic anthropology^[21]. Such a synthetic consilience is an ideal towards which to aim, but one which should be subject to constant challenge. Rather than restricting the possibilities to a panoptic database or a subordination of all to phylogeny, understanding a complex adaptive system like human migration can be conceived as a system in which incommensurable, scale-dependent, and dynamic components produce emergent results through interacting feedback processes^[22].

Up until 2001 or 2002, the dominant model for explaining Pacific migration was Bellwood’s “Express train” or “Out of Taiwan” (OOT) model^[23-25]. In its broadest form, this model held that people moved from South China into Taiwan around 5000 years before present (YBP), followed by a demic diffusion of Austronesian-speaking peoples south from Taiwan on the wave of the adoption of agricultural practices for growing rice around 3000 YBP. They moved into Near Oceania, New Guinea, the Bismarck Archipelago, and the Solomons, founding the Lapita culture, and then into remote Oceania, ultimately reached New Zealand, Madagascar, and possibly even South America. The model was portrayed as the synthesis of genetics, linguistics, and archeology first suggested by Cavalli-Sforza^[26]. At a conference held

in 2001 to discuss the efflorescence of this Farming/Language Hypothesis, it became apparent that no consensus could be reached about the hypothesis and that the OOT model was under criticism. Indeed, the conference papers were published under the less than celebratory title *Examining the Farming/Language Hypothesis*^[27,28].

The problems with the OOT model were manifold. mtDNA evidence seemed to confirm the model, but Y chromosome evidence favored one of the other major alternatives, the so-called “Slow boat” model or “out of Island Southeast Asia” in which the origin point of movement was South China or Island Southeast Asia^[29]. Specifically, recent Y chromosome and mtDNA analyses confirmed Wee’s Daic NPC origin hypothesis, thereby undermining the OOT model and suggesting that the area now beneath South China is an original homeland for the Daic peoples. This more complex account leaves room for two other models, Terrell’s “entangled bank” and Green’s “triple I (intrusion, integration, and innovation)”^[30,31].

It is tempting to place all four models on a continuum from OOT to tangled bank, but there are profound ontological differences between them. The “Express train” model is phylogenetic, that is, arborescent or tree-like, whereas the entangled bank model is reticulate or rhizomatic. One emphasizes origins, initial settlement, and subsequent splits, whereas the other emphasizes a continuous process of interaction and admixture^[32]. Having differing models creates problems; any genetic, archeological, or linguistic data will be arranged and analyzed in preset, model-specific ways, thereby restricting means of testing between them. Thus, synthesis becomes unlikely.

The key to success in human movement has been their diversity and adaptability, which enable them to establish a wide variety of means to survive in every environment around the world. Thus, for example, humans not only moved across the substantial sea barrier but were also able to adapt to crossing the complex ecological boundary of Wallacea between Island Southeast Asia and Melanesia. New Guinea, the Bismarcks, and the Solomons are hotspots of linguistic, genetic, and cultural diversity, so it is vital to take into account the various local and specific forms of movement and interaction. The pattern of cultural and linguistic diversity in which the lowlanders but not the highlanders are Austronesian suggests that the highly varied terrain and climate provides for small isolated groups with great diversity and for little interaction. The Polynesians did indeed pass through as they moved into Remote Oceania, but they now appear to have had relatively restricted interaction with the other inhabitants of the islands. It is possible that their boat technology kept them largely separate and homogenous, whereas

the matrilineal kinship arrangements may explain the specificity of the admixture of Melanesian mtDNA^[33]. Furthermore, the relatively recent phase of colonization and terraforming during which Polynesians moved into the remote Pacific, occupying and transforming islands, including Hawaii, Easter Island, and New Zealand, has now become the subject of a series of debates and controversies, following a brief period of consensus around the strategic voyaging model, which is now being re-evaluated^[34].

Captain Cook was the first to recognize that the people of the Pacific were of one nation and asked the question that still lingers today: “How shall we account for this nation spreading itself so far over this vast ocean?”^[35] Cook was of two minds, entertaining the possibility that Polynesians had the technical and cognitive capacity to deliberately settle the islands, while also wondering if some of the islands had been found accidentally. Much of his ambiguity on this issue is reflected in his difficulties in understanding the chart drawn by the Tahitian, Tupaia, whom Cook took with him when he left Tahiti on his first voyage on Endeavour in 1769. Tupaia was the leading Pacific navigator of the day and, in effect, showed Cook around, drawing a chart of all the islands he knew while they traveled together. Tupaia’s chart, which was undecipherable until recently, was a puzzle for Cook because many of the islands seemed to be positioned incorrectly, thus giving Cook severe reservations about Tupaia’s geographical knowledge^[36]. Recently, two French oceanists re-analyzed the chart and found that “Tupaia’s Chart, while having the appearance of a map, is in fact a mosaic of sailing directions or plotting diagrams drawn on paper.” They conclude,

“...unraveling of the Chart... highlights the difficulties of understanding or sharing knowledge on both sides. Cook, in his own words, believed Tupaia was drawing a map. Tupaia seems indeed to have tried to include distance in his plotting diagrams, thereby going beyond the traditional system of representation. Cook clearly remained fixed in his Cartesian world, adding cardinal points to Tupaia’s Chart. But both could look at the manuscript and see their own system represented: Cook reading islands on a grid and Tupaia reading islands radiating out from different centers.”^[37]

In other words, Cook and Tupaia worked with differing epistemological and ontological assumptions about space and time and how they can be represented, assumptions that were incommensurable and mutually unrecognized. They both thought they were drawing a map but did not realize that they had no common agreement about what maps are or how they record and enable movement. Although they each had an effective system of navigation, they were operating within completely different socio-technical-religious networks.

For Cook and his fellow enlightenment European navigators and explorers, the system was one of calculation and long-distance control central to the establishment of empire; for Tupaia and his fellow Polynesian navigators, the system was one of exploration and settlement by kin-based replication^[38,39].

The prevailing orthodox explanation of movement into Remote Oceania has been one of deliberate strategic voyaging through the deployment of a complex of technologies and socio-technical skills, including canoes capable of windward sailing, a sophisticated body of navigational, environmental, and topographical knowledge, along with social institutions for storing, teaching, and reproducing that knowledge. Irwin^[40] set the paradigm with computer simulations showing the navigators would have strategically chosen to start off exploring against the wind, thereby ensuring a safe return downwind, leaving the most difficult route, sailing downwind to New Zealand with no assurance of return, until last. This paradigm seemed to be confirmed by a multitude of replica voyages and by Chambers' molecular genetics^[41,42]. However, Atholl Anderson^[43], a constant critic of this model, argues against the likelihood that early canoes had the required windward capacities. He recently proposed a model based on the early voyagers having simple canoes and opportunistically using long-term variability in wind patterns due to El Niño and the Southern Oscillation (ENSO) to sail eastwards and southwards across the Pacific^[44]. Other models are now proposed based on simulations, evolving canoe design, subsistence strategies, and so on, thereby opening the field to many widely differing understandings of where, when, how, with what, and why people moved into and throughout the Pacific^[45-47].

This pattern of early agreement or dominance of a single model, followed by a proliferation of new research in a variety of disciplines revealing flaws in the early model, and provoking calls for a new synthesis that has not yet emerged, has been played out in every great human movement, including Out of Africa, Into Europe, Into Asia, and Into the Americas. Although it is self-evident that the move into the Pacific was by sea, only recently has maritime movement started to challenge the terrestrial orthodoxy as a key component in all the great migrations, but especially Into the Americas and Out of Africa along the "Great Southern Arc." Both migrations are now conceived as a process of "coastal migration," suggesting a mix of strand lopping and voyaging^[48-52].

Migration into the Americas

The story in the case of the Americas is very like

that of the Pacific. A dominant paradigm, the "Clovis first" model, has been overthrown by once controversial but now accepted archeological dating and by rethinking the possible entry routes. One of the controversial human occupation sites in question, Monte Verde in Southern Chile, is now largely accepted as dated at about 14 500 YBP, which makes it difficult to accommodate on the Clovis first model. This model was based on the assumption that migration into Alaska was only possible across the Beringian land bridge after the Late Glacial Maximum (LGM) at about 13 000 YBP, when an ice-free corridor opened. An alternative coastal route is now plausible given accumulating archeological evidence of human occupation along the West coast, especially on the islands off California. Such evidence has been hard to obtain because of the rise in sea levels after the LGM^[53].

What has really challenged the assumption of terrestrial movement across a land bridge is the articulation of a coastal migration model in which people could have followed the "kelp highway" from Japan to Baja, California and then to Latin and South America^[54]. This model opens up the possibility of a much earlier timeframe for migration into the Americas, as well as multiple groups overlapping each other and penetrating the interior simultaneously. However, as in the Pacific example, there is no agreement on the number, routes, or dates of migrations^[55-57]. Some genetic studies support a single migration across the Beringian land bridge, and others support multiple entries, as suggested by the recent genome sequencing of the hair of a Paleo-Eskimo^[55,58-61]. In contrast, Hubbe *et al.*^[62] studied a large number of Paleo-American skulls unearthed in Brazil and dated around 11 000 YBP paint a picture that differs radically from the genetic story based on studies of modern Native Americans. He found that these skulls were anatomically distinct from those of Native Americans, bearing more similarity to those of the ancestral populations of Australian aborigines and Melanesians. Hence, they concluded that there were at least two distinct migrations into the Americas. There is some evidence that the land bridge may have been flooded as early as 11 000 YBP, which supports a coastal migration route, along with other possible overland routes^[63].

Thus, it appears that the great migrations into Southeast Asia, the Pacific, and the Americas may have used a coastal path. Furthermore, these migrations could only have occurred with the deployment of socio-technical complexes sharing broad characteristics. They would also have common climate constraints and sea level changes. In addition, the forms of movement and interaction would have been entirely dependent on the specific historical context. The interactive complexity of those movements have not yet been brought into

focus because of the constraints of earlier cognitive trails established in looking for isolated technical and material signs of genes, artifacts, and other proxies and markers, and because the role of social cognition has not yet been fully understood and included in the complex.

The work of many disparate archeologists suggests that all forms of movement would have been dependent on a social technology of kinship, a network of relatedness, bonding, and obligations that enables the transmission of property and knowledge across generations through a classification of friends, enemies, and strangers. These conceptions of kinship and relatedness are social and cultural constructs and do not map directly onto genetic and biological relationships. Hence, it is necessary to find ways in which the differing stories of relatedness and movement can work together.

Gamble^[5] suggested that the development of complex forms of social cognition is a prerequisite for overcoming the limitations of co-presence and extending relationships in space and time: reaching Australia required kinship just as much as boats. A view that is consonant with Robin Dunbar's "social brain hypothesis." Dunbar^[64] argues that "primate societies are implicit social contracts established to solve the ecological problems of survival and reproduction more effectively than they could do on their own. Primate societies work as effectively as they do in this respect because they are based on deep social bonding that is cognitively expensive. Thus it is the computational demands of managing complex interactions that has driven neocortical evolution." This concept of the dynamics of human neocortical evolution as social rather than technological fits well with models proposed by Stanley Ambrose, emphasizing the co-development of language, symbolization, and compound tool making in Africa around 300 000 YBP^[65], and with Marwick's claim^[66], which states that language and symbolization developed with the extension of exchange networks. In a large part, the symbolization and feedback essential to the development of such social networks depends on keeping track of relatedness and kinship through forms of telling, such as performing and representation, storytelling, singing, dancing, painting, building, and weaving^[67,68]. It is now apparent that each of the major human dispersals need reconceiving, not as simple mass migrations or demic diffusions, but as human movements that were relatively fast and strategic, requiring great flexibility in a diversity of environments, necessitating complex information exchange systems that allow group planning and feedback^[69]. Such information exchange systems are typically an integral component of a socio-cognitive-technical complex in which a wider interacting system of relationships, language, materials, genes, and people were co-produced during human movement^[66]. A salient example

of this is the Maori concept of whakapapa, where their epistemological framework and taxonomy is based on the kinship and genealogy expressed through the canoes that brought the different groups to New Zealand^[70].

In addition to the social and cognitive components, appropriate material technologies are required for developing a strategic approach to moving into an unknown environment. For example, in the case of the Inuit and Eskimos, such technologies and skills included string, needles, clothing, shelter, fire, boats or canoes, and wolf taming, allowing them to create a "survivable microclimate."^[10,71-75] Human movement from a performative/emergent perspective is a continuously evolving complex adaptive system with multiple interacting and transforming components, including genes, environments, language, cognition, materials, and social technologies constrained by the conditions for possibility, such as climate and sea levels; genes, behaviour, or artifacts alone cannot determine it.

Conclusion

How then does this concept of human movement through the environment shape the ways in which to consider how to follow trails of genes, proxies, and markers, trails which are themselves co-producing a diversity of cognitive environments? How should the reflexive process of understanding how humans came to be the way they are as a species being conceived? As indicated earlier, there is an ongoing attempt at synthesis and consilience, wherein geneticists, linguists, archaeologists, and so on, are constantly reviewing each other's data and models for clues on origins, dating, and connections. However, while such a dynamic consilience is laudable as goal-directed research, it is less desirable if it moves towards an insistence on commensurability between disciplines or towards subordination to the norms of one discipline. Three things need to be kept clearly in mind. First, because it is in the nature of science that all disciplines are crucially dependent on their ontological assumptions and models, it is vital that such assumptions and models be challenged with alternative conceptions. Second, the suggested performative conception of human movement as a complex adaptive system ought to be reflected in the ways the disciplines involved interact. Rather than aiming towards synthesis and commensuration alone, such an approach should be held in tension with that of a complex adaptive system, thereby allowing the relevant disciplines to interact and create an emergent outcome from that dynamic. A principal reason for such a suggestion is that this approach to knowledge production, movement, and assemblage is thoroughly biological. In contrast, an approach using engineering or

physics aims at technocratic problem solving rather than attempting to understand processes that are historical and contingent, interactive and emergent. Finally, indigenous perspectives must be included. Much research has the implication of telling indigenous inhabitants who they really are, where they come from, who they are related to, and what counts as authoritative knowledge. Such matters of identity, relationship, and authority are central to every cultural group's concept of themselves and are intensely political. Thus, the people who are directly affected must also have a voice in the process. Palsson^[76] has proposed the inclusion of "Inuit epigenetics," local notions of naming, subjectivity, and relatedness. While Claudio Aporta has shown that the Inuit solve their specific local problems of "passing on information about territory from season to season and generation to generation" resulting from the reality that "they can only travel in the Arctic in the winter after the snow creates a new blank territory"^[77]. To travel across unmarked territory Inuit deploy a socio-cognitive technology of knowledge communication and exchange in the form of a "network of lived story trails," a form of knowledge movement and assemblage, that, like Tupaia's, is unrecognized in the wider society but has proved superior to GPS-based navigation^[78]. Such examples suggest the necessity of including indigenous epistemologies, along with indigenous conceptions of relatedness and disease etiology^[79-82].

A key example of the kinds of problems that arise if such a wide perspective is adopted is that of denominating populations. Namely, who gets to define the level at which the phenomena under examination operates? Is it at the individual, population, or group level? Also, how are the characteristics of the relevant population and its boundary conditions determined, and how are the relationships between contemporary and ancient populations established? These questions cannot be settled externally to the standards of the disciplines, nor can they be settled internally; partly because classification systems, taxonomies, and divisions into types have an inherent arbitrariness and conventionality, and partly because groups are in interaction with each other and are ultimately defined in relational terms. In the case of NPC, there is a clear difference between the genetic approach, which operates at the population level, and the haplomic approach, which operates at the individual level. Even more profoundly challenging is Simons' haplomic analysis, which shows that humans have inherited a genetic signature from gorillas that does not appear to be present in chimpanzees. This haplomic segment is towards where the chromosomes cross, a location that is associated with NPC, so the impact of this finding, if confirmed, is relevant to a range of aspects of human and primate evolution and taxonomy^[83].

The question of whether a population should be defined in demographic units, genetic units, or haplogroups is further complicated by the possibility of completely different forms of groups or types emerging along with new conceptions of the evolutionary process. For example, Woese^[84] and Goldenfeld *et al.*^[85] claimed that the genetic code itself and its resilience to change cannot be explained under Darwinian evolution or the so-called new synthesis with molecular biology. In their view, microbial and pre-Darwinian evolution is driven by horizontal gene transfer. They argue that evolution is reticulate, that phylogenetic trees are merely conventional ways of ordering data, and that organisms need to be considered not as individual entities, but as communities in which the key processes are communication, movement, and assemblage. Consequently, the concept of "species" becomes less viable with the recognition of wandering "cosmopolitan genes," and, with viruses playing a major role in storing and moving genetic information, evolution then becomes a Lamarckian-process of interactive co-production^[86].

The discipline of genetics is, of course, not alone in having fundamental ontological issues arise from disagreements about what should be considered an appropriate theoretical framework within which to explain change, the appropriate units or groups or markers to locate and follow, and the appropriate scales of analysis. In effect, there are differing narratives of spatiality and temporality within and between disciplines. Archeology, anthropology, history, linguistics, and any other discipline concerned with explaining change have no transcendental way of resolving these issues; they are framework-dependent and depend on which group, entity, or process, at what scale, over what period, is deemed to be fixed, and which is deemed to be changing. Archeology, for example, has two other great difficulties, the paucity of the archeological record and the consequent sudden changes in dating or new material evidence, which result in controversies and paradigm switches. Sometimes, this has occurred without adequate empirical warrant as in the case of *Homo floresiensis*, where an entirely new human species has been claimed on the basis of a single skull. More important for the story of NPC is the recent work of Rose^[87], who found considerable archeological evidence that large numbers of people occupied the region that is now the Persian Gulf from about 100 000 YBP. This appears to be incompatible with a simple "Out of Africa" genetic story; rather it implies a large and completely overlooked population and further complicates the diasporas back from Southern and Southeast into Southwest Asia^[88,89]. The refugia of the Gulf Oasis that Rose revealed would open the possibility of a transmission route for NPC from Southeast Asia to the Arabian Peninsula, North African coast, and Levant.

Pääbo's laboratory made the equally significant genetic finding that Neanderthals and humans share so much genetic heritage that they should hardly be described as separate species anymore^[90]. Taken together, these findings, both archeological and haplomic, provide the basis for an interactive account that underpins a complex adaptive system. This interactive account may also induce a resurgence of Thorne and Wolpoff's multiregional hypothesis as it clearly undermines the current replacement model in which *Homo sapiens* replaces Neanderthals and all other ancestral lineages^[91-93]. These findings may also suggest a possible Phoenician and Maghrebian connection in the NPC story, specifically via the Phoenician seafaring network that extended throughout the Mediterranean and up the Atlantic littoral, and, hence, may suggest further locations to search for low-level incidence of NPC in Portugal, Ireland, and Cornwall^[94,95].

It was these kinds of evidential and framework assumption problems that Tom Dillehay, who excavated the Monte Verde site, had to confront in the most damning of criticisms from the "Clovis first" establishment. Over many years, his critics simply "knew" that his dating must be wrong because they unquestioningly assumed that the only entry route into the Americas was over the Beringia land bridge after the LGM. Following the long-delayed and begrudging acceptance of his empirical work, Dillehay^[96] wrote a reflective piece on how to proceed in understanding the peopling of the Americas that can be extended to all studies of human movement and historical change. He argues this about the question of how people populated the Americas:

It must be answered at all scales and by all disciplines. Along these lines, researchers need to anticipate the first peopling process empirically and theoretically, observe its material, skeletal, and molecular correlates, and its variation and linkage at different scales, and relate them to similar issues on a global scale, meaning cross-cultural comparison to the study of early migration behavior in Old World archaeology, as well. Variability in the peopling process can be studied by a wide range of paradigms, including biological, ecological, and anthropological paradigms. Flexibility between local, hemispherical, and global questions, between context and artifact, between essentialism and materialism, between reductionism and emergence, and between different datasets to create inclusive analyses and more theoretical understanding of the process in an interdisciplinary manner is one goal. Another is to integrate the sheer complexity of multiple databases beyond the traditional focal points of sites, artifacts, genes, and skeletons and integrate them into a descriptive and analytical whole. To do so requires both an interdisciplinary scientific and theoretical framework^[96].

Such an integrated process cannot be one of synthesis and commensurability alone; it must allow the productive tension of working with and against an emergent non-linear process of interactive multiplicity and incommensurability.

The preceding discussion leaves a key question: how do these concepts and considerations help to identify the etiology, early detection, and, eventually, treatment of NPC? First, they provide a framework for understanding the contribution of biomarkers in the context of population migrations, which, in turn, provides insight into NPC incidence/occurrence. In contrast, with a simple gene story, haploid ("haplomic") sequence-typing promises to help resolve the complex inheritance and interaction patterns of portions of the inherited two human half-genomes^[7]. Second, they open the possibility of understanding the specific meanings of NPC's genomic complexity, which remains unclear.

The thrust of the foregoing discussion is that there are widely differing models of human movement as well as differing models of how to assemble the relevant data. All models are highly dependent on their underlying assumptions, their spatio-temporal scales, and their selection and definition of variables. It is suggested that the inclusion of the dynamics of a socio-cognitive-technical complex is essential to such modelling and that a synthetic phylogenetic approach to data assemblage be held in tension with a historically dynamic, reticulate, complex adaptive system approach.

This leaves the question addressed in a recent collection of papers: "Can we really read history from the genetic data?"^[97] The authors acknowledged that "historical processes are not amenable to experiment and control, but it is possible to simulate a world and to test that simulation."^[97] Simulations have, for example, used a wide range of variables to test between a unique origin model and a multiregional model for human dispersals out of Africa and find in favor of a unique origin^[98]. Oppenheimer has compared what he labels as phenetic and phylogeographic approaches and found a complex Asian prehistory for Polynesian migration that is telling against the express train OOT^[99]. However, Greenhill *et al.*^[100] have shown that a phylogenetic language test rules out the entangled bank model and partly confirms the OOT model. These simulations, though still contradictory and in need of refinement, are nonetheless working towards enabling a critical re-evaluation of genetic history models such as those of Olsson^[101] and Wells^[102], which give an overly simplistic primacy to genetics as being based in very limited sets of discontinuous genetic markers and lacking a clearly articulated understanding of human movement. As the biologist Hurler^[103] pointed out, a hypothesis needs to be clear on dispersal mechanisms to be testable, a point illustrated by the directionality of clinal patterns. For

example, in Europe, there are opposing clines, e.g. Y chromosomal haplogroup 9 decreases in frequency from Southwest Asia to Northwest Europe, indicating Neolithic gene flow, whereas haplogroup 1 has a cline in the opposite direction, supposedly representing Paleolithic “resistance.” Likewise, in Polynesia, the mtDNA cline with the Neolithic 9 bp deletion is of highest frequency at the extremity of dispersal. Hurles^[103] made the fundamental point that “...the direction of a cline need not indicate its point of origin. The crucial difference may be in its mechanism of spread.” He goes on to make the equally fundamental point that “...extant genetic diversity is ... a suite of prehistoric signals of different time depths... Each allele has its own history which may be a mixed one. Each locus contains multiple alleles and therefore a set of stories... an individual can only reveal part of one story and there is no guarantee that you will get parts of the same story if you sample one individual from each location... An entire population must be assayed to get a fuller picture of each history that has contributed to the whole.” Hunley *et al.*^[104], for example, in their genetic/linguistic/geographic analysis of Northern Melanesia, found a lack of “treeness” and model fitting and likewise call for a higher resolution of the genetic data. Harpending^[105] suggests generating a simulated data set from known histories followed by challenging practitioners of haplotype history to reconstruct what happened given the simulated data. This strategy is now viable given the anticipated availability of complete continuous genetic information using haplomic technology^[7].

However, although such simulations may be a way forward for archeogenetics and provide a temporal framework for the human family tree, they are based in a phylogenetic arborescent framework. As Hurles^[103] put it, “archaeology and genetics are both highly resistant to horizontal transmission.” Such phylogenetic computer models need to be held in tension with biologically reticulate forms of modeling. Additional capacity in testing is needed to allow for multiple dynamic and functional scales and cognitive networks, which Gershenson^[106] and Tang^[107] claims is possible. The task ahead, then, is to give as much clarity and precision as possible to as many variables as possible, as well as to articulate and make apparent as many assumptions as possible and subsequently simulate and test them in the real world. By analogy, such an approach should be used in conceiving, understanding, and treating cancers, including NPC. Research on cancer to date has been essentially reductionist, but it can be radically reconceived with the profoundly different ontology of a complex adaptive system that allows dynamic interaction of heterogeneous variables at multiple scales, an approach that, if adopted, could be developed as “archeo-haplomics.”^[7,108-110] Holding the two approaches in tension may be the most productive way of following trails of knowledge and opening up a fuller understanding of NPC and other epigenetically complex diseases.

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