



Testing modern human out-of-Africa dispersal models and implications for modern human origins



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ABSTRACT

The modern human expansion process out of Africa has important implications for understanding the genetic and phenotypic structure of extant populations. While intensely debated, the primary hypotheses focus on either a single dispersal or multiple dispersals out of the continent. Here, we use the human fossil record from Africa and the Levant, as well as an exceptionally large dataset of Holocene human crania sampled from Asia, to model ancestor–descendant relationships along hypothetical dispersal routes. We test the spatial and temporal predictions of competing out-of-Africa models by assessing the correlation of geographical distances between populations and measures of population differentiation derived from quantitative cranial phenotype data. Our results support a model in which extant Australo-Melanesians are descendants of an initial dispersal out of Africa by early anatomically modern humans, while all other populations are descendants of a later migration wave. Our results have implications for understanding the complexity of modern human origins and diversity.

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1. Introduction

For most of the late twentieth century, discussion on human evolution and modern human origins, or anthropogeny (Varki et al., 2008), focused on validating or falsifying the polarizing models of either multiregional evolution or African origins and replacement of other hominins. Consensus on Africa as the primary birthplace for modern humans has emerged from palaeontological and genetic evidence, placing the common ancestral population between approximately 100 and 200 thousand years ago (~ka; White et al., 2003; McDougall et al., 2005; Fu et al., 2013b; Poznik et al., 2013; Scozzari et al., 2014). At the same time, hominin interbreeding has been proposed in order to explain the genetic affinities between extant and extinct hominin populations (Green et al., 2010; Reich et al., 2010, 2011; Hammer et al., 2011; Mendez et al., 2013;

Prüfer et al., 2014; Sankararaman et al., 2014; The Sigma Type 2 Diabetes Consortium, 2014; Vernot and Akey, 2014). Similarly, a revival of the ‘assimilation’ hypothesis in human palaeontology (Smith et al., 1989, 2005) has encouraged continued assessment of taxonomically ambiguous fossils as descendants of hominin interbreeding events (Liu et al., 2010; Rogers Ackermann, 2010). As a result, the anthropogeny discussion has shifted toward assessing the degree, timing, and location of admixture between hominin populations (Sankararaman et al., 2012; Cooper and Stringer, 2013; Sankararaman et al., 2014). However, an alternative view is that genetic and phenotypic resemblance between extant and extinct populations is a consequence of deep population substructure in Africa, as well as drift following the out-of-Africa expansion (Mirazón Lahr and Foley, 1994; Mirazón Lahr, 1996; Green et al., 2010; Blum and Jakobsson, 2011; Ghirotto et al., 2011; Eriksson and Manica, 2012, 2014; Lowery et al., 2013; Reyes-Centeno et al., 2014). In this view, the context of the geographical and temporal niches occupied by recent hominins can explain, at least in part, the resemblance between Holocene populations and some Pleistocene

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hominins. This view suggests that genetic and phenotypic plesiomorphic traits in certain extant populations reflect differential diversity exported outside of Africa, particularly if the dispersal pattern out of the continent consists of multiple exits.

Given these competing views, understanding the spatial and temporal distribution of hominin populations in the Middle–Late Pleistocene is necessary for developing a coherent anthropogeny theory. Here, we review competing out-of-Africa dispersal hypotheses previously proposed from multidisciplinary evidence. We then design a test for assessing their spatio-temporal predictions using measures of cranial diversity between extant human populations and Pleistocene anatomically modern human (AMH) populations, or ‘palaeo-demes’ (Howell, 1999). Using a large craniometric dataset, we test the expected relationship of hypothetical ancestral palaeo-demes from Africa and the Levant and descendant Holocene populations from Asia, as compared to hypothetical geographical routes of dispersal predicted under different out-of-Africa models.

1.1. The serial founder effect and eastward expansion hypothesis

Support for the origins of AMHs in Africa and their expansion out of that continent comes from the consistent observation that genetic (Eller, 1999; Harpending and Rogers, 2000; Prugnolle et al., 2005; Ramachandran et al., 2005; Liu et al., 2006; Li et al., 2008; Deshpande et al., 2009), linguistic (Atkinson, 2011), and cranial phenotypic (Manica et al., 2007; von Cramon-Taubadel and Lycett, 2008; Betti et al., 2009) diversity decreases with increasing distances from Sub-Saharan Africa. This pattern—referred to as a cascading bottleneck (Harpending and Rogers, 2000) or serial founder (Ramachandran et al., 2005) effect—is usually interpreted to represent a single dispersal event, with an iterative loss of diversity during modern human expansion caused by small bottlenecks and a loss in diversity following each successive founding process. Biological diversity decreases primarily along a latitudinal axis in Eurasia, consistent with a series of short, simple terrestrial migration routes, avoiding major geographic barriers (Liu et al., 2006; Ramachandran and Rosenberg, 2011). This eastward expansion (EE) scenario results in increasing rates of population differentiation and genetic linkage disequilibrium with increasing distances from Africa (Ramachandran et al., 2005; Jakobsson et al., 2008). The EE hypothesis is compatible with a scenario in which expanding AMHs admixed with other hominin populations, but where their genetic contributions would have had to be small (DeGiorgio et al., 2009).

1.2. The multiple dispersals and southern route hypothesis

An alternative hypothesis that is also consistent with decreasing diversity from Africa is a multiple dispersals (MD) scenario, whereby AMHs expanded out of the continent at different time-scales and via distinct geographical routes (Mirazón Lahr and Foley, 1994; Mirazón Lahr, 1996). The MD hypothesis was derived primarily from comparative craniometric studies and associations with the available palaeoenvironmental record. It predicts that a first, opportunistic dispersal between 50 and 100 ka involved a rapid migration primarily along a coastal route, through the southern Arabian Peninsula, reaching Southeast Asia at roughly the same time that a second dispersal through the Levant prompted colonization of the rest of Eurasia between ~40 and 50 ka. Isolated populations throughout Southeast Asia are proposed to retain the signal of the initial ‘southern route’ dispersal, while others are palimpsests of the two dispersals. Hypothetical ‘relic’ populations include Australians, Melanesians, Papuans, Dravidian speakers of South Asia, and short-statured ‘Negrito’ populations of Southeast Asian islands, such as the Andaman Islanders of the Bay of Bengal

and the Aeta/Agta of the Philippines. Following a biogeographical approach, the designation of ‘relics’ is in reference to the ecological context of populations that have become isolated as a result of occupying geographical refugia or exploiting specific ecological niches. The MD scenario predicts that these populations retain plesiomorphic traits because they diverged first from a structured ancestral African population, have remained isolated from subsequent population expansions, and consisted of smaller population sizes. A MD scenario has been questioned on the basis of autosomal genetic data (Wollstein et al., 2010; Reich et al., 2011) but has been supported by some recent genomic studies sampling proposed relic populations (Ghirotto et al., 2011; Rasmussen et al., 2011; Reyes-Centeno et al., 2014).

1.3. The multiple dispersals with isolation hypothesis

In an amendment to the MD hypothesis, the multiple dispersals with isolation (MDI) scenario suggests that Australians are the only isolated descendants of the southern route dispersal, while Papuans, Melanesians, and possibly the Aeta ‘Negrito’ from the Philippines retain a southern route genetic signal that is detectable but obscured due to admixture with members of the second dispersal (Rasmussen et al., 2011). An isolation scenario for Australo-Melanesians is consistent with uni-parental (mitochondrial and non-recombining Y-chromosome DNA) and genome-wide data, although gene flow from outside the region during historical times is still detectable at low levels in Northern Australia (Hudjashov et al., 2007; Pugach et al., 2013). The chronological separation between the dispersals is considered to be relatively short, with the first commencing between ~75 and 62 ka, as inferred from the divergence of Africans and Australians, and the second between ~38 and 25 ka, as inferred from the divergence of East Asians and Europeans. However, dates of divergence between Africans and Eurasians have been estimated as far back as ~140 ka (Gutenkunst et al., 2009), which is more in line with a southern route dispersal interpreted to have occurred as early as the late Middle Pleistocene or during the last interglacial, between ~131 and 114 ka (Stringer, 2000; Petraglia et al., 2010; Armitage et al., 2011; Boivin et al., 2013; Reyes-Centeno et al., 2014; Scozzari et al., 2014).

1.4. The single dispersal and beachcomber arc hypothesis

Given the discrepancies between the EE and MD/MDI hypotheses, a reconciling view is that of a single wave bifurcating outside of Africa, likely in southwest Asia (Mellars, 2006; Oppenheimer, 2012). This view is broadly similar to the EE hypothesis in that population divergence outside of Africa is largely due to the geographic barrier of the Himalaya mountain range, which obstructed migrations between northern and southern Asia. The EE scenario also acknowledges the importance of a coastal ‘beachcomber arc’ migration into Australia, along the Indian Ocean rim. Based primarily on uni-parental genetic evidence, this beachcomber single dispersal (BSD) hypothesis suggests a single out-of-Africa event at ~75 ka (Oppenheimer, 2012) or less than 65 ka (Mellars et al., 2013). Like the EE scenario, BSD considers a series of founding bottlenecks during this expansion. However, in contrast to the parsimonious latitudinal gene flow of EE, BSD implies substantial migration along a longitudinal axis. For example, in addition to a dispersal along the Indian Ocean rim, the ‘beachcomber arc’ also includes the eastern Pacific Ocean rim. Furthermore, it allows for migrations from southwest Asia back into Africa. Gene flow, therefore, is much more dynamic. The implication for biological diversity is that Eurasian populations differentiated in southwest Asia, and that extant North African and non-African

populations reflect a subset of this diversity. As in the MD/MDI hypotheses, a behavioural implication is inherent in the BSD model, as the southern, coastal dispersal is largely the result of a shift towards marine resource exploitation, documented in the late Middle Pleistocene archaeological and palaeontological records of Africa (Henshilwood and Marean, 2003; Marean et al., 2007).

1.5. Testing modern human dispersal patterns

These different out-of-Africa dispersal hypotheses have been formally evaluated by some of us (Reyes-Centeno et al., 2014), testing the geographical and temporal predictions of each scenario against two independent biological datasets, namely genomic and cranial shape variables derived from modern human Holocene populations. Since spatial and temporal distances between populations are explicit in the dispersal scenarios, distinguishing between competing hypotheses is achieved by assessing the correlation of spatio-temporal distances with neutral biological distances. This approach is founded on the assumption that the primary driver of recent human evolution is genetic drift (Rogers Ackermann and Cheverud, 2004; Roseman and Weaver, 2007; Weaver et al., 2007; Reyes-Centeno et al., 2014; Weaver, 2014). In the absence of selection and assuming a common ancestral origin, cranial phenotypic differentiation in modern human populations is expected to be proportional to the geographic proximity between them (Hubbe et al., 2010; Weaver, 2014). Consensus has emerged on using cranial form as a proxy for identifying patterns of modern human population history and neutral diversification (Relethford and Harpending, 1994; Roseman, 2004; Harvati and Weaver, 2006a, b; Manica et al., 2007; Betti et al., 2009; Hubbe et al., 2009; Smith, 2009; von Cramon-Taubadel, 2009; Smith et al., 2013). Only a limited number of populations and certain cranial regions have been shown to be affected by non-stochastic evolutionary processes, such as climate-related effects on cranial phenotype. Previous work found greater support for the MDI hypothesis, supporting an initial dispersal scenario that occurred closer to the Middle-Late Pleistocene boundary (Reyes-Centeno et al., 2014). However, that study used Holocene modern human samples, relied on genetic divergence and hypothetical 'archaeological divergence' estimates to control for a temporal component in the models, and was limited to a sample size of ten populations. Another approach is to analyse Holocene and Pleistocene populations in tandem, such that the former can be considered descended from the latter. This approach has been employed with craniometric data for testing competing dispersal scenarios for the peopling of the Americas from Asia (Hubbe et al., 2010). Drawing from this method, the use of African and Levantine Pleistocene fossil palaeo-demes as ancestral to Holocene populations is used here to control for the temporal dimension of competing dispersal hypotheses following the proposal that the fossil record can serve to represent spatiotemporally bounded biological populations, or palaeo-demes (Howell, 1999).

Single dispersal models such as EE and BSD predict continuity in the cranial phenotype of early AMHs and the later fossil populations in Africa. In this view, morphological diversity during the out of Africa event would reflect features primarily observed in a later Late Pleistocene palaeo-deme (LPPD). By contrast, multiple dispersal scenarios such as MD and MDI predict that isolated, relic descendants of the first dispersal would show closer affinity to the earliest AMHs while all other extant populations would show closer affinities to the LPPD. In such a scenario, two ancestral palaeo-deme populations account for the diversity exported outside of Africa (Fig. 1b).

Because the competing scenarios suggest that AMH dispersal(s) occurred between ~135 and 25 ka, fossils within this time frame

must be considered; however, the human fossil record from this period is scarce and fragmentary. In East Africa, the earliest relatively complete AMH adult crania is the Herto BOU-VP-16/1 specimen, dated to ~160 ka (White et al., 2003; McCarthy and Lucas, 2014). In the Levant, the earliest AMH adult crania are at the Qafzeh and Skhul sites, dated to between ~135 and 80 ka (MacCurdy, 1936; Vandermeersch, 1981; Schwarcz et al., 1988; Grün et al., 2005). Since this region is often thought to represent an extension of African ecosystems (Howell, 1999; Klein, 2000), the Qafzeh/Skhul specimens can be included in a human origins palaeo-deme. Notably, some African specimens within or somewhat older than this time frame, such as Ngaloba LH-18 (Magori and Day, 1983), Singa (Stringer, 1979; McDermott et al., 1996), and the Jebel Irhoud specimens (Ennouchi, 1962; Grün and Stringer, 1991; Hublin, 2001), are considered to represent early *Homo sapiens*, but retain some less modern elements in their cranial morphology (Stringer, 1974; Gunz et al., 2009; Harvati et al., 2011). Consequently, these specimens are not representative of a hypothetical AMH origins palaeo-deme. Few adult crania from Africa or the Levant are known in the later part of the Late Pleistocene. The relatively complete specimens of Hofmeyr from South Africa (Grine et al., 2007) and the Nazlet Khater 2 specimen from Egypt (Crevecoeur et al., 2009) date from ~36 ka to ~38 ka, respectively, and have been attributed to populations ancestral to Upper Palaeolithic Eurasians. As such, they can be used to represent a LPPD.

2. Materials and methods

2.1. Samples

For the hypothetical palaeo-deme samples, we included six specimens belonging to the origins palaeo-deme or the LPPD (Table 1), maximizing the number of craniometric variables that could be collected across all samples and without imputing missing values. A total of twelve standard craniometric variables (Howells, 1973; Bräuer, 1988) were available for analysis (Table 2). Data for the Skhul and Qafzeh specimens were collected by C.S. (Stringer, 1992). Published data were used for Herto BOU-VP-16/1 (White et al., 2003), Nazlet Khater 2 (Crevecoeur, 2006; Crevecoeur et al., 2009), and the Hofmeyr specimen (Grine et al., 2007, 2010; Crevecoeur et al., 2009). For the Holocene sample, we used a subset of the craniometric dataset collected by T.H. (Hanihara, 2006; Hubbe et al., 2009), totalling 2110 adult male individuals. The subset includes samples grouped according to the dispersal models tested here, comprising eighteen populations from Africa and Asia (Table 3).

We note that several studies have assessed the correlation of craniometric variables with climate parameters in order to infer environmental selection (Manica et al., 2007; Betti et al., 2009; Hubbe et al., 2009). Because distinct climate variables were used in these studies, results differ as to the degree to which climate affects each cranial measurement. In our analysis, we used only one variable (nasion–prosthion height; Table 2) that was consistently found to be under strong climate selection. However, this variable was also found to retain a strong global demographic signal by Manica et al. (2007) and to have a higher heritability value than the average of the variables sampled by Carson (2006). Continued assessment of factors affecting cranial form, including climate and diet, will allow for a better understanding of which cranial variables to use in future studies.

2.2. Measure of population differentiation

Raw cranial measurements were size-standardized by dividing each measurement by the geometric mean of all measurements,

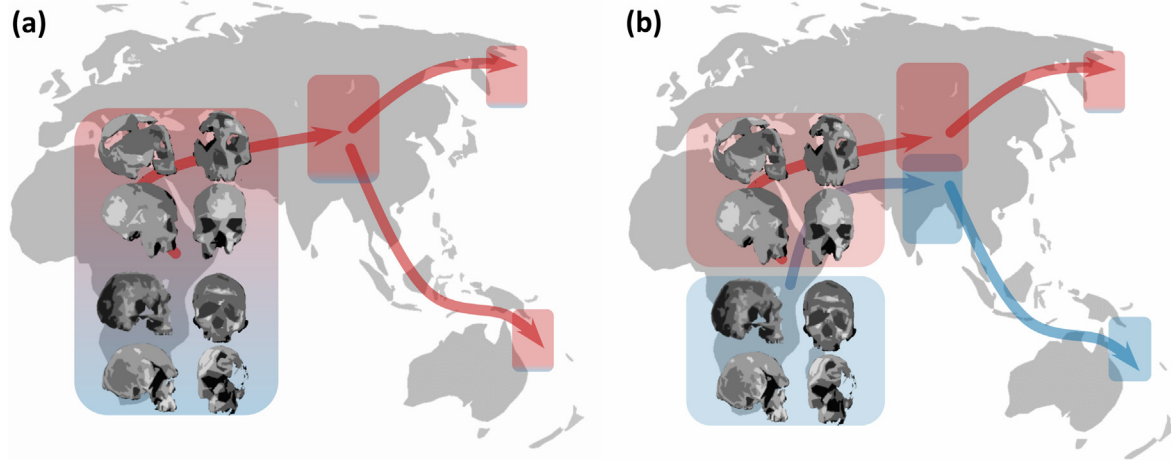


Figure 1. Study design. A schematic representation of the source population(s) in Africa under either a single dispersal (a) or multiple dispersals (b) hypothesis. In (a), continuity between early and later modern humans in Africa is expected, followed by eastward geographical continuity of Holocene populations, with decreasing diversity resulting from expansion. In (b), Middle–Late Pleistocene anatomically modern humans are expected to show affinities to descendants of an early southern route dispersal, whereas Late Pleistocene modern humans are expected to show affinities to descendants of a second dispersal. Rectangles represent demes and their size indicates intra-population diversity. For simplicity, Holocene map outlines are shown. Fossil drawings adapted from the following sources (in order of appearance from top to bottom): [Crevecoeur \(2006: Nazlet Khater 2\)](#), [Grine et al. \(2007: Hofmeyr\)](#), [Vandermeersch \(1981: Qafzeh 6\)](#), and [White et al. \(2003: Herto BOU-VP-16/1\)](#).

Table 1
Fossil Pleistocene cranial sample.

	Provenance	Specimen	Geological age (–ka)
Origins Palaeo-deme (ORIG)	Ethiopia	Herto BOU-VP-16/1	160
	Palestine/Israel	Skhul 5	80–135
		Qafzeh 6	80–135
		Qafzeh 9	80–135
Late Pleistocene palaeo-deme (LPPD)	South Africa	Hofmeyr	36
	Egypt	Nazlet Khater 2	38

Table 2
Quantitative cranial variables: linear measurements.

Bräuer (1988)	Howells (1973)	Heritability (h^2)		Howells' description
		Martínez-Abadías et al. (2009)	Carson (2006)	
M1	GOL	0.31	0.363	Maximum cranial length
M8	XCB	0.36	0.233	Maximum cranial breadth
M10	XFB	<i>n/a</i>	<i>n/a</i>	Maximum frontal breadth
M11b	AUB	0.40	0.397	Biauricular breadth
M19	MDH	<i>n/a</i>	<i>n/a</i>	Mastoid height
M29	FRC	0.11	0.144	Nasion-bregma chord
M30	PAC	0.06	0.307	Bregma-lambda chord
M43(1)	FMB	0.4	0	Bifrontal breadth
<i>n/a</i>	NPH	0.34	0.588	Nasion-prosthion height
M49a	DKB	0.33	0.170	Interorbital breadth
M52	OBH	<i>n/a</i>	0.478	Orbital height
M54	NLB	0.00	0.007	Nasal breadth
<i>n/a</i>	NLH	0.43	0.729	Nasal height

per specimen ([Darroch and Mosimann, 1985](#); [Jungers et al., 1995](#)). These size-standardized variables were used to calculate biological distances between populations. For each analysis, we calculated the levels of phenotypic (morphological) differentiation, P_{st} ([Roseman and Weaver, 2007](#)). We developed a matrix of pairwise P_{st} values representing phenotypic differentiation between populations ([Table 4](#)). P_{st} follows the quantitative analytical framework of neutral genetic evolutionary theory and is analogous to the fixation index, F_{st} , in population genetics ([Relethford and Blangero, 1990](#); [Holsinger and Weir, 2009](#)). It assumes an equal and additive model of inheritance of phenotypic traits, where phenotypic

variances are proportional to genetic variances ([Harpending and Ward, 1982](#); [Relethford and Harpending, 1994](#)). At least one of our sampled populations (Mongolians) are thought to be under strong climate selection and have been hypothesized to exhibit climate-adapted cranial morphology, therefore representing a deviation from neutrality ([Hubbe et al., 2009](#)). Because this runs contrary to the assumptions in our method, we recomputed P_{st} after removal of this population.

P_{st} acknowledges the fractional heritability of cranial traits and the added epigenetic effects on morphology. Currently, heritability estimates for cranial variables have only been ascertained in one

Table 3
Recent Holocene cranial sample.

Abb. ^a	Assigned meta- population	Geographic provenance ^b	Assigned geographic locality	Geographic coordinates		Sample size <i>n</i>
				Lat.	Long.	
BENG	Bengal Bay	Andaman Islands	Dhaka	23.71	90.41	43
EGYP	Egypt	Egypt, Sudan	Cairo	30.06	31.24	413
ESIA	Indonesia	Indonesia	Jakarta	−6.21	106.84	146
INCH	Indochina	Laos, Myanmar, Thailand, Vietnam	Bangkok	13.73	100.52	132
JAPN	Japan	Japan	Tokyo	35.66	139.82	137
LVNT	Levant	Israel, Palestine	Jerusalem	31.77	35.22	85
MLAY	Malay Peninsula	Malaysia, Singapore	Kuala Lumpur	3.14	101.69	79
MNCH	Manchuria	China (Han), Korea	Shenyang	41.81	123.43	173
MONG	Mongolia	Mongolia	Ulaanbaatar	47.92	106.9	120
NAUS	Australia North	Torres Strait Islands, Queensland	Brisbane	−27.47	153.02	57
NIND	India North	N.E. India (Indo-European), Nepal, Tibet	New Delhi	28.63	77.2	129
NMEL	Melanesia North	New Britain, New Ireland, Solomon Islands	Honiara	−9.42	159.94	121
PAPU	Papua New Guinea	Papua New Guinea	Port Moresby	−9.48	147.19	110
PHIL	Philippines	Luzon Island (Agta/Aeta 'Negrito')	Manila	14.6	120.98	20
SAUS	South Australia	New South Wales, South Australia, Western Australia	Hobart	−42.88	147.32	116
SIND	South India	India (Dravidian)	Colombo	6.93	79.86	83
SMEL	South Melanesia	New Caledonia, New Hebrides	Noumea	−22.28	166.46	67
WASI	Western Asia	Afghanistan, N.W. India (Indo-European)	Kabul	34.52	69.17	79
Total						2110

^a Abbreviation code used in data matrices.^b Ethno-linguistic affiliation in parenthesis.**Table 4**
Pairwise P_{st} values.^a

P_{st}	BENG	EGYP	ESIA	INCH	JAPN	LPPD	LVNT	MLAY	MNCH	MONG	NAUS	NIND	NMEL	ORIG	PAPU	PHIL	SAUS	SIND	SMEL	WASI
BENG	0	0.59	0.31	0.45	0.74	1.61	0.77	0.41	0.74		1.12	0.47	0.89	2.63	0.75	0.38	1.43	0.60	1.16	1.02
EGYP	0.56	0	0.35	0.43	0.27	0.70	0.08	0.58	0.42		0.68	0.24	0.45	1.78	0.36	0.75	0.79	0.22	0.61	0.17
ESIA	0.30	0.34	0	0.02	0.27	0.66	0.38	0.06	0.22		0.66	0.12	0.40	1.96	0.39	0.30	0.94	0.28	0.59	0.46
INCH	0.44	0.42	0.02	0	0.25	0.63	0.43	0.03	0.15		0.66	0.16	0.42	1.99	0.42	0.34	0.97	0.30	0.58	0.49
JAPN	0.72	0.26	0.26	0.24	0	0.63	0.25	0.40	0.15		0.70	0.16	0.40	1.84	0.49	0.63	0.90	0.33	0.59	0.25
LPPD	1.56	0.70	0.65	0.61	0.62	0	0.65	0.87	0.63		0.98	0.69	0.95	1.56	0.92	1.38	1.19	0.75	0.90	0.57
LVNT	0.74	0.08	0.37	0.42	0.24	0.65	0	0.58	0.41		0.67	0.25	0.47	1.88	0.48	0.82	0.96	0.17	0.63	0.20
MLAY	0.41	0.57	0.06	0.03	0.39	0.84	0.56	0	0.21		0.92	0.30	0.64	2.24	0.64	0.30	1.30	0.47	0.88	0.74
MNCH	0.72	0.41	0.21	0.14	0.14	0.62	0.39	0.20	0		0.87	0.24	0.51	1.92	0.56	0.62	1.18	0.51	0.74	0.41
MONG	1.20	1.02	0.63	0.54	0.46	1.11	1.00	0.51	0.34	0										
NAUS	1.10	0.67	0.65	0.65	0.69	0.95	0.66	0.91	0.86	1.72	0	0.51	0.14	1.26	0.14	1.12	0.19	0.36	0.11	0.48
NIND	0.46	0.23	0.12	0.16	0.16	0.67	0.24	0.29	0.24	0.83	0.50	0	0.22	1.93	0.26	0.47	0.68	0.16	0.35	0.20
NMEL	0.86	0.44	0.40	0.41	0.39	0.94	0.45	0.63	0.51	1.21	0.14	0.22	0	1.21	0.06	0.80	0.26	0.31	0.07	0.25
ORIG	2.52	1.73	1.89	1.93	1.79	1.51	1.81	2.17	1.87	2.02	1.21	1.86	1.17	0	1.33	1.96	1.29	2.02	1.35	1.63
PAPU	0.73	0.35	0.38	0.41	0.47	0.90	0.46	0.62	0.55	1.34	0.14	0.26	0.06	1.28	0	0.84	0.19	0.29	0.11	0.24
PHIL	0.37	0.72	0.29	0.33	0.62	1.33	0.79	0.30	0.61	0.73	1.09	0.46	0.78	1.88	0.81	0	1.35	0.58	1.03	1.03
SAUS	1.39	0.77	0.92	0.95	0.88	1.17	0.94	1.27	1.17	1.99	0.18	0.66	0.26	1.25	0.19	1.32	0	0.59	0.18	0.49
SIND	0.58	0.21	0.27	0.30	0.32	0.74	0.17	0.46	0.49	1.23	0.35	0.15	0.30	1.93	0.28	0.56	0.56	0	0.34	0.27
SMEL	1.14	0.60	0.58	0.57	0.58	0.88	0.61	0.86	0.73	1.58	0.11	0.35	0.07	1.30	0.11	1.00	0.18	0.33	0	0.31
WASI	0.98	0.17	0.44	0.47	0.24	0.56	0.19	0.72	0.40	1.06	0.47	0.19	0.25	1.59	0.23	1.00	0.48	0.26	0.31	0

^a Abbreviations correspond to Tables 1 and 3. Values are rounded to the nearest hundredth decimal. Below diagonal: P_{st} computation considering all populations; above diagonal: P_{st} computation excluding climate-adapted population. Full values and values uncorrected for sampling bias are reported in SOM Tables 1 and 2.

population using two different approaches (Carson, 2006; Martínez-Abadías et al., 2009). In these studies, estimates for each variable differ (reported in Table 2 for the variables used here), sometimes to a large degree (e.g., FMB $h^2 = 0.4$ or $h^2 = 0$). Given these discrepancies, as well as the fact that we used variables of unknown heritability and fossil populations for which no estimates are available, we use an approximate average value across the known variables, $h^2 = 0.3$. Nonetheless, heritability corrections will not affect the relative relationship between the distances calculated since the corrections are proportional between population pairs. Lastly, we used a conservative approach assuming that population sizes are equal across all samples (Pinhasi and von Cramon-Taubadel, 2009). P_{st} calculations were made in the RMET 5.0 software and corrected for sampling bias (Relethford et al., 1997) (Supplementary Online Material [SOM] Table 1). We report uncorrected values in SOM Table 2 and note that these different values do not affect the interpretations made from our analyses.

2.3. Modelling the out-of-Africa dispersal hypotheses

Out-of-Africa dispersal scenarios were modelled using geodesic distance, G , between populations along hypothetical dispersal routes (Fig. 2). Pairwise G was calculated using the PASSaGe software (Rosenberg and Anderson, 2011), which assumes a spherical shape for the Earth and a radius of 6379.336847 km (SOM Tables 5–9). The null, control model is calculated using the pairwise G between populations, without regard to geographic barriers or continuity between palaeo-demes (Hubbe et al., 2010). Addis Ababa, Ethiopia (lat. 9.02, long. 38.74) was used as the location for the palaeo-demes in all models, in order to make our study methodologically comparable to previous work (e.g., Ramachandran et al., 2005; Ghirotto et al., 2011; Reyes-Centeno et al., 2014). Waypoints were used in order to capture the complex geography of coastal migration routes for the BSD, MD, and MDI scenarios. Waypoint latitude and longitude coordinates

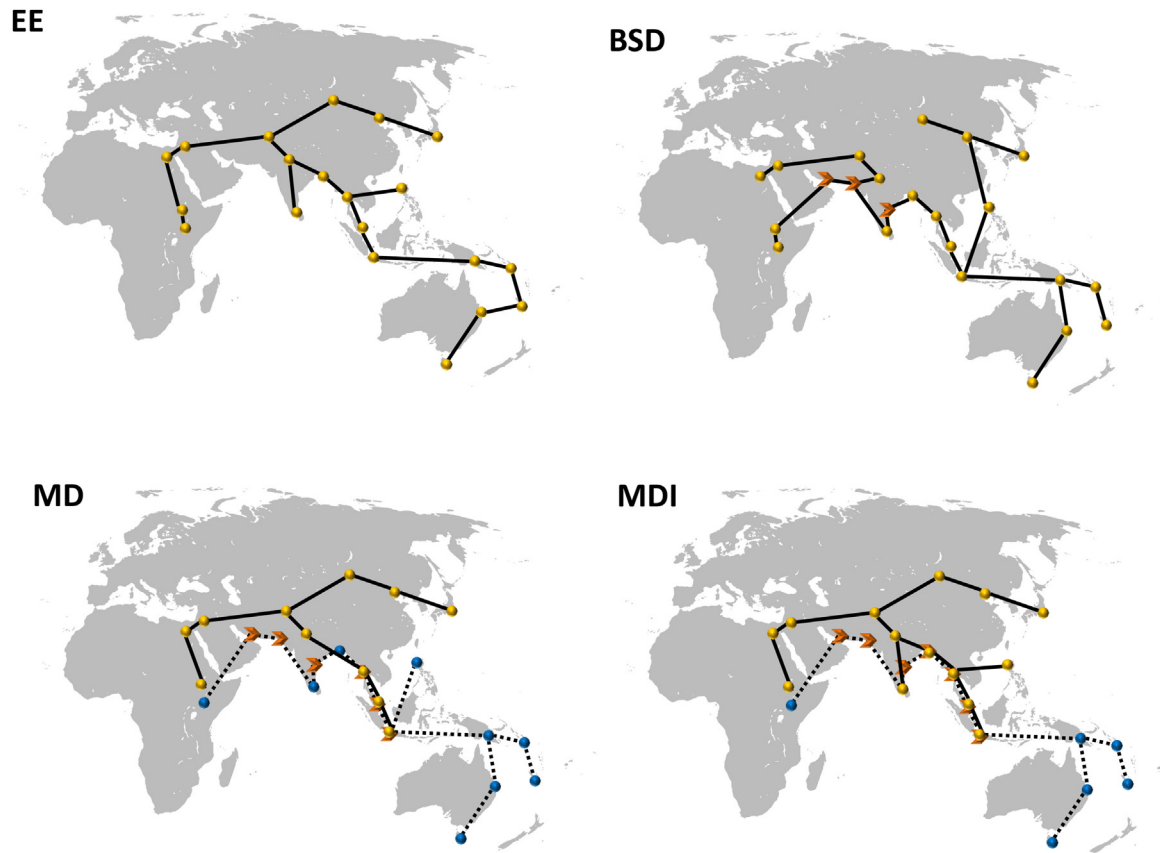


Figure 2. Out-of-Africa biogeographical models. Circles are approximate centroids of populations sampled (Table 3) and paleo-demes (Table 1), connecting lines are dispersal routes, and arrows are geographical waypoints. The eastward expansion (EE) model connects populations primarily along a latitudinal axis, avoiding geographic barriers. The 'beachcomber' single dispersal (BSD) model connects populations primarily along a coastal route. The multiple dispersals model (MD) connects hypothetical isolated, 'relic' populations (dark spheres) along a southern route (dotted lines). The multiple dispersals with isolation (MDI) model assumes that only Australo-Melanesian populations retain a strong southern route biological signal. For simplicity, Holocene map outlines are shown.

included the following: Dubai (25.27, 55.31), Karachi (24.89, 67.03), and Chennai (13.06, 80.24). We note that in the MD and MDI models, the geographical centroids of some populations were also used as waypoints. For example, Kuala Lumpur, which corresponds to the centroid of the Malaysian population, is also used as a waypoint for the southern route. This is because we sampled several populations from Southeast Asia living along a purported southern dispersal route (Indochina, Malaysia, Indonesia) but who are not considered isolated, relic populations in the MD or MDI models; therefore, we included them as descendants of the second dispersal but used the same geographical space to model the first dispersal. The evolutionary implication is that such populations are presumed to have replaced initial descendants of the first dispersal, or be highly admixed with them, obscuring a biological southern route signal. We also note that we have chosen modern points of reference (i.e., existing cities) for simplicity. Slight changes based on palaeoenvironmental reconstructions are unlikely to significantly affect G at a continental scale. In order to compare the association of P_{st} and G when considering removal of the climate-adapted population, we maintained Ulaanbaatar, Mongolia as a waypoint between the Western Asian and Manchurian populations for the EE, MD, and MDI models. The BSD model is not affected since Mongolia is a terminal node (i.e., connected by a migration route to only one other population). In all cases, therefore, G is unmodified when removing Mongolians.

In the EE model, populations are connected by geographical proximity and primarily along a latitudinal axis, avoiding major

geographic barriers (Liu et al., 2006; Ramachandran and Rosenberg, 2011). This model assumes continuity between the palaeo-demes such that the origins palaeo-deme is ancestral to the LPPD and, in turn, only the LPPD is directly ancestral to the Holocene populations (Fig. 2). The implication is that morphological diversity in Asia would primarily be an export of the diversity of the LPPD. Following this same logic, populations in the BSD model are connected along a coastal 'beachcomber arc' route. Additionally, the Holocene Egyptian and Levantine populations are presumed to represent a migration back toward Africa, from southwest Asia. In the MD model, the origins palaeo-deme is ancestral to hypothetical relic populations along a southern, coastal dispersal route. Relic populations include Dravidian speakers from India, Andamanese Islanders from the Bay of Bengal, Philippine Aeta/Agta 'Negritos,' New Guinea Papuans, Melanesians, and Australians. The LPPD is ancestral to all other populations along an initial northern dispersal route. The MDI model follows the same approach as the MD model, but in this case only New Guinea Papuans, Melanesians, and Australians are considered isolated, southern route descendants of the origins palaeo-deme. We note that from both a genetic and morphological point of view, the Aeta/Agta have been found to have closer affinities to Northern and Eastern Asian groups than to Melanesians or Australians (Hanihara, 1992, 2006; Rasmussen et al., 2011; Endicott, 2013; Migliano et al., 2013; Reyes-Centeno et al., 2014), although they have been interpreted as representing a population that is highly admixed between the two dispersal groups (Rasmussen et al., 2011; Reyes-Centeno et al., 2014).

In order to connect the separate southern and northern ancestor–descendant series in the MD and MDI models, we use a similar approach to that employed in a recent test for multiple dispersals into the Americas (Hubbe et al., 2010). Our approach differs in that we include two hypothetical ancestral populations (the palaeodemes) rather than one. In order to accommodate this, the northern and southern route descendants are connected by considering the distance of any given Holocene northern route population to the LPPD, plus the direct distance of LPPD to any given Holocene southern route population. The connection of a northern route Holocene population to the origins palaeo-deme would therefore be equal to its distance to the LPPD, plus the direct distance to the southern route population closest to Africa, plus the distance of this population to the origins palaeo-deme along the southern route. For example, in the MD model, the distance between the Western Asian population and the origins palaeo-deme would equal the distance of the Western Asian population centroid (Kabul) to the LPPD through Jerusalem and Cairo (along the northern route), plus the direct distance of LPPD to Dravidian-speaking Indians (the southern route population closest to Africa in this model), plus the distance of Dravidian Indians to the origins palaeo-deme through the Karachi and Dubai waypoints (along the southern route). Thus, $G = (G_{\text{WASI} \rightarrow \text{LVNT}} + G_{\text{LVNT} \rightarrow \text{EGYP}} + G_{\text{EGYP} \rightarrow \text{LPPD}} + G_{\text{LPPD} \rightarrow \text{SIND}} + G_{\text{SIND} \rightarrow \text{Karachi}} + G_{\text{Karachi} \rightarrow \text{Dubai}} + G_{\text{Dubai} \rightarrow \text{ORIG}})$, or $\sim 16,719$ km (SOM Table 8). The method is further exemplified by the construction of binary matrices, where 1 represents a connection between two populations along the model-specified dispersal route and 0 represents no connection (SOM Tables 10–13).

2.4. Statistical analyses

When using a pairwise distance approach, as employed here, assessing the association between two matrices is evaluated with Mantel tests, which compares their association to a null distribution. The method has been productively used for testing dispersal patterns of modern human populations (Pinhasi and von Cramon-Taubadel, 2009; Hubbe et al., 2010, 2011). Pairwise population matrices were used to test for the correlation between P_{st} and G in a simple Mantel test (Mantel, 1967). To test for significance (p -value), we ran 10k permutations of the matrix rows and columns. In all cases, we report the Pearson correlation coefficient (r) and two-tailed p -value of the permutation results. We accepted $\alpha = 0.01$ as statistically significant results, corresponding to a Bonferroni correction for multiple model tests. In order to compare competing models, we applied a Dow–Cheverud test (Dow and Cheverud, 1985). This analysis compares an observation matrix (in this case, pairwise P_{st} values) against two competing model matrices (in this case, pairwise G values for two given dispersal models). Thus, it is possible to assess whether one dispersal model correlates significantly better with morphological differentiation than another model.

3. Results

The Mantel test correlation between pairwise P_{st} and G was significant for all dispersal models (Table 5). However, the correlation coefficient for the MDI model was more than twice the value of the model with the next highest coefficient. The MDI correlation coefficient was also higher after removal of the climate-adapted population, as expected if this population deviates from the assumption of our quantitative genetics analytical framework. Dow–Cheverud tests revealed that all models fit the P_{st} values better than the control. However, only the MDI is significantly better (Table 6); furthermore, MDI is significantly better than all other competing models (Table 7). These results were upheld when

Table 5
Mantel test results.^a

Out-of-Africa models	All populations	Select populations ^b
Control	0.265 (<0.0001)	0.251 (0.001)
EE	0.334 (<0.0001)	0.311 (<0.0001)
BSD	0.281 (<0.0001)	0.223 (0.003)
MD	0.294 (0.001)	0.255 (0.001)
MDI	0.676 (<0.0001)	0.707 (<0.0001)

^a Reported values are r Pearson correlation coefficients and two-tailed p -values after 10k permutations (in parentheses).

^b After removal of climate-adapted population.

the Mongolian sample was removed. Thus, our test of out-of-Africa models supports a multiple dispersals scenario in which Australian, Papuan, and Melanesian populations descend from a southern route dispersal.

When we analysed our dataset by including only the more tightly spatio-temporally bound palaeo-deme of Qafzeh-Skhul (SOM Tables 3–4), the MDI model was again supported, albeit with a slightly lower correlation coefficient ($r = 0.658$, $p = <0.0001$; after removal of climate-adapted population: $r = 0.701$, $p = <0.0001$). While the correlation differences are minimal, the lower value may be due to the fact this restricted origins palaeo-deme does not sample an actual ancestral African population. Nevertheless, Australians, Melanesians, and Papuans had the shortest distance to the origins palaeo-deme (Table 4) and the Qafzeh-Skhul palaeo-deme (SOM Tables 3–4).

4. Discussion

4.1. One or two dispersals?

In this study, we formalized the spatio-temporal predictions of four distinct modern human out-of-Africa hypotheses and compared them to distance measures derived from a large fossil and recent modern human comparative sample. Such an approach provides an independent method for testing hypotheses derived from the archaeological record or from molecular genetic evidence. It has the advantage that it can incorporate data from AMH Pleistocene palaeo-demes, which are not represented in current palaeogenetic work. Our results indicate that the MDI model is the strongest of the four scenarios examined. In this regard, our findings are consistent with previous morphological analyses of both metric and non-metric data from regional, as well as worldwide, cranial samples (Hanihara, 2006; Stock et al., 2007; Hanihara et al., 2012), and with archaeological data that suggest an early modern human dispersal through the southern route (Armitage et al., 2011; Rose et al., 2011; Delagnes et al., 2013). Our results also agree with recent genome-wide analyses of human populations, including some sampling ancient genomes (Ghirotto et al., 2011; Rasmussen et al., 2011; Reyes-Centeno et al., 2014; Seguin-Orlando et al., 2014),

Table 6
Dow–Cheverud test: control against models.^a

Out-of-Africa models	All populations	Select populations ^b
EE	–0.119 (0.103)	–0.102 (0.189)
BSD	–0.027 (0.699)	0.060 (0.444)
MD	–0.028 (0.698)	–0.003 (0.931)
MDI	–0.388 (<0.0001)	–0.421 (<0.0001)

^a Reported values are r Pearson correlation coefficients and two-tailed p -values after 10k permutations (in parentheses). Positive correlation values indicate that the control model is a better fit with P_{st} values than the competing model, while negative correlation values indicate that the alternative model is better.

^b After removal of climate-adapted population.

Table 7
Dow–Cheverud test: MDI against competing models.^a

Out-of-Africa models	All populations	Select populations ^b
EE	0.362 (<0.0001)	0.410 (<0.0001)
BSD	0.336 (<0.0001)	0.415 (<0.0001)
MD	0.439 (<0.0001)	0.507 (<0.0001)

^a Reported values are *r* Pearson correlation coefficients and two-tailed *p*-values after 10k permutations (in parentheses). Positive correlation values indicate that the MDI model is a better fit with P_{st} values than the compared model, while negative correlation values indicate that the alternative model is better.

^b After removal of climate-adapted population.

which support multiple dispersals with an initial southern route migration. Finally, the results are compatible with palaeoclimatic reconstructions suggesting two broad windows of opportunity for dispersal out of the continent along a southern route, between ca. 140 and 115 ka and between ca. 80 and 65 ka (Blome et al., 2012; Rohling et al., 2013).

Nevertheless, our results conflict with uni-parental studies of extant modern humans, which propose a single dispersal as per the EE and BSD scenarios (e.g., Macaulay et al., 2005; Endicott et al., 2009; Fernandes et al., 2012; reviewed in: Oppenheimer, 2012). A single dispersal is also supported by the finding that all non-African modern human populations share a similar percentage of autosomal DNA with extinct Pleistocene hominin (Neanderthal) populations (Green et al., 2010; Prüfer et al., 2014) since the most parsimonious explanation for the autosomal data posits a single admixture event in Southwest Asia at the initial phases of the modern human expansion out of Africa (Green et al., 2010). Different population sizes across Eurasia are thought to have resulted in slightly higher Neanderthal genetic contribution in East Asian populations (Prüfer et al., 2014; Sankararaman et al., 2014). The recent sequencing of AMH genomes from Russia and China has shown similar or slightly stronger admixture signals than those preserved in living humans (Fu et al., 2014; Raghavan et al., 2014; Seguin-Orlando et al., 2014). These studies have also further constrained the time frame for the proposed Neanderthal-modern human interbreeding event, which is now estimated to have occurred between ~60 and 50 ka when assuming a single admixture event (Fu et al., 2014; Seguin-Orlando et al., 2014). If these estimates are correct, they imply that the out-of-Africa expansion occurred once, shortly before ~60–50 ka (although see Seguin-Orlando et al., 2014 for support of an earlier migration of Australo-Melanesian ancestors).

At the core of these conflicting findings is the question of how Australo-Melanesians, if they are the descendants of an earlier dispersal, could inherit similar levels of Neanderthal admixture as all other non-Africans and display the same derivation of uniparental markers as other non-Africans. A possible but untested answer regarding the admixture has been proposed by Weaver (2014), who suggested that this might be the result of interbreeding with Denisovans. Denisovans are close relatives of Neanderthals and have been proposed to have interbred with Australasians as well as Neanderthals (Reich et al., 2011; Skoglund and Jakobsson, 2011; Prüfer et al., 2014). That admixture event was hypothesized to have occurred in Southeast Asia as modern humans expanded along the southern route (Reich et al., 2011), possibly across the Wallace Line in Southeast Asian islands (Cooper and Stringer, 2013).

4.2. Early dispersal?

The most contentious issues in this debate are the timing of the dispersal or dispersals, how far the dispersals reached, and whether

significant traces of the hypothesized early dispersal survive in extant populations. Support for an early Late Pleistocene dispersal comes from the sites of Jebel Faya, United Arab Emirates, and the Dohfar region, Oman. Dated to between ~100 and 130 ka, these have yielded lithic assemblages argued to have been made by AMHs (Armitage et al., 2011; Rose et al., 2011; Delagnes et al., 2013). However, no hominin remains have been found in association with these artefacts, prompting intense debate concerning the taxonomic status of their makers (Mellars et al., 2013). The Qafzeh and Skhul fossils from the Levant represent clear evidence of AMHs outside of the African continent in the early Late Pleistocene. Because the origins palaeo-deme in our analysis encompasses these specimens, our results are compatible with the view that they are related to the ancestral population of Australians (Schillaci, 2008; Petraglia et al., 2010). Indeed, in comparative craniometric studies early AMHs in general, and the Qafzeh-Skhul series in particular, consistently show morphological affinities with Oceanic populations, particularly Australians and Papuans (Stringer, 1992; White et al., 2003; Grine et al., 2007; Schillaci, 2008; Gunz et al., 2009; Harvati et al., 2011). While this result would seem to support an early Late Pleistocene initial dispersal, our current test of dispersal models cannot test for an alternative later initial dispersal because of the limitations of our fossil sample (see below).

Timeframes for the out-of-Africa dispersal are also proposed on the basis of divergence date estimates derived from various genetic loci. Parsimoniously, the divergence of Africans and non-Africans can be considered an upper limit for the out-of-Africa event (Green and Shapiro, 2013). Such divergence dates depend largely on mutation rates, which have been intensely debated in the past (Roach et al., 2010; Scally and Durbin, 2012; Poznik et al., 2013). Slow mutation rates yield older dates of divergence and fast mutation rates yield younger dates. For example, estimates from modern human genetic data have ranged between ~84 and 44 ka from mtDNA data (Macaulay et al., 2005; Endicott and Ho, 2008; Endicott et al., 2009; Fernandes et al., 2012; Lippold et al., 2014); ~120 and 60 ka from Y-chromosome data (Lippold et al., 2014; Scozzari et al., 2014), and ~140 and 65 ka from nuclear data (Gutenkunst et al., 2009; Xing et al., 2010; Eriksson et al., 2012; Scally and Durbin, 2012; Reyes-Centeno et al., 2014). Calibration with fossil genomes has now served to constrain these rates for the recent human lineage (Fu et al., 2013b, 2014; Rieux et al., 2014). The most recent calibrations have confirmed a relatively fast mutation rate for uni-parental genetic loci, dating the divergence of Africans and non-Africans to ~71 ka. Studies of modern human bacterial pathogens also suggest an initial southern route dispersal between ~55 and 75 ka (Moodley et al., 2009, 2012). At the same time, calibration with the Ust'Ishim genome has also confirmed a slow nuclear mutation rate, thus producing older estimates of the dates of divergence (Fu et al., 2014).

In order to reconcile these contrasting estimates, a gradual divergence of Africans and non-Africans has been proposed, with ancestral populations in East Africa, South-western Asia, and possibly North Africa in intermittent contact with each other over an extended period of time between ~120 and 40 ka (Xing et al., 2010; Scally and Durbin, 2012). In this view, uni-parental divergence estimates reflect the most recent divergence in a long process of population separation. This hypothesis is compatible with the recent proposal that the Qafzeh-Skhul series and the Middle Palaeolithic toolmakers of the Arabian Peninsula lithic assemblages may correspond to a basal Eurasian population existing prior to ~40 ka (Fu et al., 2014; Lazaridis et al., 2014; but see Seguin-Orlando et al., 2014 for an alternative interpretation). While some fossil evidence has been used to propose an early Late Pleistocene occupation of AMH in Indonesia and China (e.g., Storm et al., 2005; Westaway et al., 2007; Liu et al., 2010), most evidence suggests first

modern human occupation of Southeast Asia between ~50 and 40 ka (Bowler et al., 2003; Barker et al., 2007; Higham et al., 2009; Demeter et al., 2012; Fu et al., 2013a).

4.3. Limitations

Our study is limited by several factors. Perhaps most importantly, it assumes that Holocene cranial phenotypic variation preserves a strong signal of ancient dispersal events rather than of more recent gene flow between populations. The observation that cranial phenotypic variance decreases as distance from Africa increases (Manica et al., 2007; von Cramon-Taubadel and Lycett, 2008; Betti et al., 2009), however, is not consistent with a significant influence of Holocene gene flow on the phenotypic structure of recent human populations. Not all available relevant early modern human specimens could be included in our palaeo-demes, due to their fragmentary preservation. The inclusion of less complete crania and other available skeletal elements from Middle–Late Pleistocene AMHs would help to more clearly assess the mode and tempo of the out-of-Africa modern human dispersal in future work. One or more of the AMH fossils included in our ancestral palaeo-demes may actually represent extinct lineages. Nonetheless, they likely closely resembled pene-contemporaneous ancestral populations. Finally, our fossil palaeo-deme samples, which date to ~160–80 ka (origins palaeo-deme) and ~37 ka (LPPD), constrain our ability to test alternative temporal frameworks for the out-of-Africa dispersal. Our results indicate that multiple dispersals out of Africa occurred before ~37 ka and later than ~135–80 ka. Because of our sample composition, however, we are unable to further constrain the temporal frame of the dispersals and cannot specifically consider the hypothesis that dispersal occurred between ~80 and 50 ka.

Our study also does not account for the effects that admixture between AMH and other hominins may have had on skeletal morphology. Such hybridization could potentially influence the structure of phenotypic variation in extant human groups, biasing our results. However, a large admixture effect is inconsistent with the observed pattern of decreasing variance with increased distances from Africa (DeGiorgio et al., 2009), making it less likely that effects of admixture significantly influence our results. In addition, we take a conservative approach in assuming equal population sizes, but incorporating estimates of effective population size, inferred either from the archaeological record or calculated from genetic data, would refine P_{St} estimates (e.g., Reyes-Centeno et al., 2014). Finally, the objective of our study was to test competing out-of-Africa hypotheses derived from the literature, rather than to develop new models. Other dispersal scenarios, which were not considered here, are therefore possible.

5. Conclusions

Developing a coherent anthropogeny thesis and understanding the process of diversification of human populations from the late Middle Pleistocene up to the present requires a biogeographical approach that requires multidisciplinary lines of evidence and a common evolutionary framework. In the absence of sufficient information, parsimonious models should be favoured over models that are more complex. However, accumulating palaeontological, archaeological, and genomics research may necessitate more complex scenarios for understanding the mode and tempo of the modern human expansion process out of Africa. There is growing recognition that some early modern human populations have little or no descendants today, while some extant populations partly derive from cryptic ancestors who have yet to be identified in the fossil record. In this study, we have used the largest modern human

cranial dataset available in a quantitative genetics analytical framework. Our test for out-of-Africa models supports multiple dispersals from Africa and relatively sustained isolation of Australo-Melanesian populations. Although we are unable to refine the time-scales of those dispersals from our work, these dispersals took place between 37 and 135 ka. Ongoing research will serve to clarify how the out-of-Africa process has shaped the genetic and phenotypic diversity of extant populations.

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Appendix A. Supplementary Online Material

Supplementary online material related to this article can be found at <http://dx.doi.org/10.1016/j.jhevol.2015.06.008>.

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