

1 Assessing connectivity despite high diversity in island  
2 populations of a malaria mosquito

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## 17 **Abstract:**

18 Documenting isolation is notoriously difficult for species with vast polymorphic  
19 populations. High proportions of shared variation impede estimation of con-  
20 nectivity, even despite leveraging information from many genetic markers. We  
21 overcome these impediments by combining classical analysis of neutral variation  
22 with assays of the structure of selected variation, demonstrated using populations  
23 of the principal African malaria vector *Anopheles gambiae*. Accurate estimation  
24 of mosquito migration is crucial for efforts to combat malaria. Modeling and  
25 cage experiments suggest that mosquito gene drive systems will enable malaria  
26 eradication, but establishing safety and efficacy requires identification of isolated  
27 populations in which to conduct field-testing. We assess Lake Victoria islands  
28 as candidate sites, finding one island 30 kilometers offshore is as differentiated  
29 from mainland samples as populations from across the continent. Collectively,  
30 our results suggest sufficient contemporary isolation of these islands to warrant  
31 consideration as field-testing locations and illustrate shared adaptive variation as  
32 a useful proxy for connectivity in highly polymorphic species.

33 The difficulties in estimating migration with genetic methods are exacerbated for large,  
34 interconnected populations exhibiting shallow population structure. Large population sizes  
35 result in high levels of polymorphism in the genome and impede accurate estimation of con-  
36 nectivity [1] and discernment of demographic independence from panmixia [2]. Population  
37 genetic methods for estimating migration using neutral markers may thus have limited util-  
38 ity when such a high proportion of diversity is shared between populations, a failing that is  
39 only partially redressed with the high quantity of markers available from massively parallel  
40 sequencing. The most powerful window into migration may instead be the distribution of  
41 selected variants [3].

42 The major African malaria vector *Anopheles gambiae sensu stricto* (henceforth *An. gam-*  
43 *biae*) is among the most genetically diverse eukaryotic species [4], with shallow population  
44 structure [4, 5] that complicates efforts to estimate connectivity from genetic data. Over-  
45 coming these obstacles to infer migration accurately is crucial for control efforts to reduce  
46 the approximately 445,000 annual deaths attributable to malaria [6]. Such vector control  
47 efforts include novel methods involving the release of genetically modified mosquitoes. The  
48 most promising involve introducing transgenes into the mosquito genome or its endosym-  
49 bionts that interrupt pathogen transmission coupled with a gene drive system to propagate  
50 the effector genes through a population [7–9]. Such systems have recently been successfully  
51 engineered in the laboratory [10]. A detailed understanding of population structure and  
52 connectivity is essential for effective implementation of any genetic control method, not least  
53 a gene drive system designed to spread in a super-Mendelian fashion.

54 Here, we analyze population structure, demographic history, and migration between pop-  
55 ulations from genome-wide variation in *An. gambiae* mosquitoes living near and on the Ssese  
56 archipelago of Lake Victoria in Uganda (Fig. 1). We augment these analyses with a demon-  
57 stration of our framework using selective sweep sharing as a proxy for connectivity when  
58 inferring migration in taxa with high variation. Islands present natural laboratories for  
59 disentangling the determinants of population structure, as gene flow—likely important in  
60 post-dry season recolonization [11]—is reduced. In addition to the high malaria prevalence  
61 of the islands (44% in children; 30% in children country-wide; [12]), we were motivated by  
62 the potential of such an island to be a field site for future tests of gene-drive vector control  
63 strategies: Geographically-isolated islands have been proposed as locales to test the dynam-  
64 ics of transgene spread while limiting their movement beyond the study population [13–16].  
65 Antecedent studies of population structure and connectivity of potential release sites are cru-  
66 cial to evaluate the success of such field trials, as well as to quantify the chance of migration  
67 of transgenic insects carrying constructs designed to propagate across mosquito populations

68 and country borders.

## 69 Results

70 The Ssesse Islands are approximately 4-50 km from the mainland, and vary in size, infras-  
71 tructure, and accessibility. Sampled islands range from Banda—a small, largely forested  
72 island of approximately 1 square kilometer with a single settlement—to Bugala—296 square  
73 kilometers, site of a 10,000 ha oil palm plantation [17], and linked to the mainland via ferry  
74 service [18]. To explore the partitioning of *An. gambiae* genetic variation in the Lake Victo-  
75 ria Basin (LVB), we sequenced the genomes of 116 mosquitoes from 5 island and 4 mainland  
76 localities (Fig. 1, Supplementary Table S1). We sequenced 10-23 individuals per site to an  
77 average depth of  $17.6 \pm 4.6$  (Supplementary Table S2). After filtering (detailed in Meth-  
78 ods), we identified 28.6 million high quality Single Nucleotide Polymorphisms (SNPs). We  
79 merged our dataset with that of the *An. gambiae* 1000 Genomes project (Ag1000G; [4]) for  
80 a combined dataset of 12.54 million SNPs (9.86 million after linkage disequilibrium pruning)  
81 in 881 individuals.



Figure 1: Map of Lake Victoria Basin study area.

Map of study area showing sampling localities on Ssesse Islands (blue) and mainland localities (red) in Lake Victoria Basin. The Ag1000G reference population, Nagongera, Tororo District, is not shown, but lies 111 km NE of Kiyindi, 57 km from the shore of Lake Victoria. Map data copyright 2018 Google.

## 82 Genetic structure

83 We analyzed LVB population structure with context from continent-wide populations [4]  
84 of *An. gambiae* and sister species *Anopheles coluzzii* mosquitoes (formerly known as *An.*  
85 *gambiae* M molecular form [19]). Both Bayesian clustering ([20]; Fig. 2a) and principal  
86 component analysis (PCA; Supplementary Fig. S1) showed LVB individuals closely related  
87 to the Ugandan reference population (Nagongera, Tororo; 0°46'12.0"N, 34°01'34.0"E; ~57  
88 km from Lake Victoria; Fig. 1). With  $\geq 6$  clusters (which optimized predictive accuracy  
89 in the clustering analysis; Supplementary Fig. S2), island samples had distinct ancestry  
90 proportions (Fig. 2a), and with  $k = 9$  clusters, we observed additional subdivision in LVB  
91 samples and the assignment of the majority of Ssese individuals' ancestry to a largely island-  
92 specific component (Figs. 2a, 2b, and Supplementary Fig. S3).

93 PCA of only LVB individuals indicated little differentiation among mainland samples  
94 in the first two components and varying degrees of differentiation on islands, with Banda,  
95 Sserinya, and Bukasa the most extreme (Fig. 2c). Twelve of 23 individuals from Bugala, the  
96 largest, most developed, and most connected island, exhibited affinity to mainland individ-  
97 uals instead of ancestry typical of the islands (Supplementary Fig. S4). As both PCA and  
98 clustering analyses revealed this differentiation, we split the Bugala sample into mainland-  
99 and island-like subsets for subsequent analyses (hereafter referenced as "Bugala (M)" and  
100 "Bugala (I)," respectively). Individuals with partial ancestry attributable to the component  
101 prevalent on the mainland and the rest to the island-specific component were present on all  
102 islands except Banda.

103 Differentiation concurred with observed population structure. Mean  $F_{ST}$  between sam-  
104 pling localities (range: 0.001-0.034) was approximately 0 ( $\leq 0.003$ ) for mainland-mainland  
105 comparisons and was highest in comparisons involving the small island Banda (Fig. 2d).  
106 Geographic distances and  $F_{ST}$  were uncorrelated (Mantel  $p = 0.88$ ; Supplementary Fig. S5).  
107 Island samples showed greater within- and between-locality sharing of genomic regions identi-

108 cal by descent (IBD), with sharing between nearby islands Sserinya, Banda and Bugala (Fig.  
109 2e). Importantly, Banda Island shared no IBD regions with mainland sites, underscoring its  
110 contemporary isolation from the mainland.

## 111 Genetic diversity

112 Consistent with the predicted decrease in genetic variation for semi-isolated island popula-  
113 tions due to inbreeding and smaller effective population sizes ( $N_e$ ), islands displayed slightly  
114 lower nucleotide diversity ( $\pi$ ; Wilcoxon rank sum test  $p < 0.001$ ; Fig. 3a), a higher propor-  
115 tion of shared to rare variants (Tajima's  $D$ ;  $p < 0.001$ ; Fig. 3b), and more linkage among  
116 SNPs (LD;  $r^2$ ;  $p < 0.001$ ; Fig. 3f). They were however, similar in inbreeding coefficient ( $F$ ;  
117  $p = 0.0719$ ; Fig. 3c), number of long runs of homozygosity ( $F_{ROH}$ ;  $p = 0.182$ ; Fig. 3d), and  
118 proportions of low frequency SNPs (Fig. 3e). The small island Banda was the most extreme  
119 in these measures.

## 120 Demographic history

121 To test islands for isolation and demographic independence from the mainland, we inferred  
122 the population history of LVB samples by estimating long-term and recent trends in  $N_e$  using  
123 stairway plots [21] based on the site frequency spectrum (SFS; Fig. 4a) and patterns of IBD  
124 sharing ([22]; Fig. 4b), respectively. Short-term final mainland sizes were unrealistically  
125 high, likely due to low samples sizes for each locality, but island-mainland differences were  
126 nonetheless informative. In both, islands had consistently lower  $N_e$  compared to mainland  
127 populations extending back 500 generations ( $\sim 50$  years) and often severely fluctuated,  
128 particularly in the last 250 generations ( $\sim 22$  years). Mainland sites Wamala and Kaazi had  
129 island-like recent histories, with Wamala abruptly switching to an island-like pattern around  
130 2005.

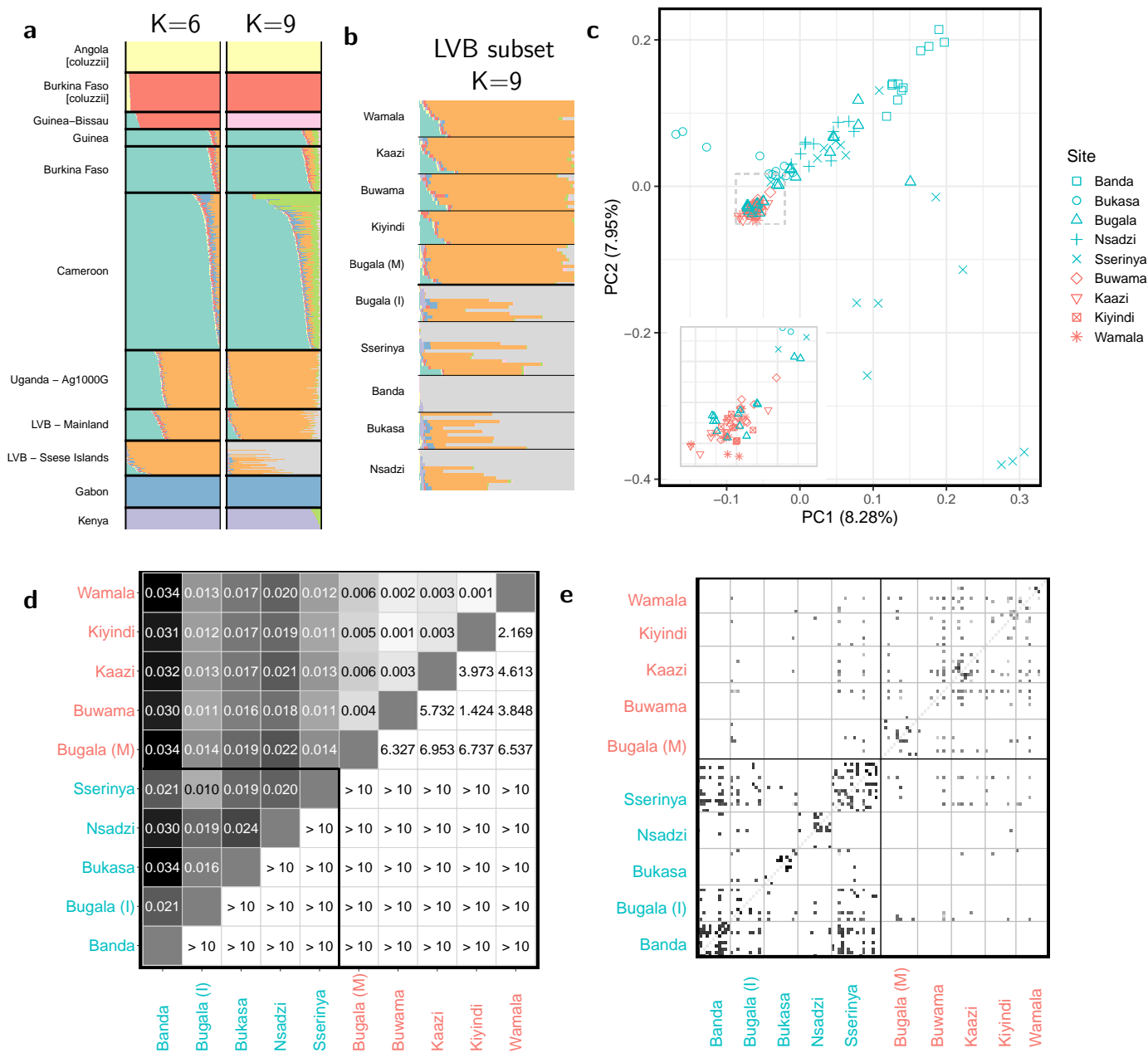


Figure 2: (Caption on next page.)



Figure 2: Population structure in the Lake Victoria Basin.

Analyses are based on chromosome 3 to avoid segregating inversions on other chromosome, unless otherwise noted. (A) ADMIXTURE-inferred ancestry of individuals in Lake Victoria Basin. Results based on analysis of LVB and Ag1000G merged dataset. Analysis is restricted to *A. gambiae s. s.*. Clustering shown for  $k = 6$  clusters, which minimizes cross validation error, and  $k = 9$  clusters, the lowest  $k$  for which island individuals have the majority of their ancestry assigned to an island-specific cluster. (B) Results of the clustering analysis with  $k = 9$  clusters for LVB individuals, split by sampling locality. (C) Plot of first two components of PCA of Lake Victoria Basin individuals showing locality of origin. Mainland individuals are colored red, while island individuals are blue, and point shape indicates sampling locality. Based on these results and that of ADMIXTURE analysis, the island sample of Bugala was split into mainland- and island-like subpopulations (“Bugala (M)” and “Bugala (I),” respectively) for subsequent analyses (Fig. S4). (D) Heatmap of  $F_{ST}$  between sites (lower triangle) and associated  $z$ -score computed via block jackknife (upper triangle). “Bugala (M)” and “Bugala (I)” are the mainland- and island-like subpopulations of Bugala. (E) Proportion of genome-wide pairwise IBD sharing between individuals, based on the full genome. Each small square represents a comparison between two individuals, and darker colors indicate a higher proportion of the two genomes is in IBD, shaded on a logarithmic scale. Individuals are grouped by locality.

131 To all pairs of LVB localities we fit an isolation-with-migration (IM) demographic model  
132 using  $\delta a \delta i$ , in which an ancestral population splits into two populations, allowing exponential  
133 growth and continuous asymmetrical migration between the daughter populations (Supple-  
134 mentary Figs. S6, S7). In all comparisons involving islands and some between mainland  
135 sites, the best fitting model as chosen via AIC had zero migration (Supplementary Tables  
136 S3, S4, and S5). Time since population split was much more recent for mainland-mainland  
137 comparisons (excluding Bugala, median: 361 years) than those involving islands (island-  
138 island median: 7,128 years; island-mainland median: 4,043 years). Island-island split time  
139 confidence intervals typically did not overlap those involving mainland sites.

## 140 Selection

141 As beneficial variants would be the most likely signatures of past gene flow to persist, we next  
142 examined signatures of selective sweeps for insight into migration. Identifying signatures of

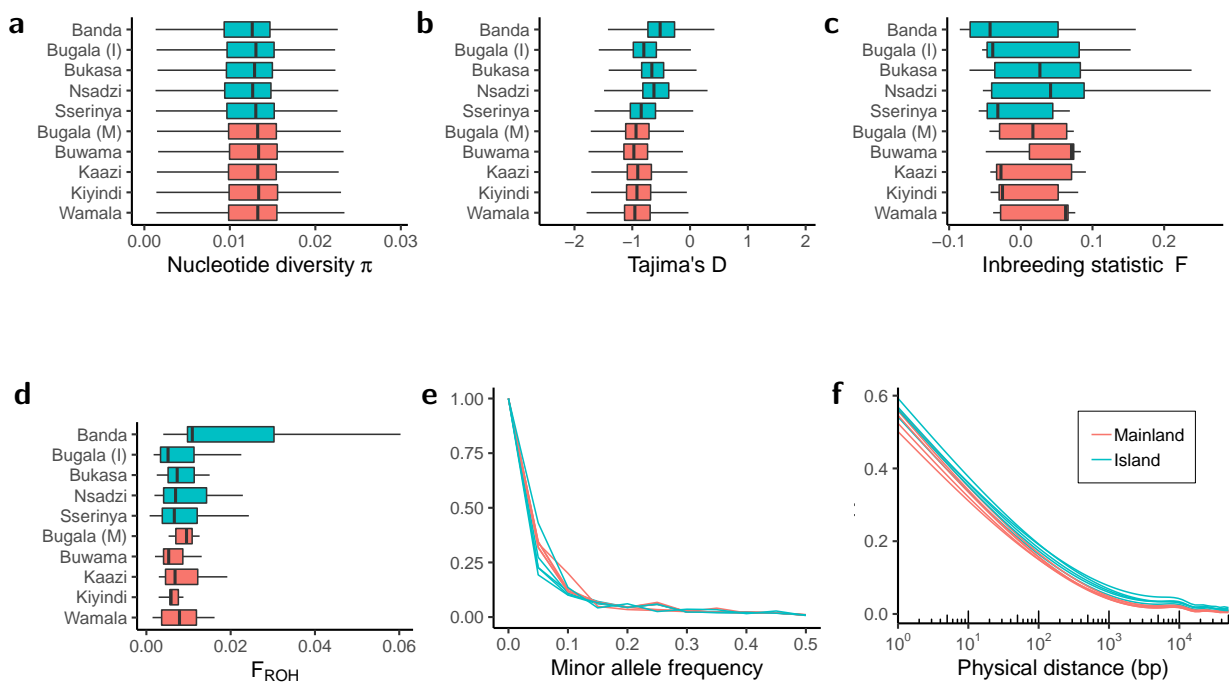


Figure 3: Diversity metrics in the Lake Victoria Basin samples.

Shown are a (A) boxplot of nucleotide diversity ( $\pi$ ; in 10 kilobase windows), (B) boxplot of Tajima's  $D$  (in 10 kilobase windows), (C) boxplot of inbreeding statistic ( $F$ ), (D) boxplot of length of runs of homozygosity ( $F_{ROH}$ ), (E) histogram of Minor Allele Frequency (MAF), and (F) decay in linkage disequilibrium ( $r^2$ ), all grouped by sampling locality. For all boxplots, outlier points are not shown.

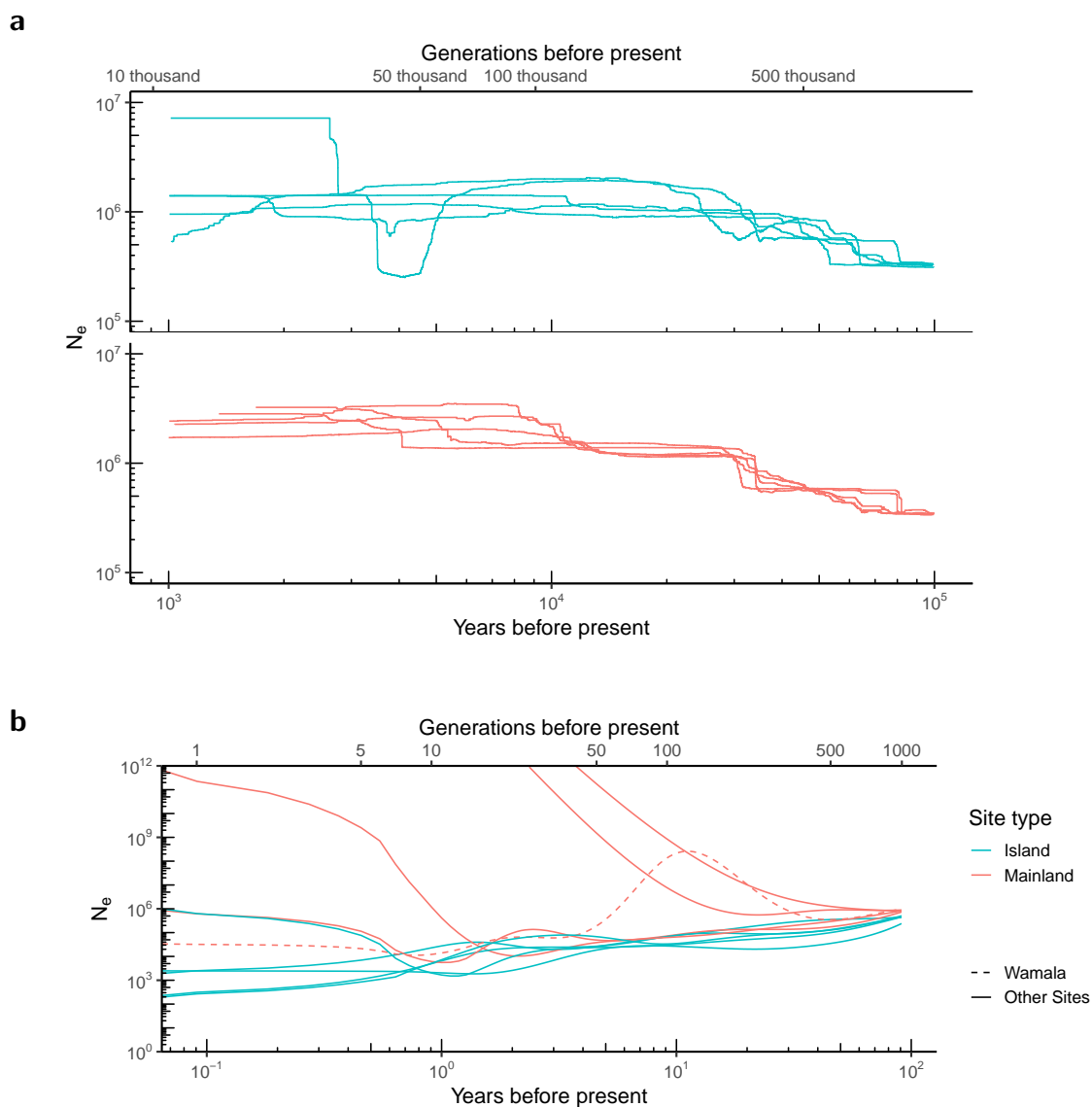


Figure 4: Population history of the Lake Victoria Basin samples.

(A) Long-term evolutionary population histories inferred via stairway plots for island and mainland samples. (B) Contemporary or short-term effective population size ( $N_e$ ) history inferred using sharing of regions that are identical by descent (IBD). Wamala, a mainland locality showing island-like fluctuations in population size, is indicated with a dashed line. Plot truncated to exclude implausibly high estimates that are likely an artifact of sample size.

143 selection in the same genomic region in populations with independent lineages would be  
144 consistent with several scenarios [23]: (i) independent parallel selective sweeps on *de novo*  
145 mutations, (ii) independent parallel selective sweeps on shared ancestral variation, or (iii)  
146 selective sweeps on variants transferred via gene flow. As we were most interested in the  
147 transfer of adaptive variants for its insight into migration (iii), we distinguished between the  
148 alternative scenarios as follows.

149 We would expect independent sweeps on novel mutations (i) to exhibit differences in  
150 genetic background between the two populations, evidenced by distinct haplotype clusters,  
151 each comprising near-identical haplotypes separated by individual haplotypes lacking signa-  
152 tures of a selective sweep. In both other scenarios (ii-iii), we would instead expect haplotypes  
153 with the sweep to group together when clustered by genetic distance. By itself, haplotype  
154 information does not differentiate sweeps targeting standing ancestral variation (ii) from  
155 those targeting adaptive variants spread through gene flow (iii), but additional information  
156 such as geographic distance between the populations, estimates of gene flow inferred from  
157 other regions of the genome, and assessment of gene flow between other nearby populations,  
158 may suggest that one of these scenarios is the more likely.

159 While the sharing of a sweep may indicate migration between populations, the inverse  
160 would be suggestive—though not conclusive—of barriers to gene flow. A lack of sharing of  
161 a selective sweep signal between two populations may indicate no migration is occurring.  
162 However, it would also be consistent with the occurrence of migration that is subsequently  
163 countered by the local effects of selection or lost to genetic drift.

164 We first compared mainland Uganda and the Ssesse Islands, reasoning that shared signa-  
165 tures of sweeps at a genomic location may indicate migration is occurring with the islands,  
166 while the absence was suggestive of isolation. We identified sweeps in the LVB using genome  
167 scans of between- and within-locality statistics, including  $F_{ST}$  ([24], Supplementary Fig. S8),  
168 Extended Haplotype Homozygosity (XP-EHH, [25], Supplementary Fig. S8), and haplotype

169 homozygosity (H12, [26], Supplementary Fig. S9). To test for sweeps that were variable  
170 within the LVB, we identified locality-specific sweeps (found at only one sampling site in  
171 the LVB), sweeps that were found in our island localities but not mainland LVB localities,  
172 and sweeps that were found only in our mainland LVB localities (all defined as H12 > 99th  
173 percentile). To add additional country-level context, we then intersected these regions with  
174 those under putative selection in a mainland Ugandan reference population (H12 > 95th  
175 percentile; [4]).

176 Some genomic locations had heterogeneous selection signals within the LVB and within  
177 Uganda, indicative of potential geographic barriers to gene flow or local variation in selective  
178 regimes. Locality-specific putative sweeps were more prevalent on island than LVB mainland  
179 localities (mean per locality: island = 52.4; mainland = 26.8), concordant with increased  
180 isolation of the islands (Supplementary Table S6). Sweeps detected only or primarily in  
181 mainland LVB localities were shared with the Ag1000G Ugandan reference population more  
182 often (8 of 37; 22%) than those found only or primarily on islands (1 of 21, 5%; Supplementary  
183 Tables S7 and S8), again indicative of some barriers to gene flow with the islands.

184 We next reasoned that continent-wide selective sweeps, with broadly distributed selective  
185 advantage, would be the most likely to be shared via gene flow. Widespread sweeps that were  
186 absent or at extremely low frequency on the islands would be a strong suggestion against  
187 contemporary gene flow, and those that conversely were present on the islands would be  
188 indicative that gene flow had occurred, if the alternative scenarios could be excluded as  
189 outlined above. To identify these regions, we intersected our set of sweeps with those under  
190 putative selection in populations across the continent (H12 > 95th percentile in Ag1000G;  
191 [4]).

192 As expected, outlier regions included known selective sweep targets from elsewhere in  
193 Africa ([4], Supplementary Table S9). All sweeps found in the reference Uganda popula-  
194 tion [4] were detected in at least some sampling localities in our LVB dataset, except the

195 sweep targeting *Vgsc*, which was likely excluded during filtration of the region adjacent to  
196 the centromere. For instance, the large genomic region spanning the cluster of insecticide  
197 resistance-associated cytochrome P450s (*Cyp6p*) on chromosome arm 2R, including *Cyp6p3*  
198 which is upregulated in mosquitoes with permethrin and bendiocarb resistance [27], exhib-  
199 ited low diversity, an excess of low frequency polymorphisms (Tajima's  $D$ ), and elevated  
200 haplotype homozygosity (H12) within the LVB populations (Supplementary Figs. S9, S10).  
201 Pairwise statistics ( $F_{ST}$  and XP-EHH) indicated low differentiation between LVB localities,  
202 as expected for a continent-wide sweep (Supplementary Figs. S8). The signal was found in  
203 every LVB site, including all islands. Hierarchical clustering of LVB and Ag1000G haplotypes  
204 revealed clades with low inter-haplotype diversity, expected after selection rapidly increases  
205 the frequency of a haplotype containing adaptive variation (Supplementary Fig. S11). Con-  
206 sistent with previous results [4], these clusters of closely related haplotypes on independent  
207 lineages indicate that multiple parallel sweeps targeting the *Cyp6p* region have occurred in  
208 several genetic backgrounds at numerous localities across Africa. Within Uganda, since al-  
209 most all mainland and island individuals carry haplotypes from a single cluster, the selected  
210 haplotype of this cluster likely spread to near-fixation via gene flow.

211 In contrast, some sweeps with continent-wide prevalence including the reference Ugan-  
212 dan population [4] were found at all mainland LVB sites but had colonized the islands  
213 incompletely. For example, a region on chromosome arm 2L (2L:2,900,000-3,000,000) was  
214 found in all assayed Ag1000G populations and LVB mainland sites, but found on no island  
215 but Sserinya (Supplementary Table S8). As in previous studies [4], independent clusters  
216 of low-diversity haplotypes in varied genetic backgrounds suggest multiple sweeps targeting  
217 the cluster of genes encoding glutathione S-transferases (*Gste1-Gste7*), including one sweep  
218 specific to Uganda. This Ugandan sweep was similarly confined largely to the mainland  
219 in the LVB. These sweeps at targets of selection throughout the continent that are largely  
220 restricted to the mainland are suggestive of strong barriers to gene flow to the islands, ei-

221 ther due to lack of connectivity or the countering effects of selection or drift. Other sweeps  
222 had colonized the islands incompletely. The sweep targeting cytochrome P450 gene *Cyp9k1*  
223 likely arose multiple times independently, since Ugandan haplotypes do not cluster with low  
224 diversity clusters from elsewhere in Africa. Within the LVB, the sweep signature is found  
225 on some, but not all islands, suggesting some barrier to gene flow or local selection limiting  
226 the spread of the sweep.

227 Two regions exhibited selection signals similar in amplitude to known insecticide-related  
228 loci, with elevated between-locality differentiation, low diversity, and extended homozygos-  
229 ity (Supplementary Figs. [S8](#), [S9](#), [S12](#), and [S13](#)). The first, at 2L:34.1 Mb, contains many  
230 genes, including a cluster involved in chorion formation [28] near the signal peak. Haplotype  
231 clustering revealed a group of closely-related Ugandan individuals, consistent with a geo-  
232 graphically bounded selective sweep (Supplementary Fig. [S14](#)). The selected variation had  
233 not fully colonized the islands or the LVB mainland sites, however, suggesting some barriers  
234 to gene flow, loss due to drift at some localities, or local differences in selective pressure  
235 within the LVB. Elsewhere in Africa, clustering analysis revealed other low-variation clades  
236 in distinct genetic backgrounds in, *e.g.*, Cameroon and Angola, suggesting parallel selection  
237 on independent mutations at this locus.

238 The second putative sweep, at X:9.2 Mb, coincided precisely with eye-specific diacyl-  
239 glycerol kinase (AGAP000519, chrX:9,215,505-9,266,532). Low diversity haplotypes formed  
240 a single cluster including LVB haplotypes overwhelmingly from the islands (Supplementary  
241 Fig. [S15](#)). Transfer via gene flow between islands but not to the mainland is reasonable,  
242 given the connectivity patterns we have inferred from neutral variation. Additionally, lo-  
243 cal selection may be countering the spread of the sweep to the mainland. However, more  
244 surprisingly, these island haplotypes with evidence of a selective sweep were most closely  
245 related to haplotypes from distant locations, primarily Gabon and Burkina Faso rather than  
246 Uganda. This sharing of extended haplotypes between islands and distant localities is con-

247 sistent with either gene flow or independent sweeps targeting ancestral standing variation.  
248 Of these alternatives, extremely long distance gene flow that persists only on islands seems  
249 less likely.

## 250 Discussion

251 Understanding the population genetics of island *Anopheles gambiae* has both evolutionary  
252 and practical importance. A limited number of genetic investigations have been conducted  
253 on oceanic [29–32] and lacustrine islands [33–36], though the latter have been limited in the  
254 type or count of molecular markers used. In contrast to shallow population structure across  
255 Africa [4, 5], partitioning of genetic variation on islands suggests varying isolation. Using  
256 a genome-wide dataset, we found differentiation between the Ssesse Islands to be relatively  
257 high in the context of continent-wide structure, with the differentiation between Banda Island  
258 (only 30 km offshore) and mainland localities on par with or higher than for populations on  
259 opposite sides of the continent (*e.g.*, Banda vs. Wamala,  $F_{ST} = 0.034$ ; mainland Uganda vs.  
260 Burkina Faso,  $F_{ST} = 0.007$  [4]). The Ssesse Islands are approximately as differentiated as all  
261 but the most outlying oceanic islands tested (*e.g.* mainland Tanzania vs. Comoros, 690-830  
262 km apart,  $F_{ST} = 0.199-0.250$  [31]). Patterns of haplotype sharing did include direct evidence  
263 for the recent exchange of migrants between nearby islands, but analyses based on haplotype  
264 sharing, Bayesian clustering, and demographic reconstruction included no evidence of direct  
265 sharing between Banda and the mainland. Banda is nonetheless connected to other islands  
266 and thereby indirectly connected to the mainland, and additional sampling may reveal signs  
267 of admixture. Additional sampling on Banda and other islands that are disjunct from the  
268 rest of the archipelago would be prudent when assessing potential field testing locations.

269 The name “Ssesse” derives from another arthropod vector, the tsetse fly (*Glossina* spp.)  
270 The tsetse-mediated arrival of sleeping sickness in 1902 brought “enormous mortality” [37,



271 pp. 332] to the 20 thousand residents, who were evacuated in 1909 [37, 38]. Though en-  
272 couraged to return by 1920, the human population numbered only 4 thousand in 1941 [37]  
273 and took until 1980 to double [39], but has since rapidly risen to over 62 thousand (2015,  
274 projected; [18, 40]). The impacts on mosquito populations of this prolonged depression in  
275 human population size, coupled with water barriers to mosquito migration, are reflected in  
276 the distinctive demographic histories of island *An. gambiae* populations, which were smaller  
277 and fluctuated more than mainland localities, echoing previous results [34, 36]. Two main-  
278 land sites had island-like recent population histories, with Wamala abruptly switching from  
279 a mainland-like to island-like growth pattern around 2005. This coincides precisely with a  
280  $\geq 20\%$  reduction from 2000-2010 in the *Plasmodium falciparum* parasite rate (PfPR<sub>2-10</sub>; a  
281 measure of malaria transmission intensity) in Mityana, the district containing Wamala [41].

282     Though previous *Anopheles* population genetic studies have inferred gene flow even  
283 among species [4, 42], we inferred that no genetic exchange had occurred since the split  
284 between island sites and between islands and the mainland. Island pairs were inferred to  
285 have split far deeper in the past (5,000-14,000 years ago) than mainland sites (typically < 500  
286 years ago), on par with the inferred split time between Uganda and Kenya (approximately  
287 4,000 years ago; [4]). Although bootstrapping-derived confidence intervals permit some cer-  
288 tainty, our model fit is not optimal likely due to low sample sizes and high levels of shared  
289 ancestral variation, and additional sampling is necessary to clarify population history. Our  
290 inferred lack of gene flow to the islands appears contradictory to the presence of individuals  
291 who share ancestry with the mainland on all islands but Banda. We cannot dismiss the  
292 possibility that this indicates actual migration occurs. If so, effects of migration would have  
293 to be sufficiently countered by local selection to limit its effect on allele frequency spectra,  
294 rendering effective migration (as estimated in population history inference) zero. The ap-  
295 parent contradiction can also be resolved if shared ancestry between islands and mainland  
296 suggested by the clustering result is interpreted as retention of shared ancestral polymor-

297 phism or the existence of inadequately sampled ancestral variation [43], rather than recent  
298 admixture. This interpretation is consistent with the affinity we observed between the Sses  
299 Islands and West Africa in the structure of adaptive variation.

300 Discerning whether the absence of observed gene flow is due to lack of connectivity, the  
301 opposition of selection, or the stochasticity of genetic drift is difficult. Instead we must rely  
302 on estimates of the strength of selection in the two locales to inform our conclusions. For  
303 example, we would expect that an insecticide sweep found all over Africa would spread in  
304 island mosquito populations with insecticide treated bed nets, despite the considerable effect  
305 of genetic drift in small populations. As insecticide treated bed net usage is present on the  
306 islands [18], variation conferring a major selective advantage related to insecticides would  
307 be expected to spread to and persist on the islands if migration allows the transfer, and the  
308 strongest evidence of a lack of contemporary connectivity is therefore the absence of a sweep  
309 on the islands that is widespread on the continent.

310 We found two sweeps on insecticide-related genes that are common targets of selection  
311 elsewhere but which have incompletely colonized the Sses Islands: one on cytochrome P450  
312 monooxygenase *Cyp9K1* [44, 45] present on some islands, and another on glutathione S-  
313 transferase genes (*Gste1-Gste7*; [46–49]) at extremely low frequency on the islands. That  
314 the selective sweeps targeting these loci [4] have not fully colonized the islands despite the  
315 advantage in detoxifying pyrethroids and DDT suggests a lack of contemporary exchange.  
316 However, the sweep targeting the *Cyp6p* cluster was found on all islands, confirming past  
317 gene flow had occurred at some point. Although these distributions confirm that past mi-  
318 gration from the mainland to islands has occurred and we are unable to exclude low levels of  
319 contemporary gene flow, taken together our data are consistent with potentially high degrees  
320 of isolation on contemporary timescales for some islands of the Sses archipelago.

321 Our investigation also identified two previously unknown signatures of selection. For  
322 the first, on chromosome arm 2L and encompassing many genes, haplotypes with sweeps in

323 distinct genetic backgrounds across Africa suggest the region has been affected by multiple  
324 independent convergent sweeps. In Uganda, most individuals with the sweep are from the  
325 mainland, suggesting a local origin and spread via short distance migration. The putative  
326 target of the second sweep is diacylglycerol kinase on the X-chromosome, a homolog of  
327 retinal degeneration A (*rdgA*) in *Drosophila*. The gene is highly pleiotropic, contributing to  
328 signal transduction in the fly visual system [50, 51], but also olfactory [52] and auditory [53]  
329 sensory processing. It has been recently implicated in nutritional homeostasis in *Drosophila*  
330 [54] and is known to interact with the TOR pathway [55], which has been identified as a  
331 target of ecological adaptation in *Drosophila* [56, 57] and *An. gambiae* [58]. The sweep  
332 appears largely confined to island individuals in the LVB, but the cluster of haplotypes also  
333 includes those from Gabon, Burkina Faso, and Kenya. Shared extended haplotypes suggest  
334 a single sweep event spread by gene flow or selection on standing ancestral variation, not  
335 independent selection on *de novo* mutations. Possible explanations include long distance  
336 migration of an adaptive variant persisting on only the islands or, more reasonably, selection  
337 on standing ancestral variation. We have not found obvious candidate targets of selection,  
338 *e.g.* coding changes, which may be due to imperfect annotation of the genome or the likely  
339 possibility that the target is a non-coding regulator of transcription or was filtered from  
340 our dataset. Further functional studies would be needed to clarify the selective advantage  
341 that these haplotypes confer. Interestingly, the putative sweep coincides with a similar  
342 region of low diversity in a cryptic subgroup of *Anopheles gambiae sensu lato* (GOUNDRY;  
343 [42]), suggesting possible parallel selective events on independent mutations or adaptive  
344 introgression.

345 Population structure investigations are paramount for informing the design and deploy-  
346 ment of control strategies, including field trials of transgenic mosquitoes. We demonstrate  
347 alternatives to simple extrapolation of migration rates from differentiation, which is fraught  
348 [59] particularly given the assumption of equilibrium between the evolutionary forces of

349 migration and drift [59–61], an unlikely state for huge *An. gambiae* populations [3]. We sug-  
350 gest that future assessments of connectivity include, as we have, the spatial distribution of  
351 adaptive variation, identification of recent migrants via haplotype sharing, and demographic  
352 history modeling, from which we have inferred the Ssesse Islands to be relatively isolated on  
353 contemporary time scales. Though we cannot exclude the possibility of a small amount of  
354 gene flow over evolutionary time between our most isolated islands and the mainland, the  
355 data are consistent with a sufficiently low amount of gene flow that it becomes reasonable  
356 to consider these islands as isolated on short time frames.

357 A completely isolated population of mosquitoes is not a reasonable expectation given  
358 mosquitoes' propensity for active and even passive (human-aided or windborne) dispersal  
359 [16], potentially up to hundreds of kilometers [11]. Although no island, lacustrine or oceanic,  
360 is completely isolated, such localities may still be ideal for initial gene drive field testing,  
361 as the geographical barriers maximize isolation to the extent possible [16], and absolute  
362 isolation on evolutionary timescales is unnecessary given the relatively short timeframe of  
363 small-scale field tests. Thus, the probability of contemporary migration may be sufficiently  
364 low to qualify some Ssesse Islands as candidate field sites. Additionally, the assessment of the  
365 islands' suitability as potential sites for field trials of genetically modified mosquitoes must  
366 also consider the logistical ease of access and monitoring that the bounded geography of a  
367 small lacustrine island with low human population density affords initial field tests. Due  
368 consideration should be provided to these characteristics of small lake islands that may be  
369 appealing to regulators, field scientists, local communities, and other stakeholders. Given  
370 such features and the probable rarity of migration, the Ssesse Islands may be logical and  
371 tractable candidates for initial field tests of genetically modified *An. gambiae* mosquitoes,  
372 warranting further entomological study.

## 373 **Materials and Methods**

374 **Experimental design** Mosquitoes were sampled from 5 of the Ssesse Islands in Lake Vic-  
375 toria, Uganda (Banda, Bukasa, Bugala, Nsadzi, and Sserinya) and 4 mainland sampling  
376 localities (Buwama, Kaazi, Kiyindi, and Wamala) at varying distances from the lake in May  
377 and June, 2015. Sampling took place between 4:40 and 8:15 over a 30 day period as follows:  
378 Indoor resting mosquitoes were collected from residences via mouth or mechanical aspirators  
379 and subsequently identified morphologically to species group. Female mosquitoes assigned  
380 to the *An. gambiae sensu lato* complex based on morphology ( $N=575$ ) were included in  
381 further analyses. All mosquitoes were preserved with silica desiccant and transported to the  
382 University of Notre Dame, Indiana, U.S.A. for analysis.

383 **DNA extraction, Library preparation, and Whole Genome Sequencing** Animals  
384 were assigned to species level via a PCR-based assay [62] using DNA present in a single leg  
385 or wing. DNA from individual *An. gambiae s. s.*  $N=116$  mosquitoes was extracted from  
386 the whole body via phenol-chloroform extraction [63] and then quantified via fluorometry  
387 (PicoGreen). Automated library preparation took place at the NYU Langone Medical Center  
388 with the Biomek SPRIWorks HT system using KAPA Library Preparation Kits, and libraries  
389 were sequenced on the Illumina HiSeq 2500 with 100 paired end cycles.

390 **Mapping and SNP calling, filtering** Software version information is provided in Sup-  
391 plementary Table S10. After quality filtering and trimming using ea-utils' fastq-mcf (-l 15  
392 -q 15 -w 4; [64]), reads were mapped to the *An. gambiae* reference genome (AgamP4 PEST;  
393 [65, 66]) using BWA aln and sampe with default parameters [67].

394 After realignment around indels with GATK's IndelRealigner, variants were called using  
395 GATK's UnifiedGenotyper (with -stand\_call\_conf 50.0 and -stand\_emit\_conf 10.0; selected to  
396 be consistent with methods of recent comparison SNP dataset [4]) and filtered for quality [68],

397 excluding SNPs with QualByDepth (QD) < 2.0, RMSMappingQuality (MQ) < 40.0, Fisher-  
398 Strand (FS) > 60.0, HaplotypeScore > 13.0, or ReadPosRankSum < -8.0. All bioinformatic  
399 steps for read mapping and variant identification are encapsulated in the NGS-map pipeline  
400 (<https://github.com/bergeycm/NGS-map>). This yielded 33.1 million SNPs. Individuals  
401 and variants with high levels of missingness (> 10%) and variants that were not biallelic  
402 or exhibited values of HWE that were likely due to sequencing error ( $p < 0.00001$ ) were  
403 excluded from further analysis. For use in population structure inference, the SNP dataset  
404 was further pruned for linkage disequilibrium by sliding a window of 50 SNPs across the  
405 genome in 5 SNP increments and recursively removing random SNPs in pairs with  $r^2 > 0.5$   
406 using PLINK [69, 70]. After filtration, the dataset contained 28,569,621 SNPs before LD  
407 pruning and 115 individuals. SNPs unpruned for linkage disequilibrium were phased with  
408 SHAPEIT2 [71] using an effective population size ( $N_e$ ) of 1,000,000 (consistent with pre-  
409 vious demographic modeling [4]), default MCMC parameters (7 burn-in MCMC iterations,  
410 8 pruning iterations, and 20 main iterations), conditioning states for haplotype estimation  
411 ( $K = 100$ ), and window size of 2 Mb.

412 **Population structure inference** To explore population structure in a larger, continent-  
413 wide context, we merged our LVB SNP set with a recently published dataset of *Anopheles*  
414 *gambiae* individuals (from the Ag1000G project) [4]. Prior to filtering, biallelic SNPs from  
415 the LVB and Ag1000G datasets were merged using bcftools [72]. We excluded any SNP with  
416 greater than 10% missingness in either dataset, any SNPs that did not pass the accessibility  
417 filter of the Ag1000G dataset, and SNPs with MAF < 1%. After this filtration, our merged  
418 SNP dataset contained 12,537,007 SNPs.

419 After pruning the merged dataset for LD (leaving 9,861,756 SNPs) and excluding labo-  
420 ratory crosses (leaving 881 individuals), we assigned individuals' genomes to ancestry com-  
421 ponents using ADMIXTURE [20]. We created 10 replicate samples of 100,000 SNPs from

422 chromosome 3 (prior to LD-pruning), including only biallelic SNPs in euchromatic regions  
423 with MAF > 1%. These replicate datasets were pruned for LD by randomly selecting from  
424 pairs of SNPs with  $r^2 > 0.01$  in sliding windows of size 500 SNPs and with a stepsize of  
425 250 SNPs. For each replicate, we ran ADMIXTURE for 5 iterations in five-fold cross val-  
426 idation mode for values of  $k$  from 2 to 10. This resulted in 50 estimates for each value of  
427  $k$ . We assessed these results using the online version of CLUMPAK with default settings to  
428 ensure the stability of the resulting clustering [73]. CLUMPAK clusters the replicate runs'  
429 Q-matrices to produce a major cluster for each value of  $k$ , which we then visualized. The  
430 lowest cross-validation error was found for  $k = 6$  clusters, but we also display ancestry esti-  
431 mates with  $k = 9$  clusters to further explore patterns of structure with a level of subdivision  
432 at which the Ssese Island individuals are assigned a unique ancestry component.

433 We visualized population structure via principal components analysis (PCA) with PLINK  
434 [69, 70], using the LVB-Ag1000G merged dataset (excluding the outlier Kenyan population;  
435 [4]) and 3,212,485 chromosome 3 SNPs (to avoid the well-known inversions on chromosome 2  
436 and the X-chromosome) outside of heterochromatic regions (such as centromeric regions; [66];  
437 Supplementary Table S11). We next performed a PCA on the LVB dataset alone, pruning  
438 for LD and low-MAF (< 1%) SNPs on chromosome 3. Based on the results of this analyses,  
439 we split individuals from the large island of Bugala into two clusters for subsequent analyses:  
440 those that cluster with mainland individuals and those that cluster with individuals from  
441 the smaller islands.

442 We computed the pairwise fixation index ( $F_{ST}$ ) between locality samples for *An. gambiae*  
443 using the unbiased estimator of Hudson [74] as implemented in smartpca [75, 76]. To obtain  
444 overall values between sampling sites, per-SNP values were averaged across the genome  
445 excluding known inversions (*2La*, *2Rb*, and *2Rc*) and heterochromatic regions. We also  
446 computed  $z$ -scores via block jackknife, using 42 blocks of size 5 Mb. We tested for isolation  
447 by distance, or a correlation between genetic and geographic distances, with a Mantel test

448 [77] as implemented in the R package ade4 [78], using these  $F_{ST}$  estimates and Euclidean  
449 geographic distances between localities.

450 To estimate fine-scale structure and relatedness between individuals, we estimated the  
451 proportion of pairs of individuals genomes that are identical by descent (IBD) using PLINK  
452 [69, 70]. We excluded heterochromatic and inversion regions, and retained informative pairs  
453 of SNPs within 500 kb in the pairwise population concordance test.

454 **Diversity estimation** Grouping individuals by site (except for Bugala, which was split  
455 based on the results of the PCA), we calculated nucleotide diversity ( $\pi$ ) and Tajima's  $D$   
456 in nonoverlapping windows of size 10 kb, the inbreeding coefficient ( $F$ ) estimated with the  
457 method of moments, minor allele frequencies (the site frequency spectrum, SFS), and a mea-  
458 sure of linkage disequilibrium ( $r^2$ ) using VCFtools (Danecek2011). For  $r^2$ , we computed  
459 the measure for all SNPs (unpruned for linkage) within 50 kb of a random set of 100 SNPs  
460 with  $MAF > 10\%$  and corrected for differences in sample size by subtracting  $1/n$ , where  $n$   
461 equaled the number of sampled chromosomes per site. To visualize decay in LD, we plotted  
462  $r^2$  between SNPs against their physical distance in base pairs, first smoothing the data by  
463 fitting a generalized additive model (GAM) to them. We also inferred runs of homozygos-  
464 ity using PLINK [69, 70] to compare their length ( $F_{ROH}$ ), requiring 10 homozygous SNPs  
465 spanning a distance of 100 kb and allowing for 3 heterozygous and 5 missing SNPs in the  
466 window. Runs of homozygosity were inferred using LD-pruned SNPs outside of inversions or  
467 heterochromatic regions. We tested the significance of differences in these statistics between  
468 island and mainland categories using a two-sided Wilcoxon rank sum test.

469 **Demographic history inference** To estimate the contemporary or short-term  $N_e$  for  
470 each site, we inferred regions of IBD from unphased data with IBDseq [79] and analyzed  
471 them with IBDNe [22]. We restricted our analysis to SNPs from chromosome 3 to avoid  
472 inverted regions. We allowed a minimum IBD tract length of 0.005 cM (or 5 kb), scaling



473 it down from the recommended length for human genomes due to mosquitoes' high level of  
474 heterozygosity [4] and assumed a constant recombination rate of 2.0 cM/Mb (after [80]).

475 To estimate the long-term evolutionary demographic history of mosquitoes on and near  
476 the Ssesse Islands, including a long-term estimate of  $N_e$  [81], we inferred population demo-  
477 graphic history for each site via stairway plots using the full site frequency spectra based  
478 on SNPs on chromosome 3 with heterochromatic regions and regions within 5 kb of a gene  
479 excluded [21].

480 We also inferred a “two-population” isolation-with-migration (IM) demographic model  
481 with  $\delta a \delta i$  [82, 83] in which the ancestral population splits to form two daughter populations  
482 that are allowed to grow exponentially and exchange migrants asymmetrically, as described  
483 in the main text. For  $\delta a \delta i$ -based analyses, we used the full dataset of SNPs on chromosome  
484 3, not pruned for LD but with heterochromatic regions and regions within 5 kb of a gene  
485 masked. We polarized the SNPs using outgroup information from *Anopheles merus* and *An.*  
486 *merus* [84]. We fit this two-population model and the same model without migration to all  
487 pairs of locality samples, choosing the optimal model using the Godambe Information Matrix  
488 and an adjusted likelihood ratio test to compare the two nested models. We compared the  
489 test statistic to a  $\chi^2$  distribution and rejected the null model if the p-value for the test statistic  
490 was  $< 0.05$ . For both, singletons and doubletons private to one population were masked from  
491 the analysis and a parameter encompassing genotype uncertainty was included in the models  
492 and found to be low (mean = 0.0.70%). We assessed the goodness-of-fit visually using the  
493 residuals of the comparison between model and data frequency spectra (Supplementary Fig.  
494 S7). Using the site frequency spectrum, we projected down to 2-6 fewer chromosomes than  
495 the total for the smaller population to maximize information given missing data. We set the  
496 grid points to  $\{n, n + 10, n + 20\}$ , where  $n$  = the number of chromosomes. Bounds for  $N_e$   
497 scalars were  $\nu \in (0.01, 10, 000)$ , for time were  $T \in (1e-8, 0.1)$ , for migration were  $m \in (1e-$   
498  $8, 10)$ , and for genotyping uncertainty were  $p_{misid} \in (1e-8, 1)$ . Parameters were perturbed

499 before allowing up to 1000 iterations for optimization. We estimated parameter uncertainty  
500 using the Fisher information matrix and 100 bootstrap replicates of 1 Mb from the dataset. If  
501 the Hessian was found to be not invertible when computing the Fisher information matrix,  
502 the results of that iteration were excluded from the analysis. For population size change  
503 parameters,  $\nu$ , optimized values for one or both populations were often close to the upper  
504 limit. Due to this runaway behavior, common in analyses of the SFS [85], we excluded the  
505 population size change from our interpretation.

506 To translate  $\delta a \delta i$ - and stairway plot-based estimates of  $N_e$  and time to individuals and  
507 years respectively, we assumed a generation time of 11 per year and a mutation rate of  $3.5e-9$   
508 per generation [4].

509 **Selection inference** To infer candidate genes and regions with selection histories that  
510 varied geographically, we compared allele frequencies and haplotype diversity between the  
511 sampling sites. To infer differing selection between sampling sites, we computed  $F_{ST}$  between  
512 all populations in windows of size 10 kb using the estimator of Weir and Cockerham [24]  
513 (as implemented in VCFtools [86]), and H12 (as implemented in SelectionHapStats [26])  
514 and XP-EHH on a per-site basis (as implemented in selscan [87]) to detect long stretches of  
515 homozygosity in a given population considered alone or relative to another population [25].  
516 For XP-EHH, EHH was calculated in windows of size 100 kb in each direction from core  
517 SNPs, allowing EHH decay curves to extend up to 1 Mb from the core, and SNPs with MAF  
518  $< 0.05$  were excluded from consideration as a core SNP. As we lacked a fine-scale genetic map  
519 for *Anopheles*, we assumed a constant recombination rate of 2.0 cM/Mb (after [80]). Scores  
520 were normalized within chromosomal arms and the X-chromosome. The between-locality  
521 statistics,  $F_{ST}$  and XP-EHH, were summarized using the composite selection score [CSS;  
522 [88, 89]].

523 We plotted these statistics across the genome to identify candidate regions with signa-

524 tures of selection, including high differentiation between samples from different localities,  
525 reduced variability within a sample, and extended haplotype homozygosity. To identify re-  
526 gions of the genome showing signatures of selection specific to certain geographic areas, we  
527 identified genomic regions with elevated H12 in a subset of localities, and confirmed both ele-  
528 vated differentiation (as inferred from  $F_{ST}$ ) and evidence of differing selective sweep histories  
529 (as inferred from XP-EHH). Excluding the mainland-like portion of Bugala, we identified  
530 putative locality-specific sweeps (H12 over 99<sup>th</sup> percentile in one population), island-specific  
531 sweeps (H12 over 99<sup>th</sup> percentile in 4 or more of the 5 island localities but 0 or 1 mainland  
532 localities), or LVB mainland-specific sweeps (H12 over 99<sup>th</sup> percentile in 3 or more of the 4  
533 island localities but 0 or 1 island localities). To place these putative sweeps in their continen-  
534 tal context, for the region of each putative locality-, island-, or LVB mainland-specific sweep,  
535 we determined if the H12 values of each of the Ag1000G populations (excluding Kenya due  
536 to its signatures of admixture and recent population decline; [4]) were in the top 5% for that  
537 population, indicating a possible selective sweep at the same location.

538 We further explored the haplotype structure and putative functional impact of loci for  
539 which we detected signatures of potential selection to determine the count and geographic  
540 distribution of independent selective sweeps. To provide necessary context for the recon-  
541 struction of sweeps and quantify long distance haplotype sharing between populations, we  
542 included data from several other *An. gambiae* populations across Africa (Burkina Faso,  
543 Cameroon, Gabon, Guinea, Guinea-Bissau, Kenya, and other Ugandan individuals; [4]). We  
544 computed the pairwise distance matrix as the raw number of base pairs that differed and  
545 grouped haplotypes via hierarchical clustering analysis (implemented in the hclust R func-  
546 tion) in regions of size 100 kb centered on each peak in pairwise  $F_{ST}$  or XP-EHH, or the  
547 average of peaks, in the case for multiple nearby spikes. As short terminal branches can  
548 result from a beneficial allele and linked variants rising to fixation during a recent selective  
549 sweep, we identified such clusters by cutting the tree at a height of 0.4 SNP differences per

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## 822 **Data and materials availability**

823 All scripts used in the analysis are available at <https://github.com/bergeycm/Anopheles>  
824 [\\_gambiae\\_structure\\_LVB](#) and released under the GNU General Public License v3. Sequenc-  
825 ing read data for the LVB individuals are deposited in the NCBI Short Read Archive (SRA)  
826 under BioProject accession PRJNA493853.

## 827 **Author Contributions**

828 C.M.B., J.K.K., and N.J.B. designed the study; C.M.B., M.L., R.M.W., and J.K.K. col-  
829 lected biological samples; C.M.B. analyzed the data; C.M.B., M.C.F., and N.J.B. wrote the  
830 manuscript; M.C.F., J.K.K., and N.J.B. supervised the research; C.M.B., M.L., R.M.W.,  
831 M.C.F., J.K.K., and N.J.B. edited the manuscript.

## 832 **Conflict of Interest Statement**

833 The authors declare no competing financial interests.

834 **Supplemental Material for: Assessing connectivity**  
835 **despite high diversity in island populations of a**  
836 **malaria mosquito**

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838 K. Kayondo, and Nora J. Besansky

839 **Tables**

Table S1: Sampling sites and coordinates.

Location	Latitude	Longitude	Sample Count
Banda	-0.25893	32.39594	11
Bugala - Bugoma	-0.26697	32.07936	11
Bugala - Lutoboka	-0.31624	32.29246	7
Bugala - Mweena	-0.32806	32.31113	5
Bukasa	-0.48609	32.45091	11
Buwama	0.02077	32.10574	11
Kaazi	-0.31831	31.88183	11
Kiyindi	0.27558	33.14699	10
Nsadzi	-0.08632	32.58895	11
Sserinya	-0.26476	32.37228	16
Wamala	0.40811	31.99609	11

Table S2: List of individuals included in study with mean depth of sequencing coverage.

ID	Field ID	Island	Site	Mean depth
LVB2015-1	CM-KSB-J5	Nsadzi	Kansambwe	20.40
LVB2015-2	K-KSB-E1	Nsadzi	Kansambwe	24.50
LVB2015-3	RM-KSB-G1	Nsadzi	Kansambwe	17.90
LVB2015-4	NKG-F-G3	Bukasa	Nakibanga	4.90
LVB2015-6	NKG-F-H1	Bukasa	Nakibanga	15.80
LVB2015-7	NKG-K-I1	Bukasa	Nakibanga	15.80
LVB2015-8	NKG-K-K1	Bukasa	Nakibanga	19.90
LVB2015-9	NKG-M-C1	Bukasa	Nakibanga	22.30
LVB2015-10	NKG-M-D1	Bukasa	Nakibanga	20.30
LVB2015-11	NKG-M-F1	Bukasa	Nakibanga	23.90
LVB2015-14	MWN-K-A1	Bugala	Mweena	21.20
LVB2015-15	MWN-K-C2	Bugala	Mweena	18.30
LVB2015-16	MWN-P-D1	Bugala	Mweena	5.34
LVB2015-17	MWN-R-E1	Bugala	Mweena	22.60
LVB2015-18	MWN-R-F1	Bugala	Mweena	17.10
LVB2015-19	BDA-K-B1	Banda	Banda	14.40
LVB2015-20	BDA-K-B2	Banda	Banda	18.00

LVB2015-21	BBS-C-M1	Sserinya	Bbosa	19.70
LVB2015-22	BBS-F-F1	Sserinya	Bbosa	20.80
LVB2015-24	BBS-K-J3	Sserinya	Bbosa	22.80
LVB2015-25	BBS-K-J8	Sserinya	Bbosa	17.30
LVB2015-26	BBS-K-K2	Sserinya	Bbosa	18.20
LVB2015-27	BBS-M-L1	Sserinya	Bbosa	22.40
LVB2015-28	BBS-P-I4	Sserinya	Bbosa	23.30
LVB2015-29	BBS-R-A2	Sserinya	Bbosa	19.60
LVB2015-30	BBS-R-C1	Sserinya	Bbosa	16.10
LVB2015-32	KSS-F-E2	Sserinya	Kasisa	21.00
LVB2015-33	LBK-C-F1	Bugala	Lutoboka	21.00
LVB2015-34	LBK-C-F6	Bugala	Lutoboka	18.60
LVB2015-35	LBK-C-G6	Bugala	Lutoboka	20.90
LVB2015-36	LBK-K-E2	Bugala	Lutoboka	22.00
LVB2015-37	LBK-M-A1	Bugala	Lutoboka	18.50
LVB2015-39	LBK-R-O1	Bugala	Lutoboka	20.20
LVB2015-42	BGM-F-D1	Bugala	Bugoma	16.70
LVB2015-43	BGM-F-E2	Bugala	Bugoma	24.50
LVB2015-45	BGM-K-M2	Bugala	Bugoma	23.80
LVB2015-46	BGM-M-G1	Bugala	Bugoma	18.40
LVB2015-47	BGM-M-H2	Bugala	Bugoma	14.10
LVB2015-48	BGM-M-J1	Bugala	Bugoma	20.90
LVB2015-50	BGM-P-F9	Bugala	Bugoma	18.90
LVB2015-51	BGM-R-O2	Bugala	Bugoma	16.80
LVB2015-52	KZI-F-F001	Kaazi	Nabugabo	19.10
LVB2015-53	KZI-F-G001	Kaazi	Nabugabo	19.50
LVB2015-54	KZI-F-H001	Kaazi	Nabugabo	19.40
LVB2015-55	KZI-P-A001	Kaazi	Nabugabo	10.30
LVB2015-56	KZI-P-B005	Kaazi	Nabugabo	16.50
LVB2015-59	KZI-R-C003	Kaazi	Nabugabo	18.10
LVB2015-60	KZI-R-D007	Kaazi	Nabugabo	15.90
LVB2015-61	BWM-C-G001	Buwama	Buwama	16.10
LVB2015-62	BWM-C-H001	Buwama	Buwama	11.10
LVB2015-63	BWM-F-A001	Buwama	Buwama	20.40
LVB2015-64	BWM-F-B001	Buwama	Buwama	21.50
LVB2015-65	BWM-P-J001	Buwama	Buwama	14.80
LVB2015-66	BWM-R-C002	Buwama	Buwama	19.10

LVB2015-67	BWM-R-F005	Buwama	Buwama	22.30
LVB2015-68	NMA-C-E003	Wamala	Naama	20.30
LVB2015-69	NMA-C-F002	Wamala	Naama	17.80
LVB2015-70	NMA-F-A001	Wamala	Naama	13.10
LVB2015-71	NMA-K-B001	Wamala	Naama	22.10
LVB2015-72	NMA-K-C002	Wamala	Naama	18.00
LVB2015-73	NMA-P-G001	Wamala	Naama	18.20
LVB2015-74	NMA-P-H003	Wamala	Naama	16.60
LVB2015-76	KYD-C-G001	Kiyindi	Kiyindi	16.10
LVB2015-77	KYD-C-H001	Kiyindi	Kiyindi	11.80
LVB2015-78	KYD-C-I001	Kiyindi	Kiyindi	16.40
LVB2015-79	KYD-C-J002	Kiyindi	Kiyindi	11.50
LVB2015-80	KYD-F-A003	Kiyindi	Kiyindi	10.30
LVB2015-81	KYD-F-B004	Kiyindi	Kiyindi	21.50
LVB2015-82	KYD-K-D002	Kiyindi	Kiyindi	18.40
LVB2015-84	KYD-R-K001	Kiyindi	Kiyindi	16.80
LVB2015-89	BDA-K-E2	Banda	Banda	15.10
LVB2015-90	BDA-K-F1	Banda	Banda	25.10
LVB2015-91	BDA-M-N1	Banda	Banda	25.60
LVB2015-92	BDA-M-O4	Banda	Banda	17.60
LVB2015-93	BDA-M-Q1	Banda	Banda	39.20
LVB2015-96	CM-KSB-J2	Nsadzi	Kansambwe	9.22
LVB2015-97	CM-KSB-J3	Nsadzi	Kansambwe	10.10
LVB2015-98	CM-KSB-J6	Nsadzi	Kansambwe	16.90
LVB2015-100	K-KSB-D1	Nsadzi	Kansambwe	6.05
LVB2015-101	ML-KSB-M1	Nsadzi	Kansambwe	4.27
LVB2015-102	ML-KSB-M2	Nsadzi	Kansambwe	19.90
LVB2015-103	RM-KSB-G2	Nsadzi	Kansambwe	14.20
LVB2015-104	RM-KSB-G3	Nsadzi	Kansambwe	17.50
LVB2015-105	NKG-R-A12	Bukasa	Nakibanga	15.30
LVB2015-106	NKG-C-E1	Bukasa	Nakibanga	16.20
LVB2015-108	NKG-K-C5	Bukasa	Nakibanga	18.50
LVB2015-109	NKG-M-A1	Bukasa	Nakibanga	12.80
LVB2015-112	BDA-K-D4	Banda	Banda	12.70
LVB2015-113	BDA-K-E3	Banda	Banda	12.20
LVB2015-114	BDA-M-N5	Banda	Banda	15.00
LVB2015-115	BDA-M-P1	Banda	Banda	16.80



LVB2015-116	BBS-C-M3	Sserinya	Bbosa	16.60
LVB2015-117	BBS-K-J1	Sserinya	Bbosa	18.80
LVB2015-118	BBS-K-J11	Sserinya	Bbosa	14.60
LVB2015-120	BBS-K-K6	Sserinya	Bbosa	18.10
LVB2015-121	BBS-P-I8	Sserinya	Bbosa	15.00
LVB2015-122	BBS-R-A19	Sserinya	Bbosa	15.50
LVB2015-125	LBK-R-A5	Bugala	Lutoboka	18.10
LVB2015-126	BGM-K-K1	Bugala	Bugoma	15.20
LVB2015-128	BGM-M-H4	Bugala	Bugoma	20.30
LVB2015-129	BGM-P-F4	Bugala	Bugoma	19.00
LVB2015-130	KZI-F-G005	Kaazi	Nabugabo	18.60
LVB2015-131	KZI-P-A007	Kaazi	Nabugabo	15.80
LVB2015-132	KZI-R-C012	Kaazi	Nabugabo	15.10
LVB2015-133	KZI-R-E011	Kaazi	Nabugabo	16.30
LVB2015-134	BWM-P-I001	Buwama	Buwama	18.20
LVB2015-135	BWM-P-K002	Buwama	Buwama	19.30
LVB2015-136	BWM-R-D001	Buwama	Buwama	14.40
LVB2015-137	BWM-R-F002	Buwama	Buwama	19.90
LVB2015-138	NMA-C-E006	Wamala	Naama	21.90
LVB2015-139	NMA-C-F003	Wamala	Naama	20.40
LVB2015-140	NMA-P-G003	Wamala	Naama	18.90
LVB2015-141	NMA-R-I001	Wamala	Naama	14.10
LVB2015-142	KYD-F-B006	Kiyindi	Kiyindi	18.10
LVB2015-143	KYD-K-E003	Kiyindi	Kiyindi	14.20

Table S3: Results of two population demographic inference with IM model in  $\delta a\delta i$  when comparing island to island localities. Numbers in parentheses are bounds of 95% confidence interval computed using Fisher information matrix and 100 bootstrap replicates of 1 Mb from the dataset.

Localities	$N_a$	% Pop. 1 in Split	Pop. 1 $\nu_F$	Pop. 2 $\nu_F$	Time since split	$m_{12}$	$m_{21}$
Banda - Bugala (I)	531,000 (530,000, 532,000)	0.603 (0.596, 0.609)	1.94 (1.8, 2.09)	9,800 (7,060, 12,500)	3,290 (3,190, 3,390)	None	None
Banda - Bukasa	526,000 (525,000, 527,000)	0.568 (0.556, 0.581)	14.7 (13.7, 15.6)	9,080 (7,240, 10,900)	7,580 (7,470, 7,690)	None	None
Banda - Nsadzi	527,000 (526,000, 528,000)	0.518 (0.502, 0.534)	47.1 (39.9, 54.4)	9,880 (7,310, 12,400)	9,340 (9,160, 9,530)	None	None
Banda - Sserinya	531,000 (530,000, 532,000)	0.489 (0.464, 0.514)	10.5 (8.69, 12.4)	9,840 (7,390, 12,300)	4,430 (4,250, 4,610)	None	None
Bugala (I) - Bukasa	527,000 (526,000, 528,000)	0.49 (0.471, 0.509)	9,840 (7,850, 11,800)	536 (447, 624)	5,290 (5,170, 5,410)	None	None
Bugala (I) - Nsadzi	526,000 (525,000, 527,000)	0.56 (0.536, 0.583)	8,980 (6,920, 11,000)	128 (110, 146)	6,680 (6,440, 6,910)	None	None
Bugala (I) - Sserinya	530,000 (529,000, 531,000)	0.61 (0.571, 0.65)	5,850 (3,610, 8,090)	49 (38.3, 59.6)	2,130 (1,950, 2,300)	None	None
Bukasa - Nsadzi	527,000 (526,000, 528,000)	0.499 (0.49, 0.507)	3,420 (2,860, 3,980)	335 (293, 377)	9,340 (9,190, 9,500)	None	None
Bukasa - Sserinya	525,000 (524,000, 526,000)	0.503 (0.495, 0.51)	9,840 (7,490, 12,200)	6,760 (5,630, 7,880)	8,930 (8,780, 9,080)	None	None
Nsadzi - Sserinya	540,000 (539,000, 541,000)	0.538 (0.521, 0.554)	893 (612, 1,170)	9,900 (7,810, 12,000)	9,540 (9,280, 9,790)	None	None

Table S4: Results of two population demographic inference with IM model in  $\delta a\delta i$  when comparing island to mainland localities. Numbers in parentheses are bounds of 95% confidence interval computed using Fisher information matrix and 100 bootstrap replicates of 1 Mb from the dataset.

Localities	$N_a$	% Pop. 1 in Split	Pop. 1 $\nu_F$	Pop. 2 $\nu_F$	Time since split	$m_{12}$	$m_{21}$
Banda - Bugala (M)	522,000 (521,000, 523,000)	0.599 (0.586, 0.612)	3.83 (3.59, 4.07)	9,900 (8,410, 11,400)	5,400 (5,300, 5,500)	None	None
Banda - Buwama	522,000 (521,000, 523,000)	0.51 (0.491, 0.529)	1.09 (1.01, 1.16)	8,520 (6,830, 10,200)	3,040 (2,940, 3,150)	None	None
Banda - Kaazi	522,000 (521,000, 523,000)	0.563 (0.55, 0.575)	3.99 (3.71, 4.28)	9,960 (8,370, 11,500)	5,890 (5,760, 6,030)	None	None
Banda - Kiyindi	510,000 (509,000, 511,000)	0.568 (0.56, 0.577)	1.72 (1.69, 1.75)	9,910 (8,170, 11,600)	3,910 (3,880, 3,950)	None	None
Banda - Wamala	521,000 (520,000, 522,000)	0.562 (0.554, 0.57)	3.9 (3.66, 4.15)	7,970 (6,790, 9,140)	5,510 (5,390, 5,620)	None	None
Bugala (I) - Bugala (M)	522,000 (521,000, 523,000)	0.555 (0.543, 0.566)	1,440 (954, 1,930)	9,710 (7,420, 12,000)	4,170 (4,040, 4,300)	None	None
Bugala (I) - Buwama	523,000 (522,000, 524,000)	0.499 (0.496, 0.503)	0.215 (0.209, 0.222)	130 (2.12, 258)	190 (188, 192)	None	None
Bugala (I) - Kaazi	523,000 (522,000, 524,000)	0.366 (0.348, 0.384)	1,420 (1,210, 1,620)	8,510 (6,610, 10,400)	5,060 (4,890, 5,230)	None	None
Bugala (I) - Kiyindi	508,000 (507,000, 509,000)	0.363 (0.342, 0.383)	1,350 (1,070, 1,620)	5,910 (4,470, 7,350)	3,580 (3,420, 3,740)	None	None
Bugala (I) - Wamala	520,000 (519,000, 521,000)	0.486 (0.462, 0.51)	2,060 (1,610, 2,500)	9,270 (6,790, 11,800)	3,700 (3,570, 3,830)	None	None
Bugala (M) - Bukasa	521,000 (520,000, 522,000)	0.53 (0.508, 0.552)	9,000 (6,720, 11,300)	66.3 (52.2, 80.5)	4,830 (4,670, 4,990)	None	None
Bugala (M) - Nsadzi	535,000	0.439	9,220	7.59	4,500	None	None

	(534,000, 536,000)	(0.423, 0.455)	(7,500, 10,900)	(6.91, 8.26)	(4,390, 4,620)		
Bugala (M) - Sserinya	534,000	0.516	9,590	48.8	4,040	None	None
	(533,000, 535,000)	(0.497, 0.535)	(7,640, 11,500)	(42.4, 55.2)	(3,930, 4,160)		
Bukasa - Buwama	522,000	0.501	1.43	9,960	1,690	None	None
	(521,000, 523,000)	(0.496, 0.506)	(1.4, 1.46)	(7,250, 12,700)	(1,670, 1,710)		
Bukasa - Kaazi	522,000	0.501	41.5	9,410	5,490	None	None
	(521,000, 522,000)	(0.491, 0.51)	(33.8, 49.3)	(6,990, 11,800)	(5,320, 5,650)		
Bukasa - Kiyindi	508,000	0.361	18.6	9,220	3,360	None	None
	(507,000, 509,000)	(0.336, 0.386)	(15.8, 21.4)	(6,790, 11,600)	(3,190, 3,540)		
Bukasa - Wamala	520,000	0.39	304	8,060	5,200	None	None
	(519,000, 521,000)	(0.372, 0.409)	(257, 351)	(6,270, 9,850)	(5,050, 5,360)		
Buwama - Nsadzi	524,000	0.54	9,810	1.25	1,930	None	None
	(523,000, 525,000)	(0.502, 0.578)	(6,950, 12,700)	(1.07, 1.44)	(1,800, 2,070)		
Buwama - Sserinya	523,000	0.493	54.2	0.137	187	None	None
	(522,000, 524,000)	(0.488, 0.498)	(24.2, 84.2)	(0.134, 0.14)	(186, 189)		
Kaazi - Nsadzi	524,000	0.489	9,540	19.4	5,730	None	None
	(523,000, 525,000)	(0.47, 0.507)	(7,690, 11,400)	(16, 22.8)	(5,540, 5,910)		
Kaazi - Sserinya	523,000	0.598	6,980	104	4,550	None	None
	(522,000, 524,000)	(0.579, 0.618)	(5,440, 8,510)	(89.7, 119)	(4,410, 4,680)		
Kiyindi - Nsadzi	511,000	0.499	9,940	2.62	2,840	None	None
	(510,000, 512,000)	(0.491, 0.507)	(7,340, 12,500)	(2.26, 2.98)	(2,690, 2,990)		
Kiyindi - Sserinya	509,000	0.5	1,870	0.129	185	None	None
	(508,000, 510,000)	(0.496, 0.503)	(-5,010, 8,750)	(0.126, 0.132)	(183, 187)		
Wamala - Nsadzi	523,000	0.473	8,490	9.72	4,420	None	None
	(522,000, 524,000)	(0.454, 0.492)	(6,720, 10,200)	(8.57, 10.9)	(4,290, 4,560)		
Wamala - Sserinya	521,000	0.649	9,840	39.1	2,790	None	None
	(520,000, 522,000)	(0.643, 0.655)	(7,070, 12,600)	(38.1, 40.1)	(2,760, 2,820)		

Table S5: Results of two population demographic inference with IM model in  $\delta a \delta i$  when comparing mainland to mainland localities. Numbers in parentheses are bounds of 95% confidence interval computed using Fisher information matrix and 100 bootstrap replicates of 1 Mb from the dataset.

Localities	$N_a$	% Pop. 1 in Split	Pop. 1 $\nu_F$	Pop. 2 $\nu_F$	Time since split	$m_{12}$	$m_{21}$
Bugala (M) - Buwama	523,000 (523,000, 524,000)	0.498 (0.49, 0.506)	9,590 (802, 18,400)	1,090 (573, 1,620)	368 (320, 416)	None	None
Bugala (M) - Kaazi	521,000 (520,000, 522,000)	0.483 (0.458, 0.509)	7,570 (5,740, 9,400)	8,450 (5,860, 11,000)	2,710 (2,590, 2,830)	None	None
Bugala (M) - Kiyindi	507,000 (506,000, 508,000)	0.361 (0.318, 0.404)	1.88 (1.74, 2.01)	3,870 (1,810, 5,920)	355 (348, 362)	0.0000169 (-14.3, 14.3)	0 (-31,100, 31,100)
Bugala (M) - Wamala	521,000 (520,000, 521,000)	0.51 (0.491, 0.53)	13.1 (9.03, 17.1)	323 (-168, 814)	186 (179, 194)	0 (-162, 162)	0.00226 (-3,980, 3,980)
Buwama - Kaazi	523,000 (522,000, 524,000)	0.553 (0.357, 0.749)	706 (-764, 2,180)	186 (-101, 472)	181 (122, 239)	3.16 (-5,690, 5,690)	2.12 (-836, 841)
Buwama - Kiyindi	511,000 (510,000, 512,000)	0.322 (0.287, 0.357)	9,110 (5,390, 12,800)	9,810 (4,390, 15,200)	369 (302, 436)	761 (-80,200, 81,700)	178 (-81,200, 81,500)
Buwama - Wamala	523,000 (522,000, 524,000)	0.365 (-1,000, 1,000)	31.7 (22, 41.3)	19.7 (13.6, 25.8)	124 (107, 141)	9.27 (-578, 596)	0 (-344, 344)
Kaazi - Kiyindi	510,000 (509,000, 511,000)	0.448 (0.325, 0.571)	9,900 (1,100, 18,700)	1,670 (749, 2,600)	438 (365, 510)	923 (-64,900, 66,800)	718 (610, 825)
Kaazi - Wamala	521,000 (520,000, 522,000)	0.581 (0.515, 0.647)	9,200 (3,680, 14,700)	4,820 (2,430, 7,210)	974 (795, 1,150)	None	None
Kiyindi - Wamala	510,000 (509,000, 511,000)	0.454 (0.391, 0.518)	134 (57.9, 209)	40.3 (25.4, 55.3)	181 (166, 197)	0 (-663, 663)	0.00363 (-3.69, 3.7)

Table S6: Locality-specific (in LVB) putative sweeps based on H12 statistic.

Site	Count	Chr.	Putative Sweeps	Other sites <sup>1</sup>
Banda	44	2L	28.6 Mb; 36 Mb; 36.4 Mb; 36.9 Mb; 37.6 Mb; 38.1 Mb; 39.1 Mb; 42.2 Mb; 43.4 Mb; 43.8 Mb; 44.3 Mb; 44.9 Mb; 45.4 Mb	1 also found in BFS, GNS
		2R	4.2 Mb; 12.3 Mb; 18.3 Mb; 23.6 Mb; 29.4 Mb; 30.3 Mb; 33.7 Mb; 34.8 Mb; 35.8 Mb; 36.5 Mb; 44.1 Mb; 44.6 Mb; 49.7 Mb	1 also found in BFM, BFS, CMS, GNS, GWA; 1 also found in BFM, GWA; 5 also found in GWA
		3L	18.5 Mb; 21.6 Mb; 23.4 Mb; 23.9 Mb; 32.8 Mb	
		3R	2.6 Mb; 7.9 Mb; 29.2 Mb; 30.5 Mb; 31.3 Mb; 32.1 Mb; 33.2 Mb; 45.3 Mb; 46.4 Mb; 47 Mb	1 also found in GNS
		X	0.5 Mb; 2.1 Mb; 4.3 Mb	1 also found in AOM
Bugala (I)	24	2L	2.5 Mb; 5.5 Mb; 7.1 Mb; 19 Mb; 31.1 Mb; 43 Mb; 45.7 Mb	1 also found in AOM, BFM, BFS, CMS, GAS, GNS, UGS; 1 also found in AOM, UGS
		2R	6.7 Mb; 21.1 Mb; 24 Mb; 24.6 Mb; 35.6 Mb; 37.1 Mb; 38.6 Mb; 39 Mb; 55.9 Mb	1 also found in BFM, GWA; 2 also found in GWA
		3L	17.2 Mb; 29.5 Mb	
		3R	26 Mb; 35.8 Mb; 37.5 Mb	
		X	3.5 Mb; 5.7 Mb; 10.8 Mb	
Bukasa	112	2L	12.6 Mb; 13.6 Mb; 17.7 Mb; 20.1 Mb; 20.9 Mb; 21.6 Mb; 22.7 Mb; 23.6 Mb; 24.7 Mb; 25.4 Mb; 26.2 Mb; 26.9 Mb; 27.3 Mb; 27.8 Mb; 28.4 Mb; 29.1 Mb; 30.1 Mb; 31.5 Mb; 32.3 Mb; 33.3 Mb; 35.8 Mb; 39.4 Mb; 39.8 Mb; 40.6 Mb; 41.4 Mb; 43.1 Mb; 45.6 Mb; 48.1 Mb; 49.3 Mb	1 also found in AOM, BFM, BFS, CMS, GAS, GNS; 1 also found in BFM, GAS; 1 also found in BFS, GAS, GNS; 1 also found in BFS, GNS; 2 also found in CMS; 2 also found in GAS; 1 also found in GWA

	2R	1.3 Mb; 4.7 Mb; 5.3 Mb; 7.2 Mb; 7.6 Mb; 8 Mb; 9.7 Mb; 10.5 Mb; 12 Mb; 12.4 Mb; 13.5 Mb; 14 Mb; 15.7 Mb; 16.9 Mb; 17.5 Mb; 19.4 Mb; 22.9 Mb; 24.9 Mb; 25.8 Mb; 26.6 Mb; 29.9 Mb; 30.8 Mb; 32.4 Mb; 33.4 Mb; 35.5 Mb; 37.6 Mb; 43 Mb; 45.6 Mb; 47 Mb; 49.5 Mb; 54.8 Mb	1 also found in AOM, GAS, GWA; 2 also found in BFM; 1 also found in BFM, GWA; 3 also found in GAS, GWA; 6 also found in GWA	
	3L	7.3 Mb; 11.6 Mb; 13.1 Mb; 15.6 Mb; 18.1 Mb; 19.1 Mb; 19.8 Mb; 20.6 Mb; 24.2 Mb; 25.2 Mb; 27.3 Mb; 28 Mb; 28.7 Mb; 29.7 Mb; 30.6 Mb; 33.7 Mb; 34.7 Mb; 35.3 Mb; 36.1 Mb; 38.7 Mb; 39.9 Mb; 40.3 Mb; 41.2 Mb	2 also found in BFM; 1 also found in GAS	
	3R	5.1 Mb; 5.9 Mb; 7.2 Mb; 8.9 Mb; 12.7 Mb; 13.3 Mb; 14.1 Mb; 14.9 Mb; 15.9 Mb; 17.2 Mb; 22.3 Mb; 23.3 Mb; 23.8 Mb; 24.9 Mb; 26.8 Mb; 27.9 Mb; 31.4 Mb; 33 Mb; 35.9 Mb; 36.9 Mb	1 also found in GWA	
	X	1.7 Mb; 2.8 Mb; 4.9 Mb; 6 Mb; 7 Mb; 11.5 Mb; 12.5 Mb; 13.6 Mb; 16.7 Mb	1 also found in BFM, GAS, GWA; 4 also found in GAS	
Buwama	27	2L	14.9 Mb; 15.9 Mb; 25.1 Mb; 26.5 Mb; 31.6 Mb	1 also found in BFM, GAS; 1 also found in GWA
		2R	24.4 Mb; 39.5 Mb; 44.5 Mb; 46.3 Mb; 49.1 Mb; 53.7 Mb; 55.3 Mb	1 also found in AOM, BFM, CMS; 1 also found in BFS, CMS, GNS; 1 also found in CMS; 1 also found in GWA
		3L	2.4 Mb; 3.1 Mb; 3.6 Mb; 4.1 Mb; 10.6 Mb; 16.1 Mb; 21.7 Mb; 29.8 Mb	
		3R	18 Mb; 29.1 Mb; 35.5 Mb; 37.7 Mb; 38.4 Mb; 38.9 Mb; 40.6 Mb	1 also found in GNS

Kaazi	15	2L	8.5 Mb; 34.6 Mb	1 also found in AOM
		2R	8.3 Mb; 23 Mb	1 also found in AOM; 1 also found in GAS
		3L	3.5 Mb; 4.8 Mb; 8.6 Mb; 11.8 Mb; 13 Mb; 15.8 Mb; 25 Mb; 26.8 Mb	1 also found in BFM; 1 also found in BFM, GNS
		3R	14.7 Mb; 15.6 Mb; 46 Mb	1 also found in GNS
Kiyindi	40	2L	2 Mb; 10.6 Mb; 17.8 Mb; 22.1 Mb; 23.9 Mb; 26 Mb; 28.7 Mb; 29.9 Mb; 34.8 Mb	1 also found in AOM, BFM, BFS, CMS, GNS, UGS; 1 also found in BFS, GNS; 3 also found in GAS
		2R	19.1 Mb; 20.2 Mb; 25.9 Mb; 35.3 Mb; 36.6 Mb; 38.1 Mb; 40 Mb; 41.7 Mb; 42.4 Mb; 45.3 Mb; 48.2 Mb; 48.6 Mb; 50.1 Mb; 52.2 Mb; 53.6 Mb; 54.7 Mb; 55.1 Mb	1 also found in AOM; 1 also found in AOM, BFS, CMS, GNS, GWA; 1 also found in BFM; 2 also found in GWA
		3L	1.2 Mb; 8.9 Mb; 12.1 Mb; 12.6 Mb; 13.5 Mb; 14.8 Mb; 15.4 Mb; 16 Mb; 16.8 Mb; 19.7 Mb; 26.7 Mb	1 also found in BFM; 1 also found in GWA
		3R	38 Mb; 41.9 Mb; 48.3 Mb	
Nsadzi	47	2L	23.2 Mb; 27 Mb; 45.5 Mb	
		2R	1.6 Mb; 2.3 Mb; 3.2 Mb; 4 Mb; 8.8 Mb; 10.2 Mb; 13.2 Mb; 16.1 Mb; 20 Mb; 21.3 Mb; 24.7 Mb; 30.5 Mb; 34.2 Mb; 37.3 Mb; 41.2 Mb; 43.5 Mb; 52 Mb	1 also found in BFM, GAS; 1 also found in BFM, GWA; 1 also found in BFS, CMS, GNS; 1 also found in CMS; 2 also found in GWA
		3L	10.5 Mb; 11 Mb; 24.3 Mb; 35 Mb; 35.4 Mb; 36.8 Mb; 37.6 Mb	1 also found in GAS
		3R	3.8 Mb; 6 Mb; 7.4 Mb; 19.9 Mb; 20.5 Mb; 21.4 Mb; 23 Mb; 24.2 Mb; 27.7 Mb; 41.6 Mb; 42.2 Mb; 48.2 Mb; 49.8 Mb; 50.4 Mb	1 also found in BFS, GNS
		X	0.7 Mb; 2.3 Mb; 5.2 Mb; 7.7 Mb; 11.9 Mb; 17.9 Mb	1 also found in BFM, GAS, GWA; 1 also found in GAS



Sserinya	35	2L	22.2 Mb; 24.2 Mb; 25.7 Mb; 33.2 Mb; 34.9 Mb; 35.4 Mb; 40.2 Mb; 41.1 Mb; 45.1 Mb; 45.9 Mb; 46.8 Mb	1 also found in BFM, GNS; 1 also found in CMS, GAS; 1 also found in GAS, GNS
		2R	0.4 Mb; 7.7 Mb; 21.5 Mb; 30 Mb; 32 Mb; 36.1 Mb	3 also found in GWA
		3L	10.1 Mb; 10.9 Mb; 14.6 Mb; 34.5 Mb; 41.8 Mb	1 also found in BFS, CMS, GNS, GWA, UGS
		3R	1.9 Mb; 10 Mb; 15 Mb; 24.8 Mb; 26.2 Mb; 27 Mb; 29 Mb	1 also found in GAS
		X	5.8 Mb; 12.7 Mb; 13.1 Mb; 18.1 Mb; 18.8 Mb; 21.3 Mb	1 also found in BFM, CMS, GAS, GWA; 1 also found in BFM, GAS, GWA; 1 also found in CMS, GNS, GWA; 2 also found in GAS
Wamala	25	2L	13.4 Mb; 15.5 Mb; 17.1 Mb; 19.1 Mb; 20 Mb	2 also found in GAS
		2R	21.2 Mb; 22.2 Mb; 29.6 Mb; 38.8 Mb; 39.7 Mb; 47.6 Mb; 48.3 Mb; 48.9 Mb	2 also found in AOM; 2 also found in GWA
		3L	3.3 Mb; 7.6 Mb; 8.2 Mb	
		3R	5 Mb; 39.2 Mb; 43.2 Mb; 46.5 Mb; 47.5 Mb; 48.5 Mb; 50.5 Mb; 50.9 Mb; 51.8 Mb	

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840 <sup>1</sup> Ag1000G site codes: AOM: Angola [*coluzzii*]; BFM: Burkina Faso [*coluzzii*]; BFS: Burkina Faso [*gambiae*]; CMS: Cameroon [*gambiae*]; GAS: Gabon  
 841 [*gambiae*]; GNS: Guinea [*gambiae*]; GWA: Guinea-Bissau; UGS: Uganda [*gambiae*]

Table S7: Putative sweeps based on H12 statistic present on islands but rare or absent on LVB mainland.

Chr.	Region Start	Region End	Island Sites with Putative Sweep	Mainland Sites with Putative Sweep	Outlier Island Localities	Outlier Mainland Localities	Ag1000G Populations with Putative Sweep
2R	16,200,000	16,300,000	4 / 5	0 / 4	Banda; Bukasa; Nsadzi; Sserinya	None	Guinea-Bissau
2R	17,300,000	17,500,000	4 / 5	1 / 4	Banda; Bugala (I); Bukasa; Sserinya	Buwama	Guinea-Bissau
2R	21,000,000	21,100,000	5 / 5	1 / 4	Banda; Bugala (I); Bukasa; Nsadzi; Sserinya	Buwama	None
2R	40,400,000	40,800,000	4 / 5	1 / 4	Bugala (I); Bukasa; Nsadzi; Sserinya	Wamala	Burkina Faso [ <i>gambiae</i> ], Cameroon [ <i>gambiae</i> ], Gabon [ <i>gambiae</i> ], Guinea-Bissau
2R	41,100,000	41,200,000	4 / 5	1 / 4	Banda; Bukasa; Nsadzi; Sserinya	Wamala	Cameroon [ <i>gambiae</i> ]
2R	55,800,000	55,900,000	4 / 5	1 / 4	Banda; Bugala (I); Bukasa; Sserinya	Kiyindi	Angola [ <i>coluzzi</i> ]
2L	7,700,000	7,800,000	4 / 5	1 / 4	Banda; Bugala (I); Bukasa; Nsadzi	Buwama	Guinea-Bissau, Uganda [ <i>gambiae</i> ]
2L	8,100,000	8,200,000	4 / 5	0 / 4	Banda; Bugala (I); Nsadzi; Sserinya	None	None
2L	42,400,000	42,500,000	4 / 5	0 / 4	Banda; Bugala (I); Nsadzi; Sserinya	None	None
2L	43,500,000	43,600,000	5 / 5	1 / 4	Banda; Bugala (I); Bukasa; Nsadzi; Sserinya	Buwama	None
2L	49,000,000	49,100,000	4 / 5	1 / 4	Banda; Bugala (I); Bukasa; Sserinya	Wamala	None

3R	26,600,000	26,700,000	5 / 5	0 / 4	Banda; Bugala (I); Bukasa; Nsadzi; Sserinya	None	None
3R	36,700,000	36,800,000	4 / 5	0 / 4	Banda; Bugala (I); Bukasa; Nsadzi	None	None
3R	44,200,000	44,300,000	4 / 5	1 / 4	Banda; Bukasa; Nsadzi; Sserinya	Kiyindi	Angola [ <i>coluzzii</i> ]
3R	46,200,000	46,300,000	4 / 5	0 / 4	Banda; Bukasa; Nsadzi; Sserinya	None	None
X	6,600,000	7,000,000	4 / 5	0 / 4	Banda; Bugala (I); Bukasa; Nsadzi; Sserinya	None	Burkina Faso [ <i>coluzzii</i> ], Gabon [ <i>gambiae</i> ], Guinea-Bissau
X	8,100,000	10,700,000	4 / 5	0 / 4	Banda; Bugala (I); Bukasa; Nsadzi; Sserinya	Kiyindi	Burkina Faso [ <i>coluzzii</i> ], Burkina Faso [ <i>gambiae</i> ], Gabon [ <i>gambiae</i> ]
X	11,300,000	11,800,000	5 / 5	0 / 4	Banda; Bugala (I); Bukasa; Nsadzi; Sserinya	None	Gabon [ <i>gambiae</i> ]
X	12,900,000	13,000,000	4 / 5	0 / 4	Banda; Bugala (I); Bukasa; Sserinya	None	Gabon [ <i>gambiae</i> ]
X	14,300,000	14,400,000	5 / 5	1 / 4	Banda; Bugala (I); Bukasa; Nsadzi; Sserinya	Kaazi	Gabon [ <i>gambiae</i> ]
X	16,200,000	16,300,000	4 / 5	1 / 4	Banda; Bugala (I); Bukasa; Sserinya	Kaazi	Burkina Faso [ <i>coluzzii</i> ], Gabon [ <i>gambiae</i> ]

Table S8: Putative sweeps based on H12 statistic present on LVB mainland but rare or absent on islands.

Chr.	Region Start	Region End	Island Sites with Putative Sweep	Mainland Sites with Putative Sweep	Outlier Island Localities	Outlier Mainland Localities	Ag1000G Populations with Putative Sweep
2R	27,600,000	27,700,000	1 / 5	3 / 4	Nsadzi	Buwama; Kiyindi; Wamala	None
2R	38,000,000	38,100,000	1 / 5	3 / 4	Bugala (I)	Buwama; Kiyindi; Wamala	None
2R	42,700,000	42,800,000	0 / 5	3 / 4	None	Buwama; Kiyindi; Wamala	None
2R	45,400,000	45,500,000	1 / 5	3 / 4	Sserinya	Buwama; Kiyindi; Wamala	None
2R	46,800,000	46,900,000	1 / 5	3 / 4	Banda	Buwama; Kiyindi; Wamala	Cameroon [ <i>gambiae</i> ]
2R	48,000,000	48,100,000	1 / 5	3 / 4	Bukasa	Buwama; Kaazi; Wamala	Angola [ <i>coluzzii</i> ], Cameroon [ <i>gambiae</i> ]
2R	48,800,000	48,900,000	1 / 5	3 / 4	Nsadzi	Buwama; Kaazi; Wamala	None
2R	50,900,000	51,000,000	1 / 5	3 / 4	Bukasa	Kaazi; Kiyindi; Wamala	Burkina Faso [ <i>gambiae</i> ], Guinea [ <i>gambiae</i> ]
2R	51,500,000	51,600,000	0 / 5	3 / 4	None	Kaazi; Kiyindi; Wamala	None
2R	57,500,000	57,600,000	1 / 5	3 / 4	Banda	Buwama; Kaazi; Kiyindi	Angola [ <i>coluzzii</i> ], Guinea-Bissau
2L	2,900,000	3,000,000	1 / 5	4 / 4	Sserinya	Buwama; Kaazi; Kiyindi; Wamala	Angola [ <i>coluzzii</i> ], Burkina Faso [ <i>coluzzii</i> ], Burkina Faso [ <i>gambiae</i> ], Cameroon [ <i>gambiae</i> ], Gabon [ <i>gambiae</i> ], Guinea [ <i>gambiae</i> ], Uganda [ <i>gambiae</i> ]
2L	4,200,000	4,300,000	1 / 5	4 / 4	Bugala (I)	Buwama; Kaazi; Kiyindi; Wamala	Angola [ <i>coluzzii</i> ], Cameroon [ <i>gambiae</i> ], Gabon [ <i>gambiae</i> ], Uganda [ <i>gambiae</i> ]

2L	5,700,000	5,800,000	1 / 5	3 / 4	Bugala (I)	Buwama; Kaazi; Kiyindi	Angola [ <i>coluzzii</i> ], Guinea [ <i>gambiae</i> ], Uganda [ <i>gambiae</i> ]
2L	6,200,000	6,300,000	1 / 5	3 / 4	Bugala (I)	Kaazi; Kiyindi; Wamala	Uganda [ <i>gambiae</i> ]
2L	6,600,000	6,800,000	1 / 5	3 / 4	Bugala (I)	Kaazi; Kiyindi; Wamala	Angola [ <i>coluzzii</i> ], Cameroon [ <i>gambiae</i> ], Gabon [ <i>gambiae</i> ], Guinea [ <i>gambiae</i> ], Uganda [ <i>gambiae</i> ]
2L	10,000,000	10,100,000	1 / 5	3 / 4	Sserinya	Kaazi; Kiyindi; Wamala	None
2L	10,800,000	10,900,000	0 / 5	3 / 4	None	Kaazi; Kiyindi; Wamala	None
2L	11,300,000	11,400,000	1 / 5	3 / 4	Bugala (I)	Kaazi; Kiyindi; Wamala	Guinea-Bissau
2L	12,000,000	12,100,000	1 / 5	3 / 4	Bugala (I)	Kaazi; Kiyindi; Wamala	None
2L	12,400,000	13,000,000	0 / 5	3 / 4	Bukasa	Buwama; Kaazi; Kiyindi; Wamala	None
2L	14,500,000	14,900,000	1 / 5	3 / 4	Sserinya	Buwama; Kiyindi; Wamala	Gabon [ <i>gambiae</i> ], Uganda [ <i>gambiae</i> ]
2L	16,000,000	16,300,000	1 / 5	3 / 4	Bukasa	Buwama; Kaazi; Wamala	Gabon [ <i>gambiae</i> ]
2L	16,600,000	16,700,000	1 / 5	4 / 4	Bugala (I)	Buwama; Kaazi; Kiyindi; Wamala	None
2L	18,700,000	18,800,000	1 / 5	3 / 4	Nsadzi	Kaazi; Kiyindi; Wamala	None
2L	33,600,000	33,700,000	1 / 5	3 / 4	Bugala (I)	Buwama; Kaazi; Kiyindi	Angola [ <i>coluzzii</i> ]
2L	34,400,000	34,500,000	1 / 5	3 / 4	Sserinya	Buwama; Kaazi; Wamala	None

3R	28,500,000	28,700,000	1 / 5	4 / 4	Sserinya	Buwama; Kaazi; Kiyindi; Wamala	Burkina Faso [ <i>coluzzii</i> ], Burkina Faso [ <i>gambiae</i> ], Cameroon [ <i>gambiae</i> ], Gabon [ <i>gambiae</i> ], Guinea [ <i>gambiae</i> ], Uganda [ <i>gambiae</i> ]
3R	36,500,000	36,900,000	0 / 5	3 / 4	Nsadzi	Buwama; Kiyindi; Wamala	None
3R	43,000,000	43,100,000	0 / 5	3 / 4	None	Buwama; Kiyindi; Wamala	None
3R	43,700,000	44,100,000	0 / 5	3 / 4	Nsadzi	Buwama; Kiyindi; Wamala	Angola [ <i>coluzzii</i> ], Burkina Faso [ <i>gambiae</i> ], Guinea [ <i>gambiae</i> ], Uganda [ <i>gambiae</i> ]
3R	48,800,000	48,900,000	0 / 5	3 / 4	None	Buwama; Kiyindi; Wamala	None
3R	50,000,000	50,100,000	1 / 5	3 / 4	Sserinya	Kaazi; Kiyindi; Wamala	None
3L	7,000,000	7,100,000	1 / 5	4 / 4	Sserinya	Buwama; Kaazi; Kiyindi; Wamala	None
3L	11,500,000	11,600,000	1 / 5	3 / 4	Sserinya	Buwama; Kiyindi; Wamala	Burkina Faso [ <i>coluzzii</i> ]
3L	12,200,000	12,300,000	0 / 5	3 / 4	None	Kaazi; Kiyindi; Wamala	None
3L	13,400,000	13,500,000	0 / 5	3 / 4	None	Kaazi; Kiyindi; Wamala	None
3L	16,300,000	16,400,000	1 / 5	3 / 4	Sserinya	Buwama; Kiyindi; Wamala	Uganda [ <i>gambiae</i> ]

Table S9: Signatures of selective sweeps on known insecticide genes by site based on H12 statistic.

Chr.	Location	Insecticide Gene	Island Sites with Putative Sweep	Mainland Sites with Putative Sweep	Outlier		Ag1000G Populations with Putative Sweep	
					Island Localities	Mainland Localities		
2R	28,497,407	Cyp6p	5 / 5	4 / 4	Banda; (I); Nsadzi; Sserinya	Bugala; Bukasa; Kiyindi; Wamala	Buwama; Kaazi; Kiyindi; Wamala	Angola [ <i>coluzzii</i> ], Burkina Faso [ <i>coluzzii</i> ], Burkina Faso [ <i>gambiae</i> ], Cameroon [ <i>gambiae</i> ], Guinea [ <i>gambiae</i> ], Uganda [ <i>gambiae</i> ]
3R	28,598,038	Gste	1 / 5	4 / 4	Sserinya		Buwama; Kaazi; Kiyindi; Wamala	Burkina Faso [ <i>coluzzii</i> ], Burkina Faso [ <i>gambiae</i> ], Cameroon [ <i>gambiae</i> ], Gabon [ <i>gambiae</i> ], Guinea [ <i>gambiae</i> ], Uganda [ <i>gambiae</i> ]
X	15,241,718	Cyp9k1	3 / 5	4 / 4	Banda; Sserinya	Bukasa;	Buwama; Kaazi; Kiyindi; Wamala	Burkina Faso [ <i>coluzzii</i> ], Burkina Faso [ <i>gambiae</i> ], Gabon [ <i>gambiae</i> ], Guinea [ <i>gambiae</i> ]

Table S10: Software and versions used for major parts of analysis.

Software	Version	Citation
ea-utils	-	[64]
BWA	0.7.16a	[67]
GATK	3.8	[68]
PLINK	1.90b4.6	[69, 70]
SHAPEIT2	2.837	[71]
SAMtools/BCFtools	1.5	[72, 90]
ADMIXTURE	1.3.0	[20]
CLUMPAK	-	[73]
VCFtools	0.1.15	[86]
$\delta a\delta i$ (python package)	1.7.0	[82, 83]
Stairway plot - Jpopgen	2-beta	[21]
selscan	1.2.0a	[87]
adegenet (R package)	2.1.0	[91]
ape (R package)	5.0	[92]
RColorBrewer (R package)	1.1-2	[93]
dendextend (R package)	1.6.0	[94]
rehh (R package)	2.0.2	[95]
eigensoft	7.2.1	[75, 76]
GNU parallel	20170422	[96]
tabix	1.5	[90]
bedtools	2.26.0	[97]



Table S11: Genomic coordinates of heterochromatic and inverted regions.

Chromosome arm	Start	End	Information
2L	20,524,058	42,165,532	2La inversion [66]
2R	18,575,300	26,767,588	2Rb inversion [66]
2L	1	2,431,617	Heterochromatic region [66]
2L	5,078,962	5,788,875	Heterochromatic region [66]
2R	58,984,778	61,545,105	Heterochromatic region [66]
3L	1	1,815,119	Heterochromatic region [66]
3L	4,264,713	5,031,692	Heterochromatic region [66]
3R	38,988,757	41,860,198	Heterochromatic region [66]
3R	52,161,877	53,200,684	Heterochromatic region [66]
X	20,009,764	24,393,108	Heterochromatic region [66]

## Figures

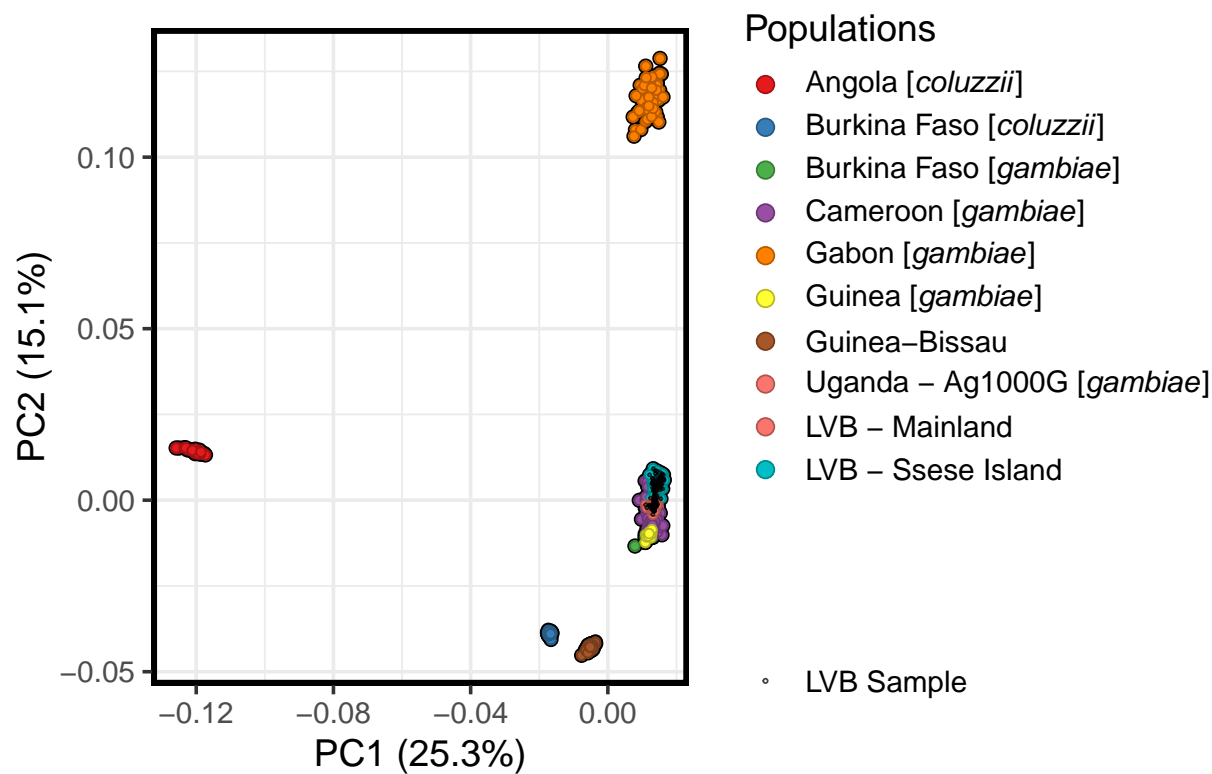


Figure S1: PCA plot of study individuals and *A. gambiae* and *A. coluzzii* individuals from reference Ag1000G populations, showing the first and second components. Kenyan population is not included, and analysis is based on chromosome 3.

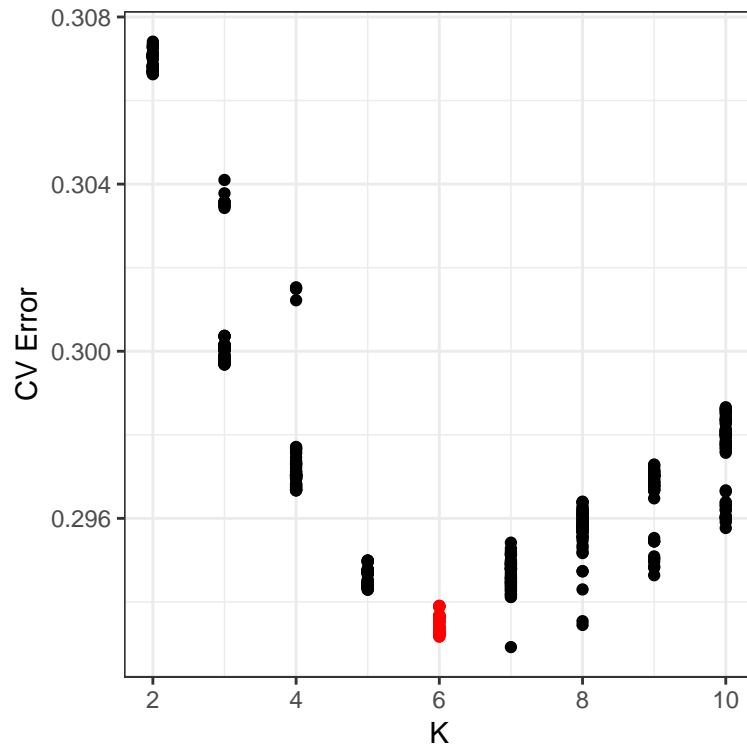


Figure S2: ADMIXTURE cross-validation error.

Cross-validation error for range of  $k$  values for ADMIXTURE analysis of Lake Victoria Basin individuals and *A. gambiae* and *A. coluzzii* Ag1000G reference populations.

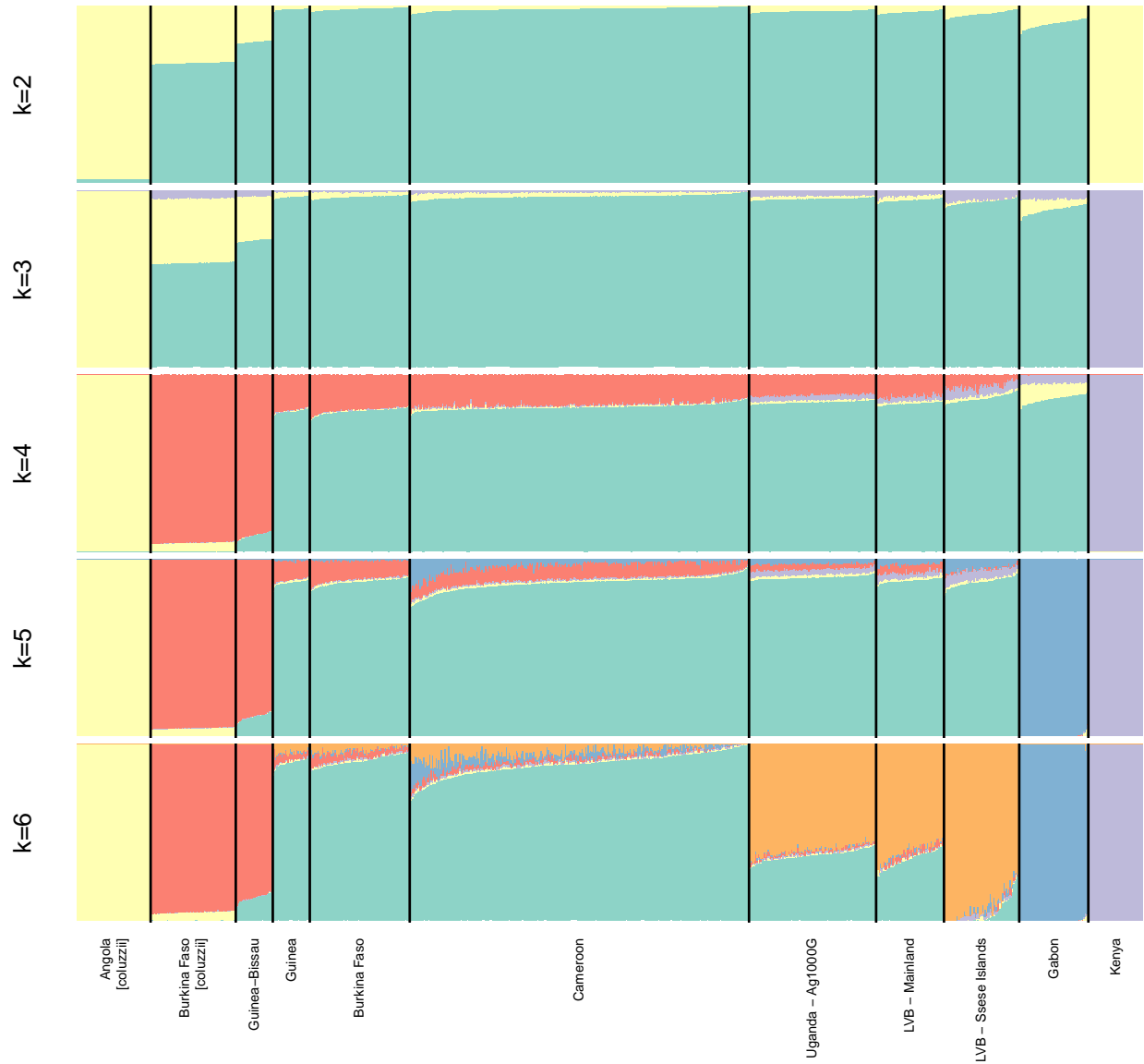


Figure S3: (Caption on next page.)

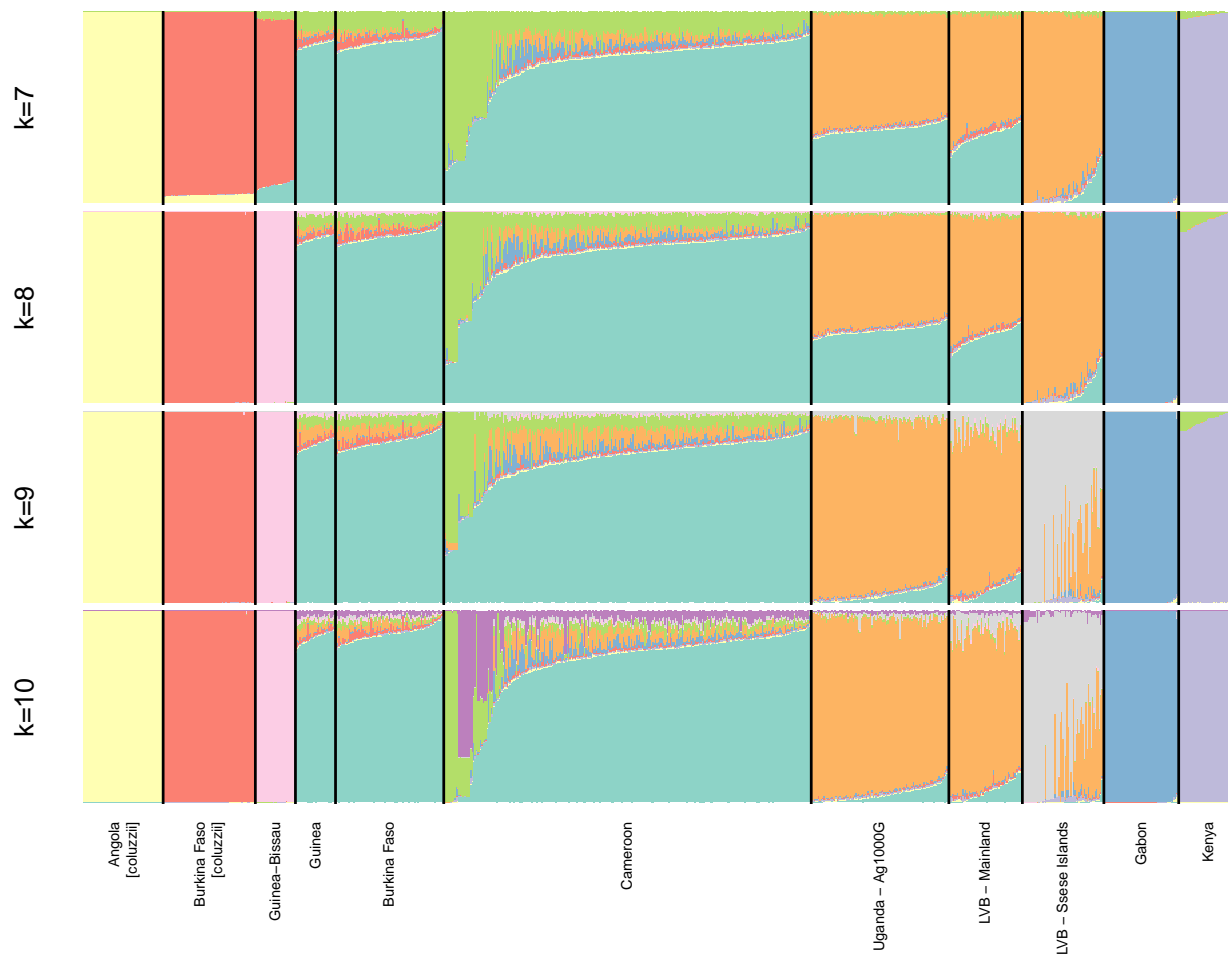


Figure S3: ADMIXTURE-inferred ancestry.

Ancestry of individuals in Lake Victoria Basin and of Ag1000G reference populations as inferred by ADMIXTURE clustering method. Samples are *A. gambiae* unless noted, and analysis is based on chromosome 3. Using  $k = 6$  clusters minimizes cross validation error (Fig. S2).

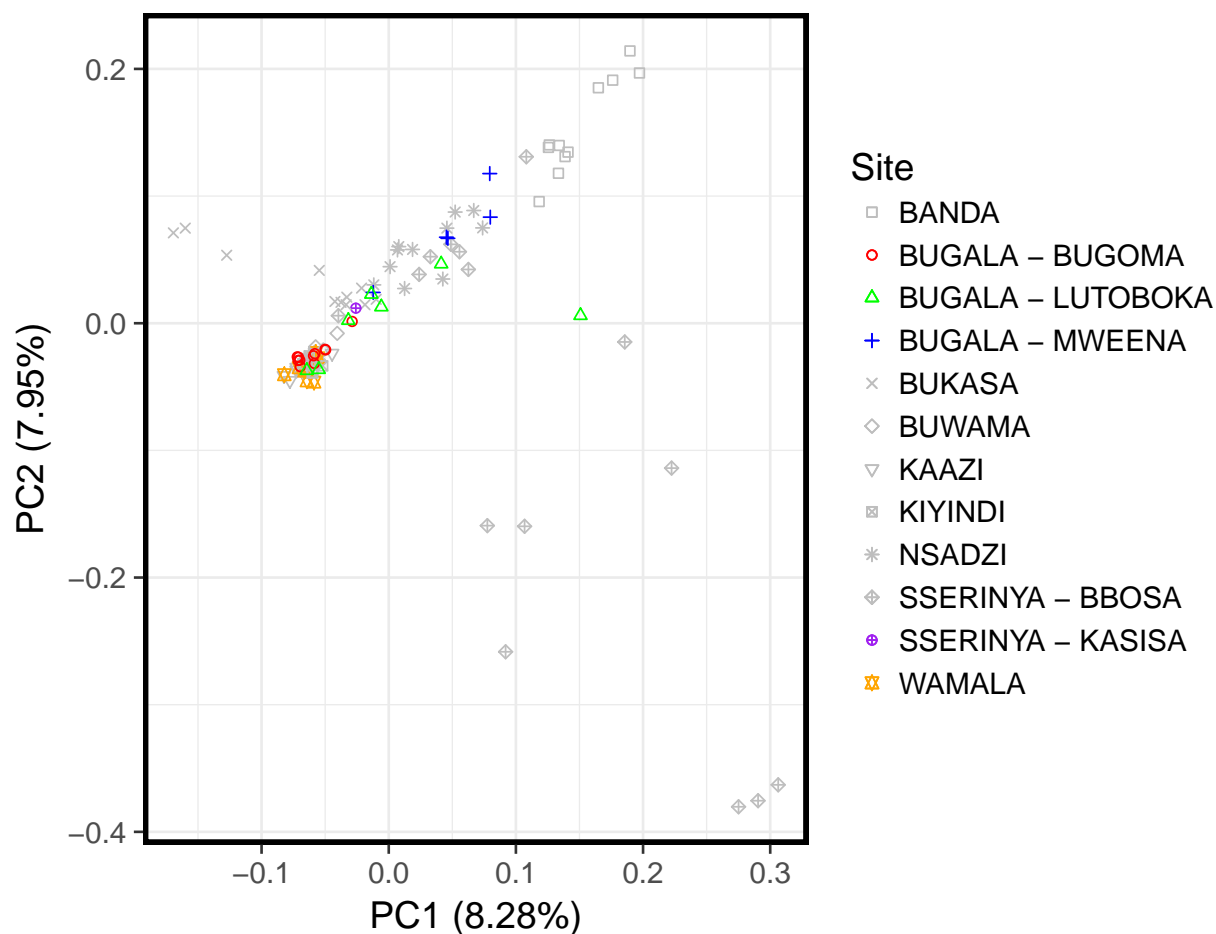


Figure S4: PCA showing Bugala subdivision.

PCA colored by sampling locations. Based on this analysis, individuals from Bugala were split into mainland- and island-like subpopulations. Samples from Sserinya Island, though sampled from two localities, were not split.

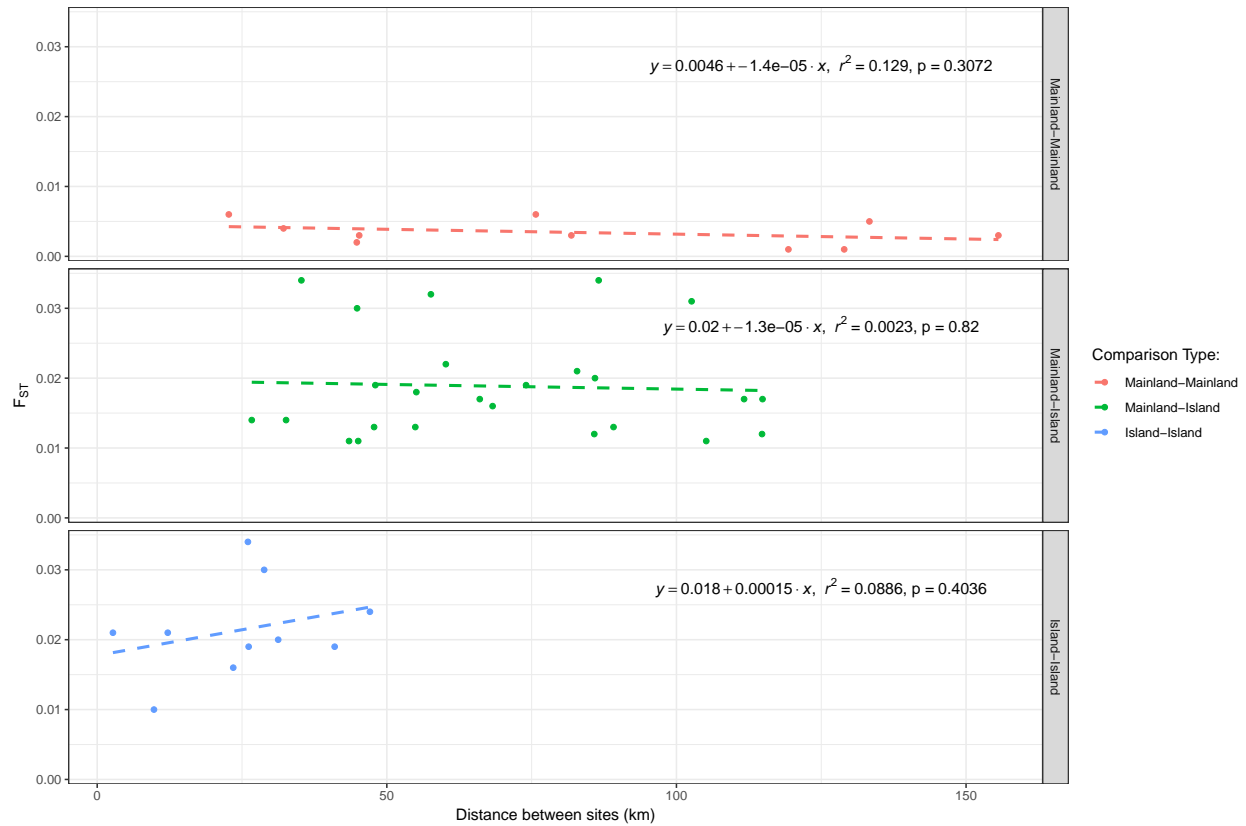


Figure S5: Correlations between genetic distance ( $F_{ST}$ ) and geographic distance between localities. The  $p$ -values are for the test that the slope is significantly different from zero.

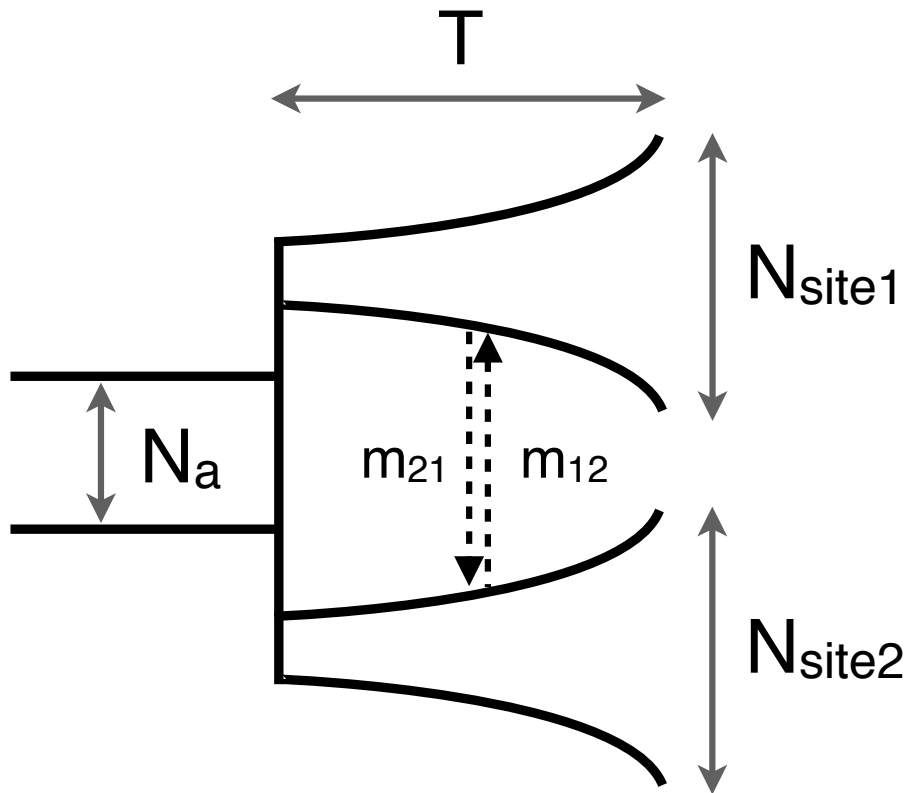


Figure S6: IM model schematics.

Schematic of model fit to data with  $\delta a \delta i$  for population history inference between all pairs of sampled sites using IM model.



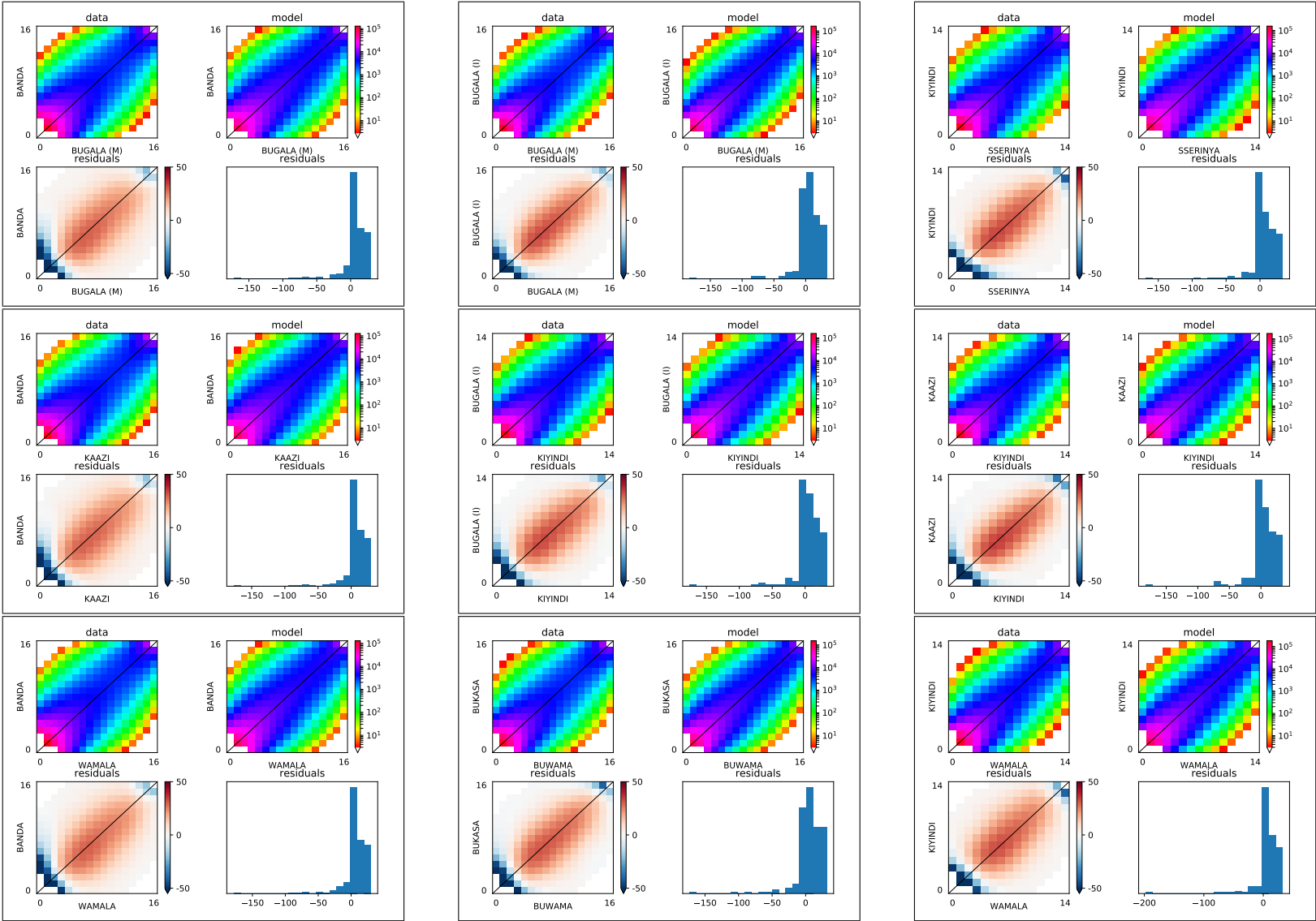
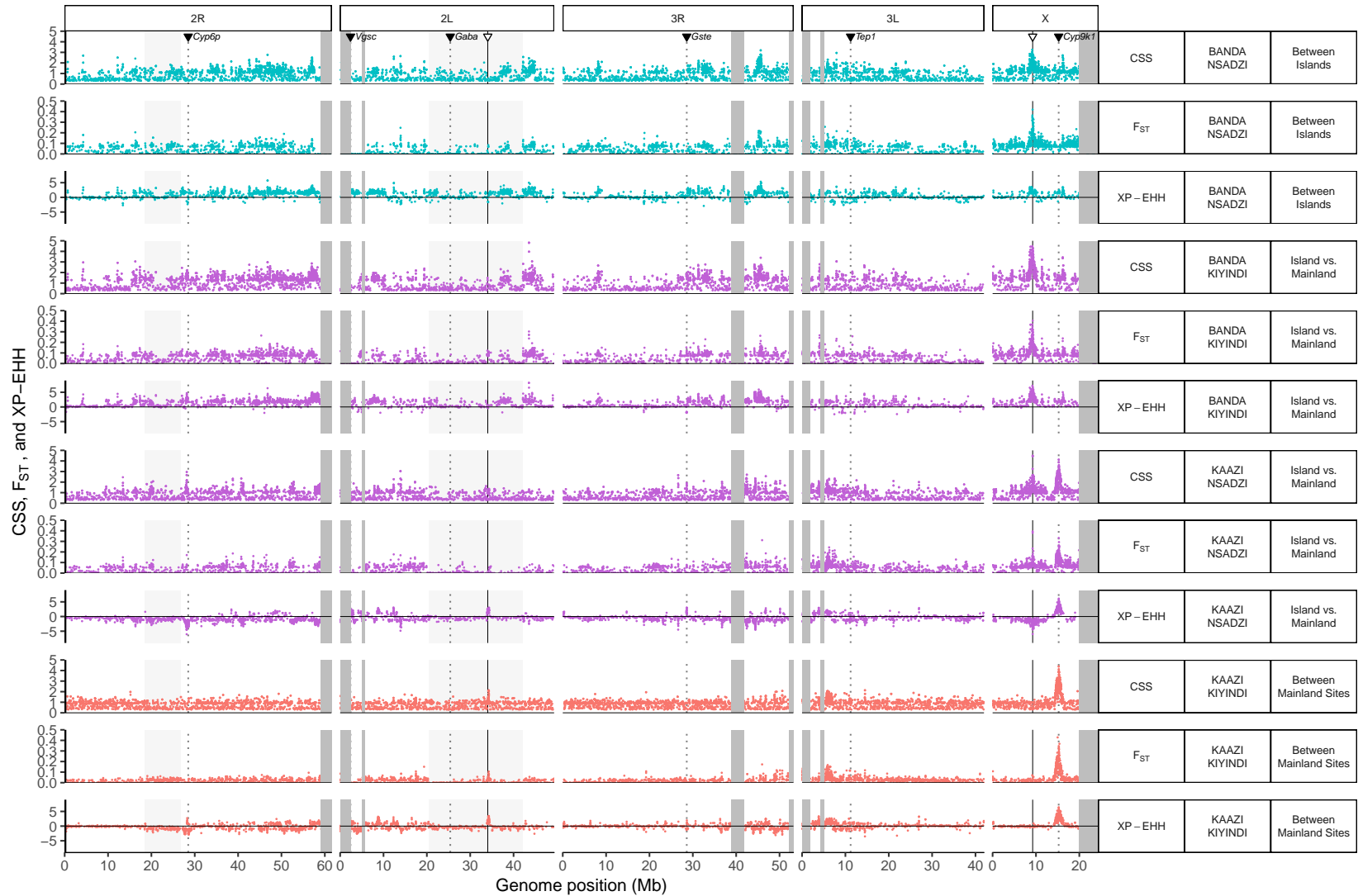


Figure S7: (Caption on next page.)

Figure S7: Two population  $\delta a \delta i$  optimization results.

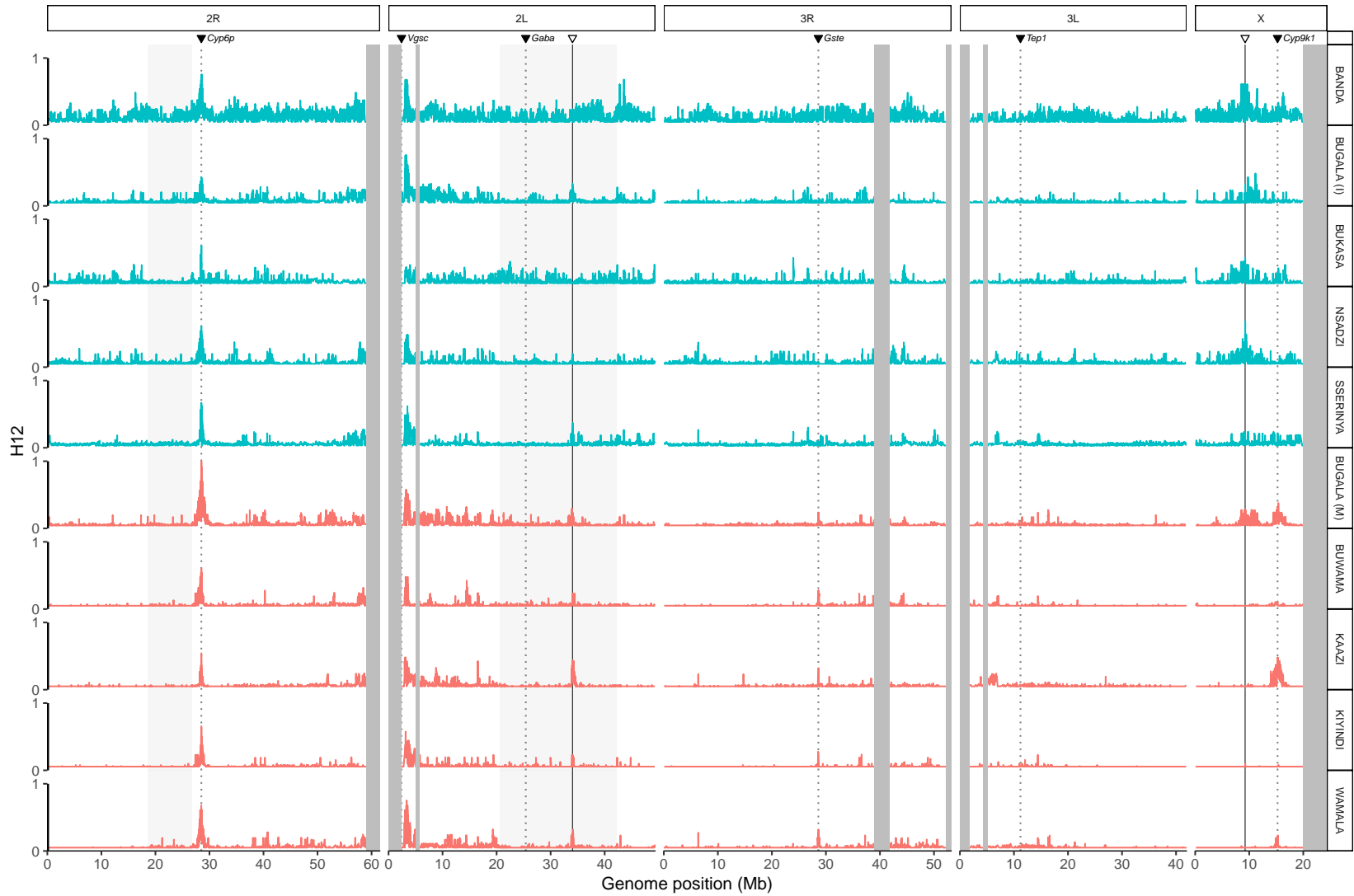
Comparison between best fitting model and data frequency spectra for two population  $\delta a \delta i$  inference. Of the pairwise comparisons for which the best model included migration, a randomly selected set of nine are shown here. Two-dimensional frequency spectra are plotted as logarithmic colormaps for the data (upper left) and model (upper right), and the bottom row plots show the residuals between model and data. Positive residuals in red indicate the model predicts too many SNPs in that entry while negative residuals in blue indicate the model predicts too few.



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Figure S8:  $F_{ST}$ , XP-EHH, and Composite Selection Score (CSS) across genome.

$F_{ST}$ , XP-EHH, and CSS averaged in windows of size 10 kb plotted across genome for pairwise comparisons of island and mainland localities. Shaded regions indicate inversions or heterochromatic regions (excluded from analysis) and dotted lines indicate known insecticide genes while solid lines indicate the two putative sweeps identified in the present study. Only several exemplar pairs of populations shown.



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Figure S9: H12 across genome.

Values of H12, a measure of haplotype homozygosity, plotted across genome. Shaded regions indicate inversions or heterochromatic regions (excluded from analysis) and dotted lines indicate known insecticide genes while solid lines indicate the two putative sweeps identified in the present study.

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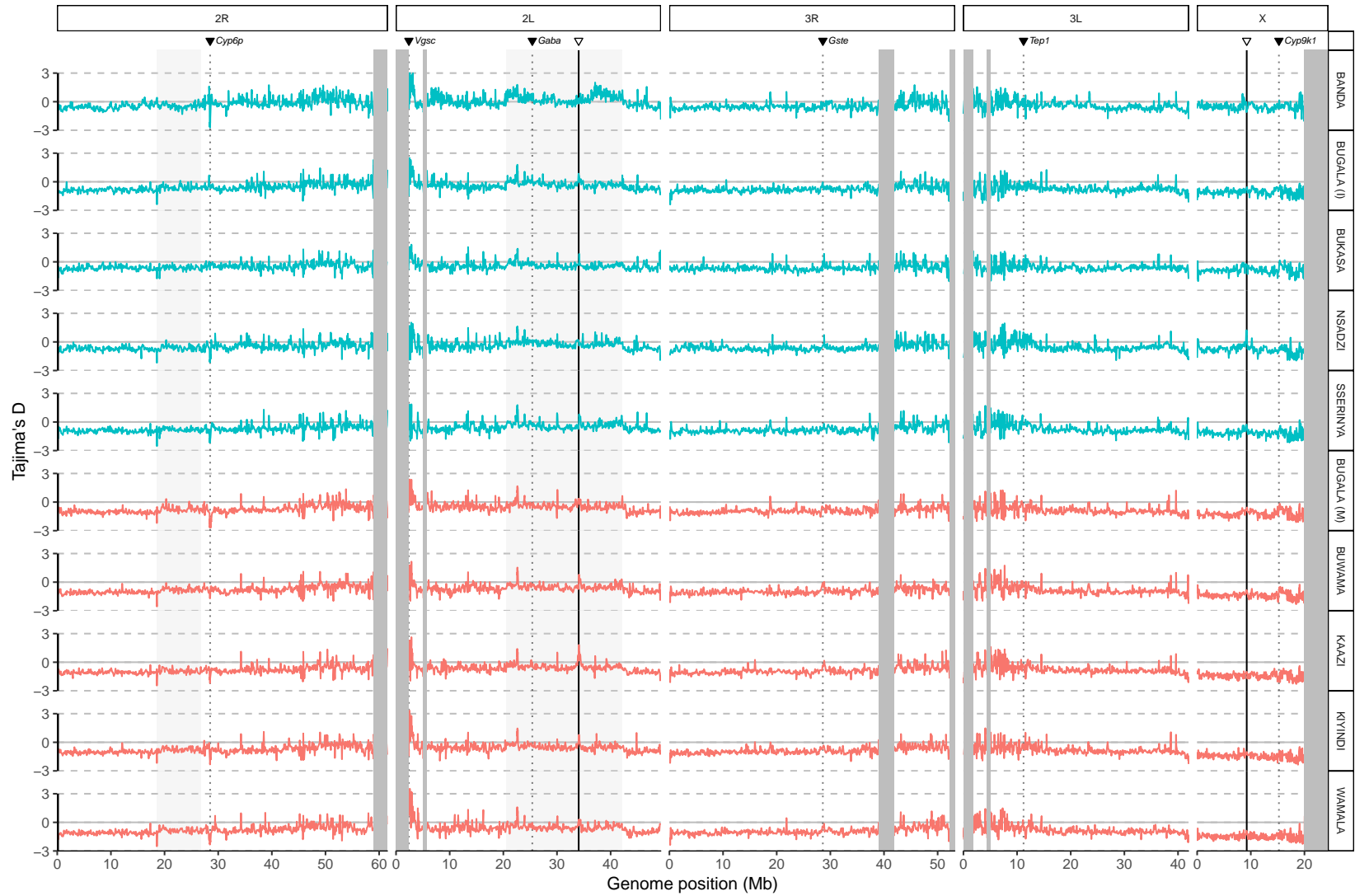


Figure S10: Tajima's  $D$  across genome.

Tajima's  $D$  plotted across genome. Shaded regions indicate inversions or heterochromatic regions (excluded from analysis) and dotted lines indicate known insecticide genes while solid lines indicate the two putative sweeps identified in the present study.

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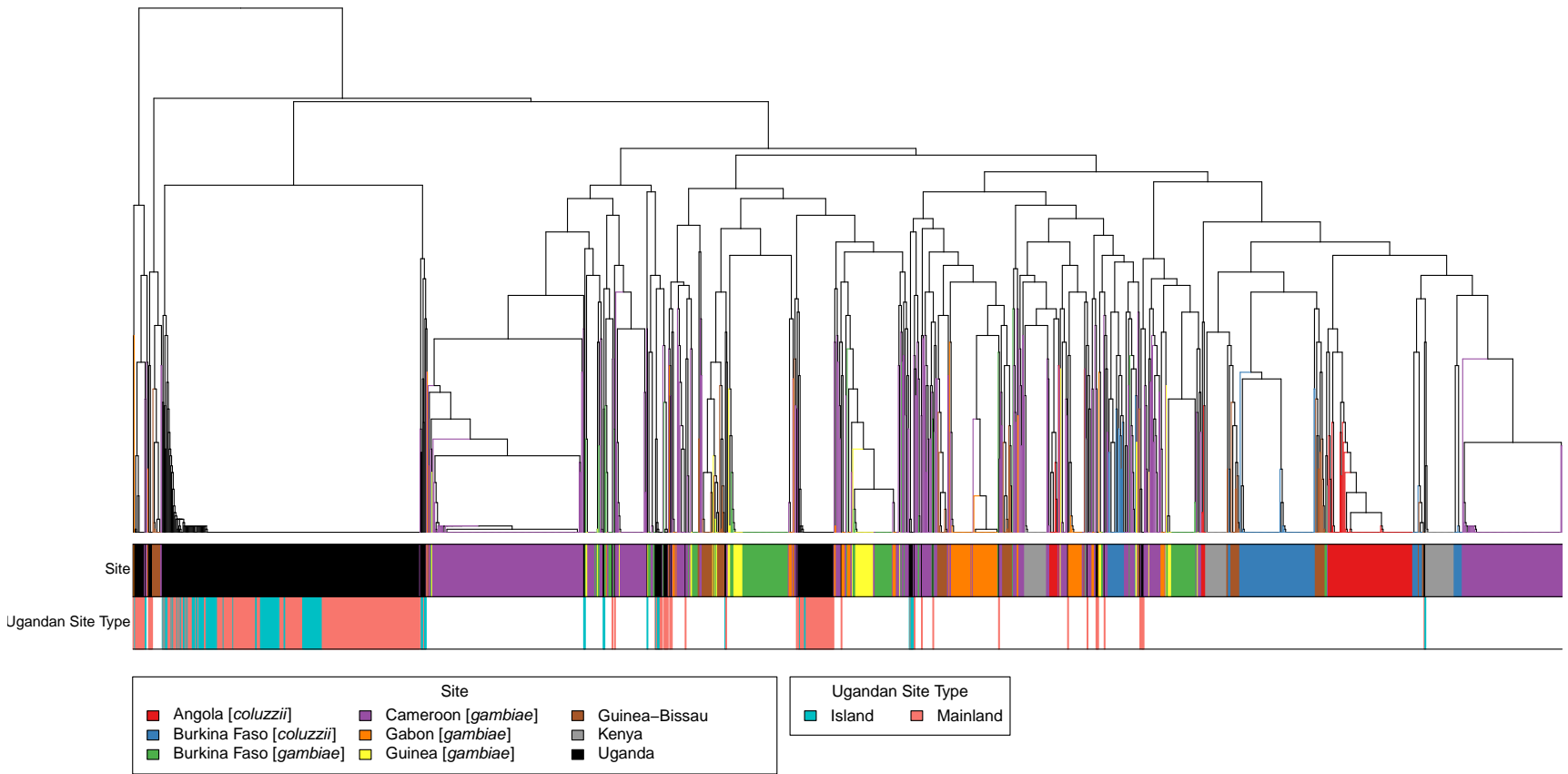


Figure S11: Tree for sweep on *Cyp6p* gene cluster on chromosome arm 2R.

Distance-based tree of haplotypes near sweep at *Cyp6p* gene cluster on chromosome arm 2R. Region shown is 10 kb up- and downstream of sweep target, centered at chr2R:28,501,972 (the approximate location of the peaks in pairwise statistics). Top color bar indicates locality, with all Ugandan individuals, from both the Ag1000G reference population and the LVB, in black. The bottom color bar differentiates the Ugandan individuals into mainland (red) and island (blue) individuals.

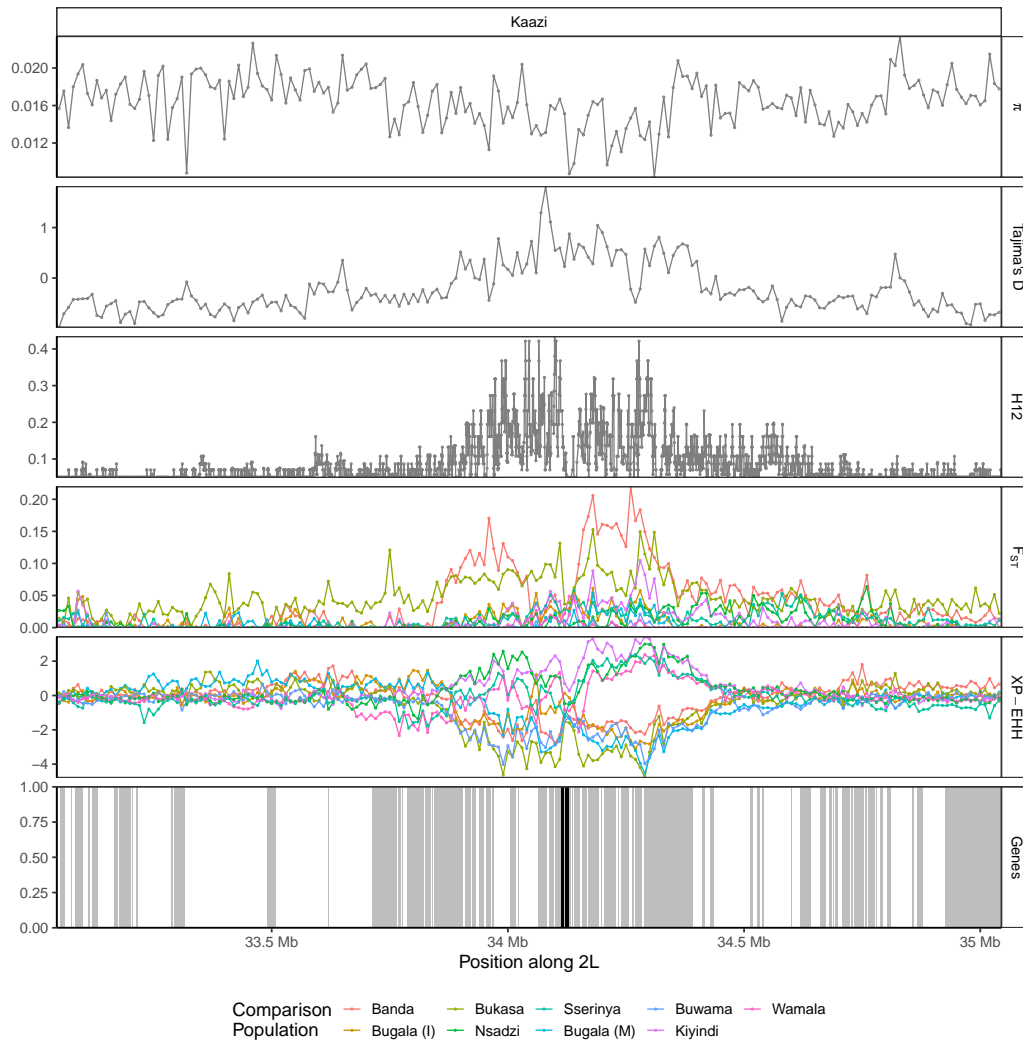


Figure S12: Selective sweep signal on chromosome 2L.

Population genetic statistics plotted near putative sweep on chromosome 2L. Focus population for all pairwise  $F_{ST}$  and XP-EHH comparisons is mainland site Kaazi, chosen to maximize peak height in these statistics. Region shown is 1 Mb up- and downstream of sweep target, centered at chr2L:34,044,820. Several genes involved in chorion formation (AGAP006549, AGAP006550, AGAP006551, AGAP006553, AGAP006554, AGAP006555 and AGAP006556) are highlighted with black vertical lines, while other genes are indicated with grey vertical lines.

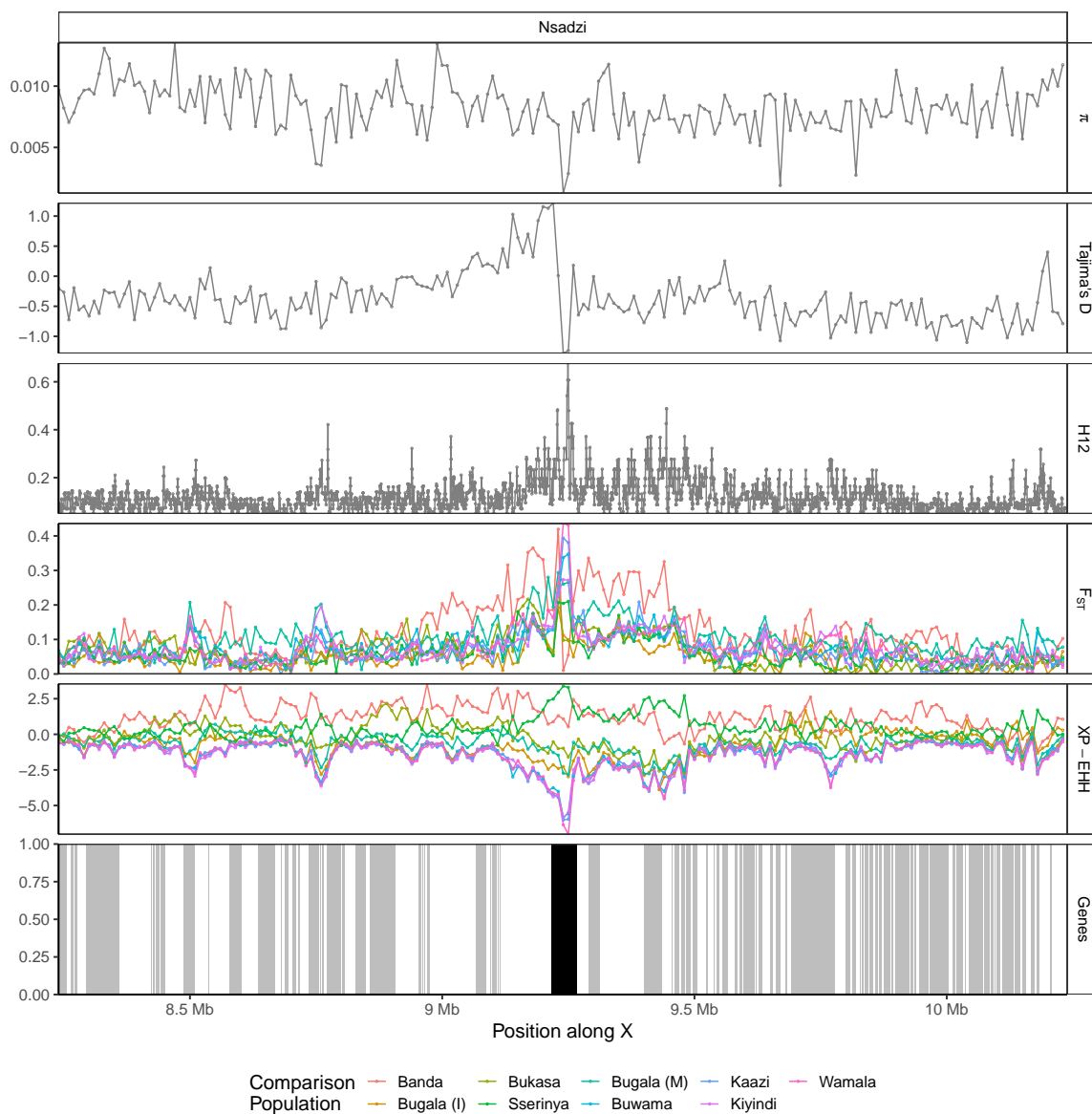


Figure S13: (Caption on next page.)

Figure S13: Selective sweep signal on X-chromosome near *rdgA* ortholog. Population genetic statistics plotted near putative sweep on X-chromosome. Focus population for all pairwise  $F_{ST}$  and XP-EHH comparisons is island site Nsadzi, chosen to maximize peak height in these statistics. Region shown is 1 Mb up- and downstream of sweep target, centered at chrX:9,238,942 (the approximate peak in pairwise statistics). The gene eye-specific diacylglycerol kinase (AGAP000519, chrX:9,215,505-9,266,532) is highlighted with a black vertical line, while other genes are indicated with gray vertical lines.



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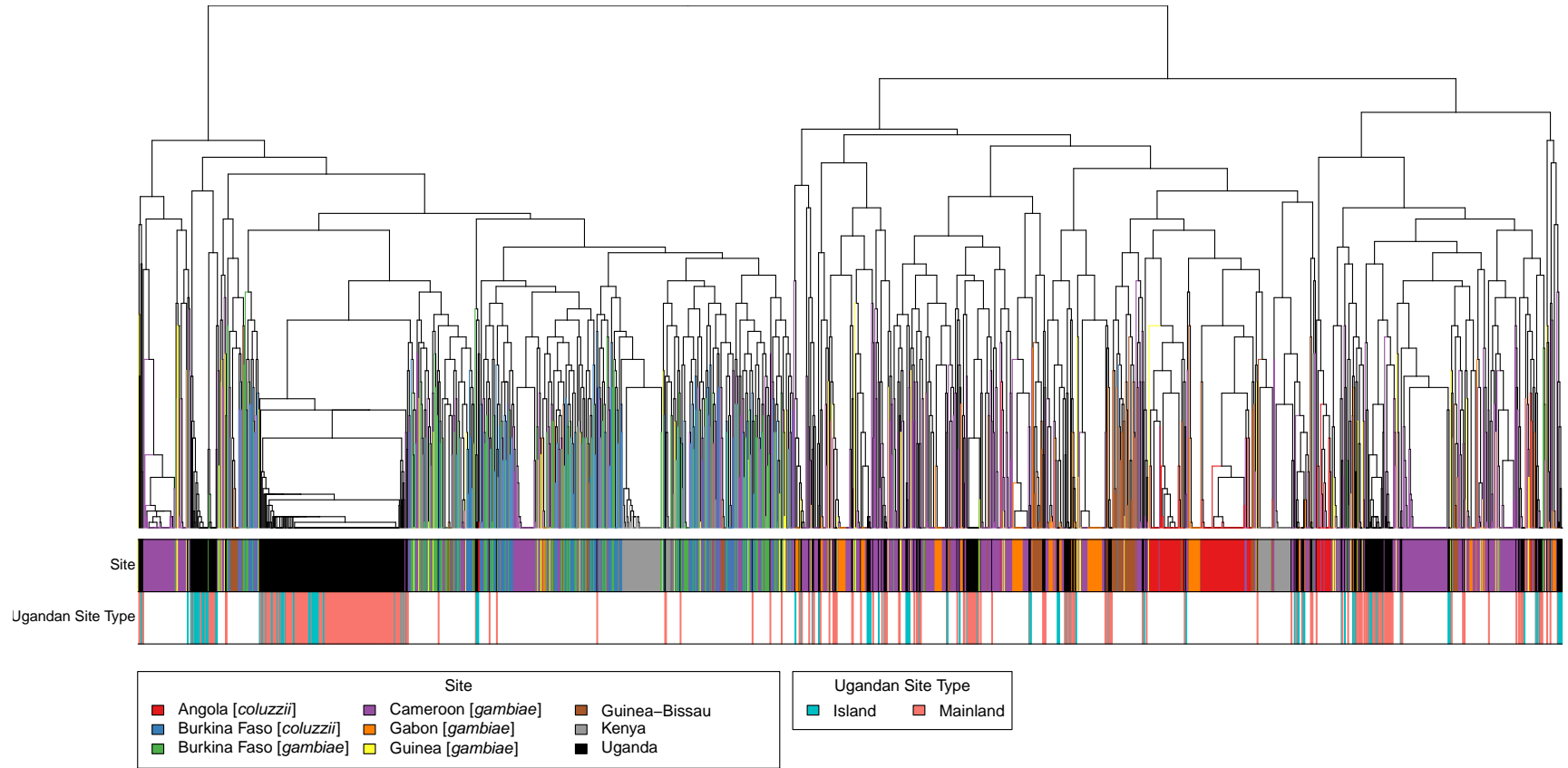


Figure S14: Tree for putative sweep on chromosome 2L.

Distance-based tree of haplotypes near putative sweep on chromosome 2L. Region shown is 10 kb up- and downstream of sweep target, centered at chr2L:34,044,820 (the approximate location of the peaks in pairwise statistics). Top color bar indicates locality, with all Ugandan individuals, from both the Ag1000G reference population and the LVB, in black. The bottom color bar differentiates the Ugandan individuals into mainland (red) and island (blue) individuals.

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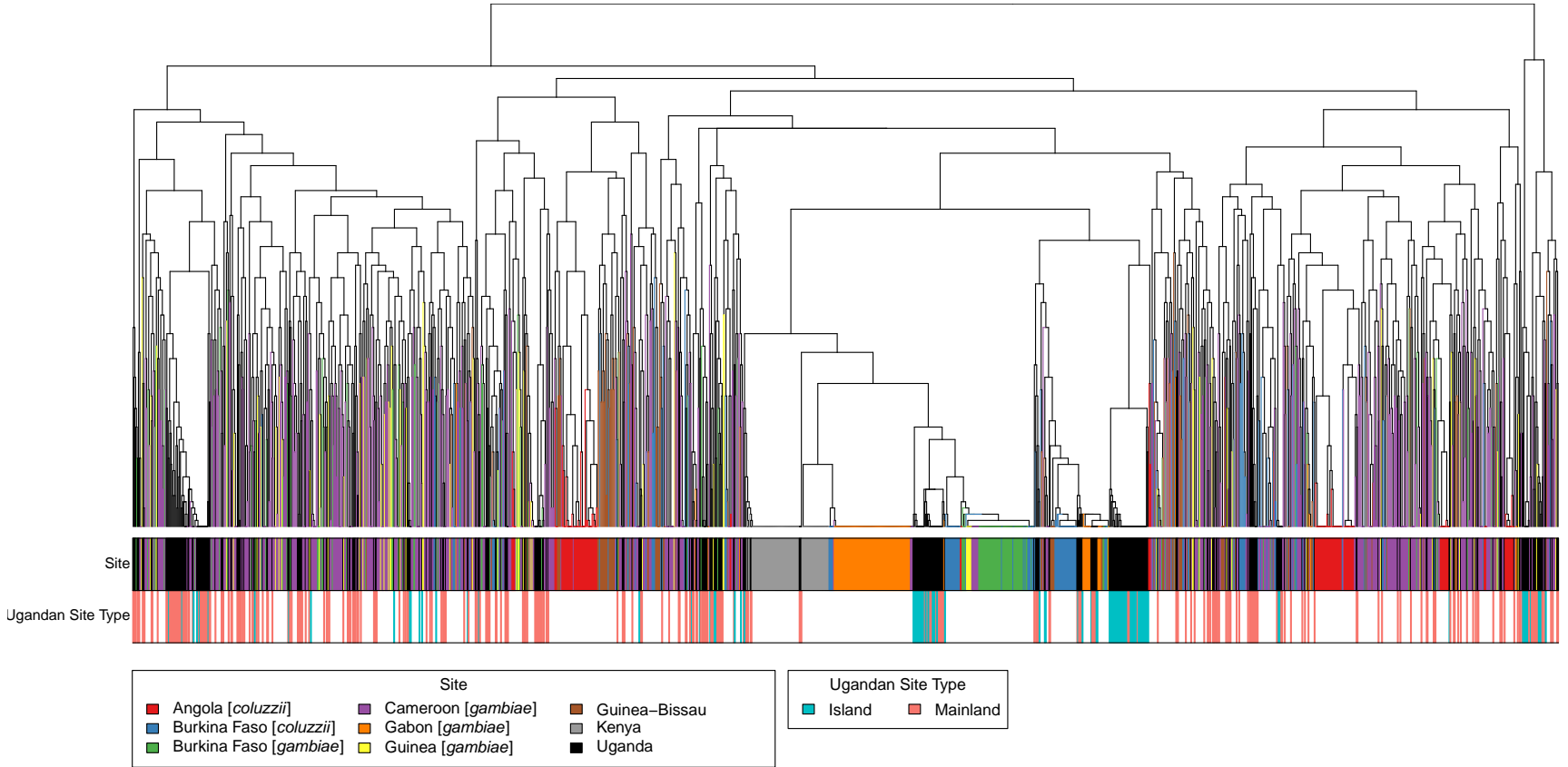


Figure S15: Tree for putative sweep on X-chromosome near *rdgA* ortholog.

Distance-based tree of haplotypes near putative sweep on X-chromosome. Region shown is 10 kb up- and downstream of sweep target, centered at chrX:9,238,942 (the approximate location of the peaks in pairwise statistics). Top color bar indicates locality, with all Ugandan individuals, from both the Ag1000G reference population and the LVB, in black. The bottom color bar differentiates the Ugandan individuals into mainland (red) and island (blue) individuals.