

# Dental Arch Asymmetry in an Isolated Adriatic Community

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**ABSTRACT** Developmental stability reflects the ability of a genotype to develop in the same way under varying environmental conditions. Deviations from developmental stability, arising from disruptive effects of environmental and genetic stresses, can be measured in terms of fluctuating asymmetry, a particularly sensitive indicator of the ability to cope with these stresses during ontogeny. In an inbred Adriatic island population, we expected dental arch fluctuating asymmetry 1) to be higher than in an outbred sample from the same island, and 2) within this population, to increase with the level of inbreeding. Due to environmental stress, we also expected to find higher fluctuating asymmetry in the outbred island population than in an urban reference group from the same country. The material consisted of 506 dental casts of 253 children from 1) the island of Hvar, and 2) Zagreb, Croatia. Three-dimensional coordinates of 26 landmarks spanning the arches were digitized. The analysis partitioned the asymmetry of arch

forms into components for directional and fluctuating bilateral asymmetry, using the appropriate Procrustes method (geometric morphometrics). The results corroborated the hypotheses. Fluctuating asymmetry was found to be higher on the island than in Zagreb in all groups and in both jaws, and increased significantly with endogamy level in the lower jaw. There was no significant directional asymmetry in the Zagreb sample and likewise none in the upper jaws of the outbred island group, but significant directional asymmetry in both jaws of the inbred population and also in the lower jaws of the outbred island group. These results suggest an environmental as well as a genetic influence on dental arch asymmetry. Although the lower jaws expressed these two stresses almost additively, the upper jaws appeared to be better buffered. The role of directional asymmetry as a potential indicator of craniofacial developmental instability clearly merits further attention. *Am J Phys Anthropol* 129:132–142, 2006. © 2005 Wiley-Liss, Inc.

Developmental stability reflects the ability of a genotype to undergo stable development of a phenotype under given environmental conditions; its opposite, developmental instability, is presumed to arise from disruptive effects of environmental and genetic stresses. In bilaterally symmetric traits, some deviations from symmetry measure the inability of an organism to cope with stresses during ontogeny. The asymmetry of a bilateral object is a formal sum of directional asymmetry and fluctuating asymmetry. In the case of directional asymmetry, one side is consistently different from the other in conformation or size. Directional asymmetry implies (but does not demonstrate the presence of) repeatable effects of environment or genotype on asymmetry, and thus conventionally does not qualify for use as a measure of developmental imprecision.

Increased fluctuating asymmetry may occur for various genetic reasons (homozygosity for deleterious recessive alleles, presence of certain dominant mutant alleles, deleterious gene combinations, aneuploidy, or chromosome aberrations) in combination with various stressors in the environment (malnutrition, extreme temperatures, or parasites: Markow, 1994, 1995; Woolf and Markow, 2003). Disruption of the genetic composition of coadapted gene complexes by inbreeding or selection for traits, so that the buffering potential is diminished, may increase the magnitude of developmental instability, resulting in increased fluctuating asymmetry. Many studies show overall fluctu-

ating asymmetry to be higher in homozygotes than in heterozygotes (e.g., Leary et al., 1984; Palmer and Strobeck, 1986; Livshits and Smouse, 1993; Leamy et al., 2002), and some reports in the literature support the hypothesis that developmental instability, resulting in increased fluctuating asymmetry, is associated with inbreeding and homozygosity. Others found no evidence for this relationship (reviewed in Markow, 1995). Patterson and Patton (1990) and Clarke (1993) argued that the foundation of the heterozygosity hypothesis (the demonstration of increased

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fluctuating asymmetry in more homozygous populations; Soulé, 1979; Vrijenhoek and Lerman, 1982) is ambiguous as long as one cannot exclude confounding effects related to the evolutionary history of the population that may independently influence fluctuating asymmetry, such as an undetected breakdown in coadaptation or differences in environmental conditions experienced during the development of individuals. Indeed, Albert and Auffray (2003) proposed within-population studies reporting correlations between individual estimates of heterozygosity. They suggested that these might provide more convincing evidence that the maintenance of developmental stability is dependent on heterozygosity (Biéumont, 1983; Leary et al., 1983, 1984, 1992).

Studies on laboratory mice (Bader, 1965) and in Japanese children (Niswander and Chung, 1965) suggested that an increase in the fluctuating asymmetry of dental dimensions may be related to inbreeding, but neither study showed a clear effect of inbreeding on dental fluctuating asymmetry. In a sample of highly inbred Tristanites, Bailit et al. (1970) found increased fluctuating asymmetry of dental dimensions (compared to the Nasioi of Bougainville, the Kwaio of Malaita, and Bostonian children), but the variation in degree of inbreeding was not found to be related to variation in degree of asymmetry of the dentition. Moreover, the investigated population had low caloric intake and poor medical care, relative to other population groups, circumstances that might both have increased fluctuating asymmetry. Suarez (1974) proposed inbreeding as responsible for increased dental fluctuating asymmetry in Neanderthals, but Doyle and Johnston (1977) suggested that values of dental fluctuating asymmetry similar to those among Neanderthals can be found in modern populations with a low inbreeding coefficient, so that fluctuating asymmetry should be attributed to environmental stress rather than inbreeding. Since then, numerous studies have considered fluctuating dental asymmetry as an indirect measure of genetic and environmental stress in various prehistoric and living human populations (e.g., DiBennardo and Bailit, 1978; Barden, 1980; Harris and Nweeia, 1980; Townsend and Brown, 1980; Ben-David et al., 1992; Hershkovitz et al., 1993).

In contrast to the relatively large number of studies about the influence of inbreeding on the fluctuating asymmetry of dental dimensions, there is little information about the influence of inbreeding on the directional and fluctuating asymmetry of dental arch form per se. Dental arch asymmetry is a common finding in normal (orthodontically untreated) children, and congenital malformations, finger-sucking, extractions, interproximal caries, and other extrinsic factors can increase dental arch asymmetry (Bishara et al., 1994). But during the mixed dentition, environmental factors may account better for asymmetry (Maurice and Kula, 1998; Šlaj et al., 2003), because growth and developmental changes are accelerated after the relatively stable period of the deciduous dentition. Maurice and Kula (1998), quantifying and describing dental arch asymmetry in children, suggested that small values of asymmetry were common and found a high degree of interarch association between the spatial positions of opposing dental landmarks, so that any asymmetry noted in one arch was usually also found in the other. In a study of siblings, Cassidy et al. (1998) showed that the left side of the human dental arch is slightly but systematically larger than the right side. They noted that the degree of asymmetry is significantly more similar within sibships than between them. How-

ever, the genetic control of dental arch asymmetry is far from understood.

The purpose of the present study was to evaluate fluctuating asymmetry of the human dental arch in the reproductively isolated population on the Adriatic island of Hvar. We hypothesized that fluctuating asymmetry in dental arches 1) would be higher in an inbred Adriatic island population than in an outbred sample from the same island, and 2) within this population, would increase with the level of inbreeding.

## MATERIALS AND METHODS

### Studied populations and material

The population of the island of Hvar as well as of other Eastern Adriatic island isolates has been the object of anthropological studies since the early 1970s. Complex ethnohistorical events, migrational patterns, and sociocultural differences (Rudan et al., 1982a,b, 1987; Jovanović, 1996) contribute to a population structure on the island of Hvar that is very suitable for analyses of genetic influences on various anthropometric traits (Rudan et al., 1986). Extensive studies of this island population include basic vocabulary (Sujoldžić, 1997), anthropometric head and body dimensions (Rudan et al., 1986), physiological (cardiorespiratory) properties (Smolej-Narančić et al., 1991; Smolej-Narančić and Rudan, 2001), quantitative and qualitative dermatoglyphic traits of the digito-palmar complex (Rudan and Schmutzer, 1976), metacarpal bone X-rays (Škarić Jurić and Rudan, 1997), analysis of erythrocytic antigens, serum proteins, and erythrocyte enzyme systems (Janićjević et al., 1994), VNTR and STR DNA polymorphisms (Martinović et al., 1998, 1999), mtDNA (Tolk et al., 2000), and Y-chromosome analyses (Barac et al., 2003).

The subdivision of the Hvar population into several villages is an important factor in reproductive isolation and in reducing intrapopulation variation for various biocultural, sociocultural, and anthropometric traits (Šimić and Rudan, 1990). The reproductive isolation, along with the small effective size of the population, results in a limited choice of reproductive partners and subsequent inbreeding (Rudan and Rudan, 2000) and a positive tendency toward isonymous marriages (which in some villages reach a proportion of 40%: Roguljić et al., 1997), thus contributing to the overall deficit of heterozygotes (Rudan and Rudan, 2000). The inbreeding coefficient of 0.0233 in this Hvar island sample is unusually high, even for an isolate population. All this renders the Hvar population suitable for investigating the influence of inbreeding on orofacial and odontometric traits (Lauc et al., 2003). Moreover, outbred individuals living under the same medically underserved circumstances serve as controls for environmental stress on the island.

From this population, we selected a sample, matched for age and sex distribution to the total elementary school population of the island, covering 20% of the total: 222 children aged 7–15 years (98 girls and 124 boys), with early mixed to complete permanent dentition. Upper and lower alginate impressions were taken and poured into dental stone. T.L. took all casts and recorded all data in May 1999. As reference sample, we used 31 Zagreb children aged 8–16 years (14 girls and 17 boys). The reference sample was matched to the Hvar sample for distribution of dentition (Lauc et al., 2000) and occlusal traits (overbite, overjet, buccal segment relationships, posterior crossbite, and medial diastema: Lauc, 2003).

## Endogamy assessment

The degree of inbreeding in offspring of consanguineous unions can be measured by the “inbreeding coefficient”  $F$ , the proportion of an autosomal genome that is expected to be homozygous through inheritance of identical genes from common ancestors (i.e., proportion of alleles identical by descent (IBD) or autozygosity). Several previous studies in the Hvar island population showed that grandparental endogamy is a very reliable indicator of inbreeding in small villages, as most (if not all) pairs of individuals will eventually be related at some point in their ancestry (Rudan and Rudan, 2000; Smolej-Narančić and Rudan, 2001). This conclusion is supported by the observation of an endogamy level of 75.5% during the 19th century (Jovanović et al., 1984), while the fraction of newcomers to the island among parents of the current population amounts to about 2%. Complete endogamy in these populations will be related to a greater expected coefficient of inbreeding in the individuals of our sample, and will (at least in some instances) potentially discriminate inbred from noninbred individuals even better than can the actual genealogical reconstruction, as the latter tends to underestimate the remote component of inbreeding (Broman and Weber, 1999; Shifman and Darvasi, 2001).

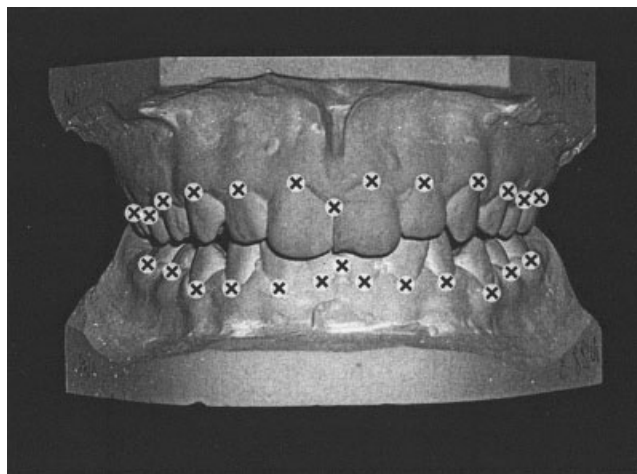
For the endogamy assessment, each child's parents provided a complete two-generation genealogical record, including places of birth and residences of the grandparents. This enabled us to assess the individual's degree of inbreeding according to his/her four grandparents. We divided the sample into three groups: a “highly endogamous” group 1 (at least three grandparents born in the same village) of 73 individuals, a “less endogamous” group 2 (two grandparents born in the same village, the other two from different villages or all grandparents from different villages of the island of Hvar) of 135 individuals, and an outbred group 3 of 14 individuals with one or more grandparents born outside the island of Hvar.

### Landmarks and preprocessing

As the mixed dentition is characterized by attrition (wear and abrasion) of the primary teeth as well as by the growth of secondary teeth, the tops of cusps could not be used as appropriate reference points for a registration of the arches. Instead, we selected 26 nonocclusal landmarks for this study, 13 per jaw: the vestibular, most cervical point of the tooth on the edge of the gingiva for the first six on either side of the midline, together with one point at the top of the medial papilla dentalis (Fig. 1). Missing teeth were noted, and the landmark was taken on the edge of the gingiva at the same position as it would have had with the tooth inserted. Digitization of landmarks was done using a Polhemus Fastrak<sup>®</sup> three-dimensional (3D) digitizer.

### Statistics and basic analyses

We approached this topic through a geometric morphometric (Bookstein, 1991) method. This way, analyses can be based on multiple traits, providing better methods for detecting stress (Leung et al., 2000), and circumventing the confounding of directional with fluctuating asymmetry that usually afflicts these studies. Palmer and Strobeck (2003) recommended that as a rule, traits that exhibit significant directional asymmetry should be excluded from fluctuating asymmetry analyses, because even if directional asymmetry is factored out statistically (Graham



**Fig. 1.** Landmark positions on dental arches. The 24 bilateral points (12 in upper and 12 in lower jaw) were placed on edge of gingiva, vestibularly, at most cervical point of tooth. Two midpoints were located at top of median papilla interdentalis.

et al., 1998), the remaining bilateral variation is likely a complex mix of directional genetic effects, directional environmental effects, and developmental instability. Instead, we quantify directional and fluctuating asymmetry as components of the total asymmetry of the complete landmark configuration under consideration. To do so, we apply the Procrustes asymmetry assessment method from Mardia et al. (2000).

The standard approach to asymmetry in anthropology is based on terms of separate measures on the left and right sides of organisms. These methods are the topic of a good-sized biometric literature (for solid reviews, see Booklage, 1992; Palmer and Strobeck, 2003; for applications to dental asymmetry, see Harris, 1992; Townsend and Farmer, 1998; Townsend et al., 1999). This classic literature begins with lists of measured variables that may or may not pertain to the positions of homologous landmarks. Our Procrustes approach is not an extension of this. Instead, it shares with other tools of geometric morphometrics the general strategy of characterizing the landmark configuration as a whole as a single geometric object. The classic language of fluctuating and directional components of asymmetry of single measures goes over without any biotheoretical change to apply in this quite different algebraic context.

Digitizing the landmarks as 3D coordinates enables us to test object symmetry by interchanging pairs of landmarks and comparing the original configurations with their relabeled reflections. The total sum of squares for squared shape distance between the original configurations and their relabeled reflections expresses what is conventionally identified with total asymmetry. The sum of squares for mean asymmetry, i.e., the squared shape distance between these two group means (original and mirrored data), corresponds to directional asymmetry, and the within-cases sum of squares around this average, which expresses the extent to which the sample fluctuates about its own mean asymmetry, corresponds to fluctuating asymmetry. For details, see the Appendix.

The main procedural steps in this method are as follows: 1) For each single form, a mirrored and appropriately relabeled form is produced. 2) The original forms,

TABLE 1. Transverse dental arch dimensions<sup>1</sup>

	Zagreb (n = 31)		Hvar (n = 222)	
	Mean ± SD (mm)	Median (minimum/maximum)	Mean ± SD (mm)	Median (minimum/maximum)
Upper jaw				
Canine–canine	35.9 ± 1.5	36.1 (32.7/38.9)	36.6 ± 3.2	36.5 (28.3/45.9)
M <sup>1</sup> –M <sup>1</sup>	49.3 ± 2.5	49.4 (42.3/56.1)	49.3 ± 3.6	49.3 (40.2/58.4)
M <sup>2</sup> –M <sup>2</sup>	54.5 ± 2.5	54.3 (49.9/61.1)	54.6 ± 3.6	54.9 (44.6/64.6)
Lower jaw				
Canine–canine	29.3 ± 1.9	29.2 (26.2/33.7)	30.0 ± 2.4	29.9 (2.37/3.72)
M <sub>1</sub> –M <sub>1</sub>	45.3 ± 2.0	45.4 (40.8/49.5)	45.9 ± 3.2	46.2 (36.3/54.0)
M <sub>2</sub> –M <sub>2</sub>	52.2 ± 2.6	51.8 (44.7/56.5)	52.5 ± 3.0	52.6 (43.4/61.7)

<sup>1</sup> Linear distances between selected antimeres. See Figure 1 for landmark positions.

together with their mirrored counterparts, are projected into shape space using a GLS Procrustes superimposition (Rohlf and Slice, 1990). 3) The vector of shape difference between each shape and its relabeled reflection is a measure of asymmetry; the sample average of these vectors is an estimate of directional asymmetry. 4) The total sum of squares of these individual vector differences is decomposed into two components, one for directional and the other for fluctuating asymmetry. In our analysis, we tested for significant directional asymmetry within several subgroups of the sample. Values of fluctuating asymmetry, averaged over subgroup, were compared between subgroups by F-tests and permutation tests (Good, 2000). Comparisons were made for upper and lower arches separately.

As Palmer and Strobeck (2003) noted, measurement error poses a serious challenge for fluctuating asymmetry analyses. We assessed measurement error by digitizing 10 randomly selected casts 10 times. The variances in fluctuating asymmetry of these sets of measurements were compared to the fluctuating asymmetry variances within the different groups under study and also to the smallest difference in fluctuating asymmetry variance between these groups. In all cases, we observed the within-group or between-group variance to be at least eight times the variance due to measurement error.

## RESULTS

Basic descriptive statistics for transverse measurements in both arches are presented in Table 1. None of these linear dimensions differ significantly (by *t*-test) between Zagreb and the island.

### Empirical shape and size distribution

Although age, sex, and dentition status were controlled in the selection of our reference sample, we still need to verify that jaw size does not differ among our groups. As size measurement we use centroid size, the square root of the sum of squared distances of the landmarks from the center-of-mass of all landmarks (Bookstein, 1991). Mean centroid size of the upper jaws in Zagreb is 786 (SD = 46, n = 31), and in Hvar, 781 (SD = 54, n = 222), which do not differ significantly by Student's *t*-test. For the lower Zagreb jaws, the mean centroid size is 695 (SD = 31), and for Hvar, 701 (SD = 35), also not statistically different; within these groups, the lower jaws are (as expected) smaller than the corresponding upper ones. The same is true for the comparison of island subgroups. In both upper and lower jaws, the outbred Hvar group does not differ

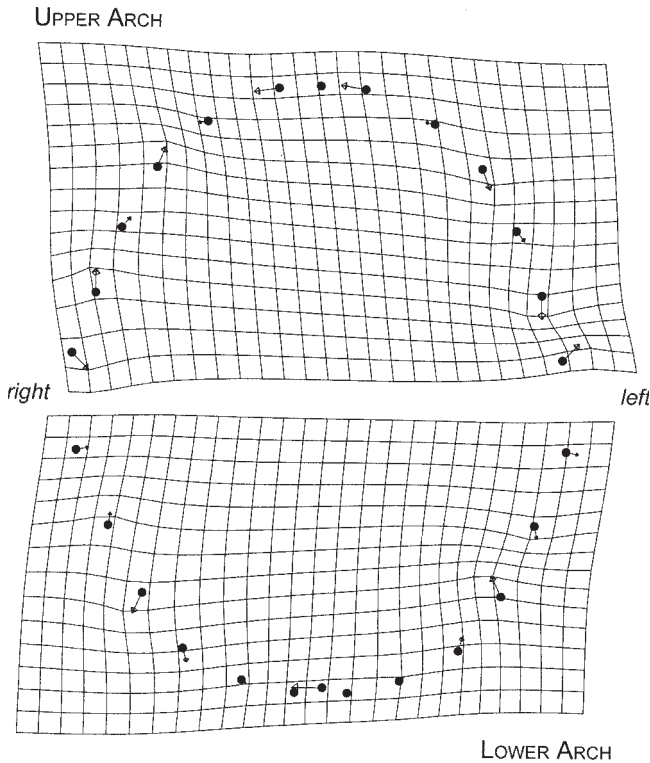
from the high or low endogamy groups in centroid size, and none of these groups differs from the Zagreb sample.

**Relative warps.** A relative warp is an eigenvector of the matrix of variances and covariances of Procrustes shape coordinates. When principal components are computed using covariances in this way, sums of squared differences of scores preserve the underlying original geometry of Procrustes distance. We used this modification of principal component analysis for shape coordinate data in order to check our configurations for factor structures. In the upper as well as in the lower jaws of the Zagreb sample, the first relative warp (RW) explains about 38% of the total variance (the second RW, ~17%; the third RW, ~9%; the fourth RW, ~6%). Those two first relative warp scores correlate largely with age ( $|r| \sim 0.5$ ), and modestly with centroid size ( $|r| \sim 0.15$ ), but *not at all* with total or fluctuating asymmetry. In other words, shape change during growth is not associated with changes in asymmetry. Dental arches from Hvar present a similar situation.

**Sex, age, and asymmetry.** In the Zagreb sample, in both jaws there is no correlation of total asymmetry with individual age, or of fluctuating asymmetry with age. Likewise, there is no connection of total or fluctuating asymmetry with centroid size of the jaw. Also, there is no significant difference between the sexes (by permutation test) in either total or fluctuating asymmetry. Likewise, the Hvar sample does not yield a statistical connection of total or fluctuating asymmetry with age, centroid size of the jaws, or sex. In short, the empirical shape and size distribution are comparable across samples, and the asymmetry measures are independent of age and sex.

### Directional asymmetry

Out of the total variation in the jaws of the Zagreb sample, the sum of squares for directional asymmetry accounts for 5% in the upper arch and for about 2% in the lower arch. These directional asymmetry values are not significant by F-test (Mardia et al., 2000); in other words, the left and right sides of the Zagreb sample do not differ in conformation (Fig. 2). In contrast, the island sample conveys a more complicated picture. Taking the whole Hvar sample together, we find highly significant directional asymmetry for both arches, but in different directions. In the maxilla, it expresses a general distortion from the symmetric mean shape toward the right side, and in the mandible, toward the left side (Fig. 3). In the upper arch, directional asymmetry explains about 5% of the total variance, but in the lower arch, 12%. In the outbred group, significant directional asymmetry is found

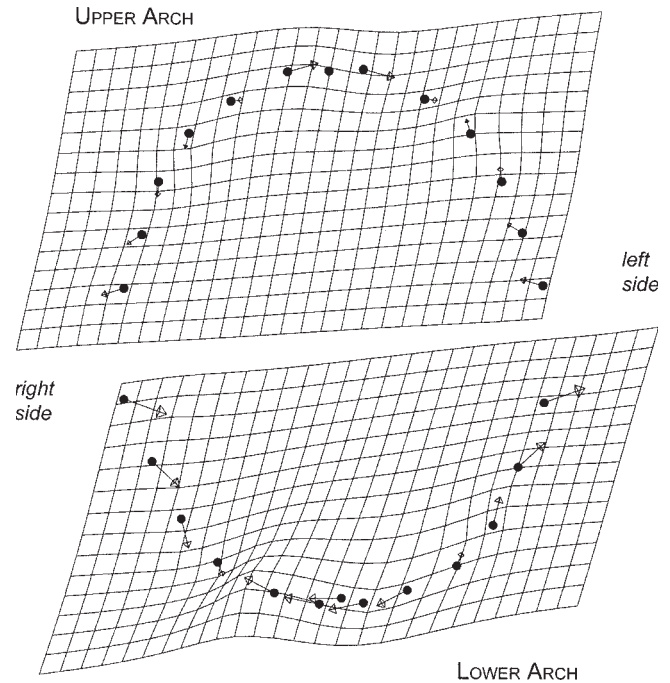


**Fig. 2.** Directional asymmetry in Zagreb sample visualized by thin-plate splines. Occlusal view. Grids show shape change between group means of original configurations and their relabeled reflections, with shape vectors (arrows) indicating specific landmark shifts magnified tenfold. In upper as well as lower jaw, grid is slightly bent toward left side of image (right side), but this is not statistically significant.

only in the lower arch, and not in the upper. The inbred group, however, is significantly directionally asymmetric in both arches, and similarly in both of its subgroups separately.

This is a convenient point at which to pause for a comparison of this way of looking at asymmetry with the conventional approaches (see Appendix). Part of the standard toolkit of geometric morphometrics (e.g., Bookstein, 1991) is the explicit construction of distance-ratios that carry a shape signal unearthed by grid analyses like these. The grid transformations here (Fig. 3) look remarkably like the uniform shears of the dental arch. If we imagine that arch as an ellipse instead of a parabola-like structure, we see that to a shear at the incisors there corresponds a pair of principal directions at  $45^\circ$  to the axis of symmetry: the distances from the midincisor point to the left and right second molars. The ratio of these distances, left over right or right over left, would be the simple shape variable most sensitive to underlying directional asymmetries, and anyone who wished to confirm these findings using conventional distance data could do so by constructing that specific distance ratio and noting that it is significantly greater than unity in one jaw of the Hvar sample, but significantly less than unity in the other jaw in Hvar. Note, too, that the component distances of these ratios are not side-specific measurements, but concern the relation between the separate sides and their joint "midline."

Comparing the directional asymmetry total vector norms (the squared lengths of the vectors of the shape dis-



**Fig. 3.** Directional asymmetry in Hvar sample visualized by thin-plate splines. Occlusal view. Grids visualize shape change between group means of original configurations and their relabeled reflections, with shape vectors (arrows) indicating specific landmark shifts magnified fivefold. Throughout both jaws, grids show general shearing, resulting in significant distortions toward right side of body in upper jaw and toward left in lower jaw at about three times the magnitude.

tances between the group means of the original configurations and their relabeled reflections), we find in the Zagreb sample estimates of 0.011 for the upper arch and of 0.009 for the lower arch, whereas in the Hvar sample, these values are at minimum two times higher: 0.026 for the upper and 0.045 for the lower arch. These numbers are dimensionless (Procrustes) squares.

In sum, in the Hvar sample, directional asymmetry is *significant* and in *different* directions in mandible and maxilla, and is three times greater in the mandible than in the maxilla. In contrast, there is no significant directional asymmetry found in the Zagreb sample anywhere.

### Fluctuating asymmetry

For the fluctuating asymmetry analysis, we calculate (in this Procrustes metric) the extent to which samples fluctuate around their own mean asymmetry by individual differences in asymmetry, specimen by specimen.

**Group comparison.** For both arches, we find significantly smaller variances in the Zagreb sample than in the sample from Hvar ( $P < 0.001$  by F-test as well as by permutation test with 5,000 permutations). Three Hvar values stood out as extreme outliers, substantially past the upper tail of all the other specimens. These subjects were therefore omitted from further analysis. Without these three, the distributions resembled the expected F-distribution shape, i.e., they were now plausibly homogenous within groups. Discarding the outliers from the groups with the higher means actually works against our hypothesis; the procedure is, in fact, conservative.

**Comparisons within Hvar.** In the Hvar sample, we compared the three subgroups: 1) outbred, 2) low endogamy, and 3) high endogamy. Figure 4 confirms that there is less fluctuating asymmetry in the panmictic urban sample than in any subsample from the island. In the upper arch, fluctuating asymmetry variance increases with endogamy, and the difference between the two endogamous groups is significant. In the lower arch, the significance of that difference perseveres; also, fluctuating asymmetry in the outbred group is slightly lower than in the low endogamy group ( $P = 0.07$ ), and significantly lower than in the high endogamy group ( $P < 0.05$ ).

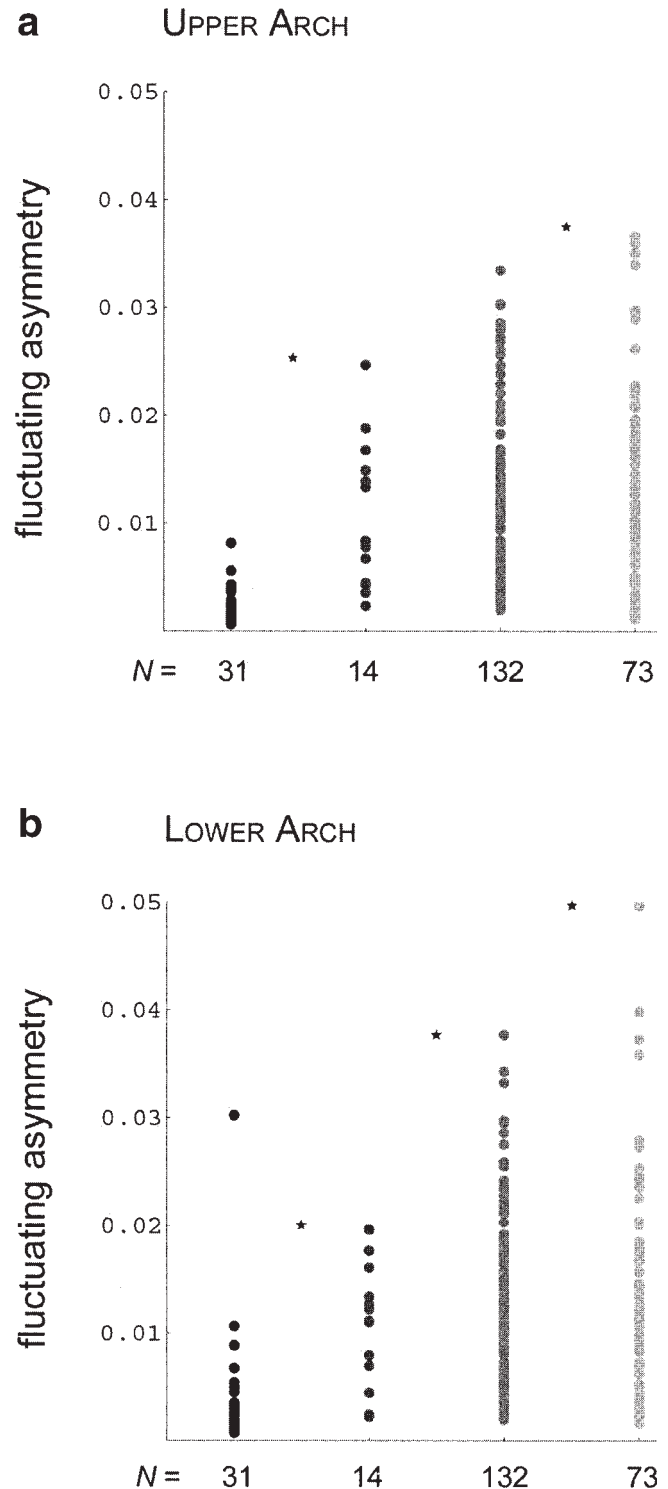
## DISCUSSION

As hypothesized, we found significantly lower fluctuating asymmetry for dental arches in the panmictic reference sample than among the outbred sample or any other sample from the inbred island population of Hvar. There were substantial differences in fluctuating asymmetry among the island population that increased with the level of endogamy. These dissimilarities in arch asymmetry were not limited to fluctuating asymmetry. The endogamous groups are consistently different in conformation of the left and right side in both arches, and the outbred group is significantly directionally asymmetric in the lower arch only, while the reference sample does not exhibit directional asymmetry in either of the arches. In their study of the influence of genetics on dental arch form, Cassidy et al. (1998) also found a systematic but very slight left-right side asymmetry to be the normal case, although here the left side is generally slightly larger than the right. In this sense, we are confident that our sample from Zagreb is a suitable reference, because here the direction of nonsignificant directional asymmetry in both arches is similar, i.e., the majority of opposing (upper and lower) landmarks shift in the same direction, mainly resulting in a shear: the right side shifting mesially, and the left side distally (Fig. 2).

### Fluctuating asymmetry

While increased fluctuating asymmetry in a highly inbred community was already reported for various traits (e.g., Livshits and Kobylansky, 1991), it has not been clear whether the developmental perturbation the individuals manifest is influenced by stressors of the environment, by genetic stressors, or by both; and, if genetic, whether the observed increased fluctuating asymmetry is the result of increased homozygosity in buffering systems or because of the presence of suboptimal recessive alleles specific to that community (perhaps a founder effect), made homozygous by inbreeding (Woolf and Markow, 2003).

The results of the present study contribute to these concerns. Of the four different subgroups we analyzed, three are from the island, and of these, two are known to be inbred. The reference group from Zagreb does not share the environment with the population from the island, but it is comparable to the outbred Hvar group in terms of its presumably very low inbreeding coefficient. Thus, this study design allows an examination of the influence on fluctuating asymmetry of both environmental circumstances (by keeping the breeding factor constant and varying the environment with the two exogamous samples from Hvar and from Zagreb) as well as inbreeding (by keeping the environment (Hvar) constant and varying the extent



**Fig. 4.** Fluctuating asymmetry. Extent to which samples fluctuate around their own mean asymmetry (within-cases sum of squares for asymmetry about their mean) is plotted per dental arch for four groups (Zagreb, solid circles; Hvar outbred, dark gray; Hvar low endogamous, medium gray; Hvar high endogamous, light gray). In both jaws, fluctuating asymmetry is higher on island than in Zagreb, and on island it increases with endogamy level (stars indicating significant differences between respective groups).

of inbreeding). We find both to be significantly connected with fluctuating asymmetry. In the environmental comparison, fluctuating asymmetry turns out to be significantly higher in Hvar than in Zagreb, while in the inbreeding comparison, fluctuating asymmetry is higher in the inbred groups than in the outbred one. Thus, we confirm that detrimental environmental circumstances (namely, little medical care) increase fluctuating asymmetry, and likewise we confirm that inbreeding increases fluctuating asymmetry in the human dental arch. The environmental impact on fluctuating asymmetry seems to exceed the inbreeding effect, inasmuch as we find considerable differences in magnitude of fluctuating asymmetry between the Zagreb and outbred Hvar group in both jaws, but a weaker signal for the “within-Hvar comparisons,” especially in the upper jaw. The latter may be due to a stronger morphological integration of the upper jaw into the craniofacial complex and thus a higher sensitivity to developmental perturbations in the lower jaw. Although this interpretation would be supported by the contention that tooth dimensions along the upper and lower dental arches are largely independently determined (Garn et al., 1968; Kieser et al., 1985), it contradicts the notion that maxillary teeth are less well-buffered than mandibular teeth (Garn et al., 1966; Harris and Nweeia, 1980; Kieser et al., 1986). However, a recent study of mice in a polluted industrial area reported an increase in chromosomal aberrations and lesions as well as in cranial fluctuating asymmetry, specifically in lower jaw dimensions (Veličković, 2004).

An immediate shortcoming in these group comparisons may be the fairly low sample size of the outbred group ( $n = 14$ ) as well as of the reference sample ( $n = 31$ ). The permutation tests and F-tests incorporate considerations of sample size, namely by losing power at smaller sizes. Any effects that either finds are thus not mere artifacts of small samples. Note also that fluctuating asymmetry, as a mean square, is not itself confounded by sample size in any way.

The question of whether fluctuating asymmetry increases because of homozygosity in buffering systems or because of suboptimal recessive alleles specific to that community cannot be answered with this one additional study. Still, Dobzhansky and Lerner’s balance or overdominance hypothesis (discussed in Woolf and Markow, 2003) gains support from our study, as it did from Livshits and Kobylansky (1991).

### Directional asymmetry

In keeping with the “widely held—yet poorly substantiated—belief that fluctuating asymmetry can act as a universal measure of developmental stability and predictor of stress” (Lens et al., 2002), we assumed that fluctuating asymmetry signaled developmental precision. Yet our samples yielded consistent differences in the extent of directionality, depending on environmental and/or genetic stress levels. Although some earlier studies did not find significant directional asymmetry in human isolates, such as Townsend and Brown (1980) in the dentition of Australian Aborigines, or Noss et al. (1983) in Pima Indians, Hershkovitz et al. (1987) in South Sinai Bedouin children did find such asymmetries, and went on to emphasize the importance of directional asymmetry in fluctuating asymmetry studies. And, indeed, Harris (1992) then observed that while some tooth crown diameters exhibited lateral-

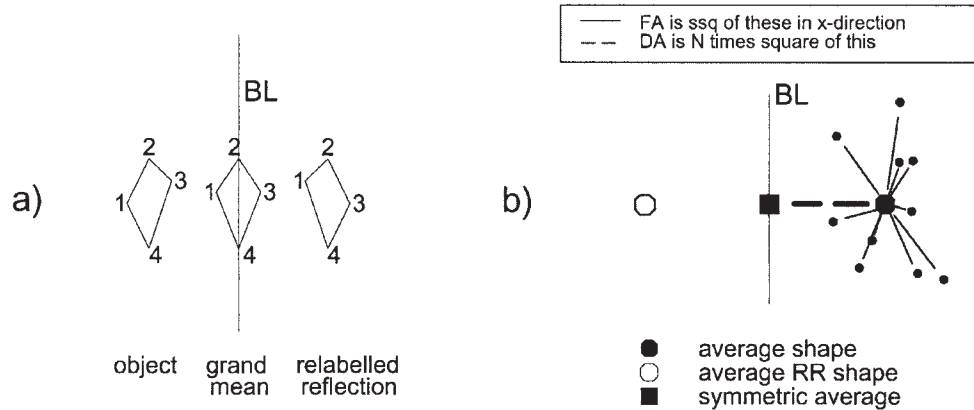
ity within studies, the pattern within and between arches appeared to be random and variable among groups. In his study of the second dentition in several human populations, he noticed the general tendency for teeth in opposite arches to exhibit opposite dominance within a population sample, in that maxillary and mandibular homologues were likely to be complementary, and conjectured that the degree of directional asymmetry was keyed to the individual’s ontogenetic stability, while cautioning about subsuming directional asymmetry within conventional measures of fluctuating asymmetry (Harris, 1992). Townsend and Farmer (1998) and Townsend et al. (1999) confirmed this intriguing reversed pattern of directional asymmetry for the deciduous dentition, but found no relationship between the left-right differences and the direction of skewness, as reported by Harris (1992). The pattern of dental arch shape we found in the mixed dentition complements findings and expectations of these studies, including the conjecture (Harris, 1992) that the *degree* of directional asymmetry may reflect a population’s level of developmental stress, while the specific *direction* may be determined by its genetic background. Along this line, our reference sample was expected to exhibit a very low directional asymmetry in comparison to the island sample, and within the inbred island sample, the arches should have shown identical patterns: right-side dominance in one jaw, paired with left-side dominance in the other. Both of these predictions were corroborated by our results.

Graham et al. (1993) found that fruit flies exposed to 10,000 mg/kg benzene showed a transition from fluctuating asymmetry to directional asymmetry (they became more right-handed for sternopleural bristles), and also suggested that directional asymmetry may be a potential indicator of developmental (in)stability. Leamy (1999) encouraged the use of directional asymmetry in comparisons among variously stressed/nonstressed or outbred/inbred populations, as he found evidence for genetic variation in directional asymmetry rather than fluctuating asymmetry for mandible characters in random-bred mice, but he reported the level of this variation to be so low that he proposed an environmental origin for phenotypic directional asymmetry variation.

In our data, directional asymmetry appears with environmental stress in the lower jaw and is present in both jaws with further inbreeding stress, and fluctuating asymmetry increases with environmental stress in both jaws and with additional inbreeding stress in the lower jaw. These results do not replicate the *transition* from fluctuating asymmetry to directional asymmetry with increasing stress, but rather demonstrate significant directional asymmetry to *co-occur* with it, and therefore support the notion that directional asymmetry itself may be an indicator of stress (Graham et al., 1993). Moreover, the results imply that the lower jaw is more prone to both environmental and also breeding stress than the upper jaw.

Our study suggests a fundamental environmental influence on dental arch asymmetry, as well as, sensitivity to inbreeding. But while the lower jaw indicates these stresses almost cumulatively, the upper jaw appears to be better buffered. The role of directional asymmetry as a potential indicator of developmental instability clearly merits further attention.

Theoretical interpretation of findings like ours must be cautious. We have very carefully operationalized the quantities here that can be operationalized (directional asymmetry, fluctuating asymmetry, and a crude summary coefficient of inbreeding), but we cannot tell from



**Fig. 5.** Fluctuating and directional asymmetry in shape space. **a:** Analysis of four-landmark form with one paired landmark and two unpaired. Shown is a total of three forms (a shape, its RR, and average of two) that might be taken as located at centers of three corresponding little drawings. BL, hyperplane of bilaterally symmetric forms; see text. **b:** Decomposition of total sum of squares for asymmetry. Each small dot stands for one specimen in simulated population of 10. Total sum of squares for asymmetry is sum of squared distances of small dots from plane BL. This sum decomposes into a term for squared distance of their average from BL plus sum of their squared horizontal differences from this average. These terms match usual construals of directional asymmetry and fluctuating asymmetry, respectively, in conventional (scalar-based) approaches.

these data whether the effect of inbreeding on these asymmetry components is via the role of inbreeding as a proxy for stress or by some other mechanism. Algebraically, we pointed to a two-way interaction (jaw by subgroup, as in Figure 4), and although we observed that the directions of contrasts underlying this complex pattern are consistent with (most of) the earlier literature, and also consistent with the interpretation of homozygosity as stress, we did not measure any other aspect of development, and so the interpretation remains just that: an interpretation, not yet an inference.

## APPENDIX

### The Procrustes approach to asymmetry: a graphical introduction

Several reviewers of an earlier draft of this article noted that the Procrustes approach to asymmetry we were exploiting was more familiar to other audiences than to the readership of this Journal. In addition to the mathematical reference by Mardia et al. (2000) that we cite in the main text, there are many earlier appearances in textbooks (Bookstein, 1991) and in primary research publications in mammalogy (e.g., Auffray et al., 1999), entomology (e.g., Smith et al., 1997; Klingenberg and McIntire, 1998; Klingenberg, 2003), and elsewhere. In Schaefer et al. (2002), we recommended this approach for general use in anthropology, and we took our own advice in such applications as Bookstein and Schaefer (2003) and Schaefer et al. (2003). For the convenience of the AJPA reader, we use this Appendix to summarize the basic approach in these earlier publications.

The explanation here, a version of that in Mardia et al. (2000), pertains to the “object symmetry” case, in which landmarks arise as either paired (left-side, right-side) or unpaired (midline) on one single image in two dimensions (2D) or three (3D). There is a fundamental operation in this scheme, which is usually called relabeled reflection (RR). As shown in Figure 5a, the relabeled reflection of a form is produced by reflecting the form in any convenient plane and then switching left and right labels (for paired

points only). We do not have to specify the plane used for the reflection, because all possible reflections have the same shape in the Procrustes analysis to follow. The Procrustes average of any form and its RR form are necessarily a perfectly symmetric form with all midline points actually collinear (or, in 3D, coplanar), and all paired points perfectly symmetrical with respect to that midline. In the usual linear approximation, such forms make up a “plane” (actually, a hyperplane) of bilaterally symmetric forms, BL. (Both Figure 5a and 5b are intended as scenes in shape space, the set of forms standardized for size, position, and orientation—not in the raw data space of, say, a digitizing tablet.) The dimension of BL is  $dn_p + (d - 1)n_u - 1 - d(d - 1)/2$ , where  $d$  is the dimension of the data space (2 or 3), and  $n_p$  and  $n_u$  are the counts of paired and unpaired landmarks. The shape of RR is the reflection in BL of the shape itself, as drawn.

For any sample of forms that include some paired landmarks, the data set that consists of all forms together with all their relabeled reflections necessarily has an exactly symmetric grand Procrustes mean, shown as the solid square in Figure 5b. This average is on BL. The average of actual forms is somewhere off the plane BL, as shown by the solid circle in Figure 5b, and the average of RR forms is the reflection of the solid disk in BL (shown here as open circle). There is a standard identity that applies to any scatter of forms and their reflections in this plane. Write  $X_{\perp i}$  for the vector from any shape  $X_i$  to the nearest point on BL, and  $\bar{X}_{\perp} = \sum_i X_{\perp i} / N$  for the vector from the sample mean shape  $\bar{X}$  to BL. (The foot of this perpendicular will be the symmetric mean shape.) By an ordinary ANOVA-like decomposition of sums of squares, we have

$$\sum \|X_{\perp i}\|^2 = N\|\bar{X}_{\perp}\|^2 + \sum \|X_{\perp i} - \bar{X}_{\perp}\|^2$$

where  $\|\cdot\|$  is Procrustes distance.

The left side is the sum of squared shape distances between all forms and their symmetrizations: a “total sum of squares for asymmetry.” One recognizes the first term on the right as  $N$  times the squared Procrustes distance of the average form from BL, and the second term on the



right as the summed squared Procrustes distances of the separate forms from their average in the direction perpendicular to *BL*, i.e., the sum of squares for asymmetry of the forms around their average asymmetry. These correspond perfectly to the classic notions of fluctuating and directional asymmetry of scalar variables as they have arisen in the literature (e.g., Palmer and Strobeck, 1986, 2003), and so we copied those terms over to this new context. (Note that the ANOVA here is only over subjects, in contrast to the two-way analysis, i.e., side by subjects, in the conventional treatment; see Boklage, 1992).

Mardia et al. (2000) presented two statistical tests for directional asymmetry. One version, a parametric F-test, presumes that asymmetry of landmark locations is distributed independently, with identical variance at all landmarks in all directions of the original image.

In our experience, this assumption is unrealistic in most applications. We recommend instead a permutation test that, in effect, flips a coin *N* times, over and over, to determine which of the paired shapes is the real version and which is the RR version. Because the total sum of squares (left side of the ANOVA above) is not affected by this permutation, the pivotal statistic is just the squared Procrustes distance between mean "pseudoleft" and "pseudoright" shapes. These are the permutation tests reported in the analyses of this paper. The grids depicted of this paper likewise express the geometry: they are warps depicting the effect of a transformation in shape space that is just double the heavy line in Figure 5b, and so allow the viewer to understand just what is asymmetrical about any directional asymmetry that is detected.

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