Week 4: Evolution of genomic architecture

Paper 1 – Chromosome inversions, Local adaptation and speciation. Kirkpatrick and Barton 2006 (Genetics)

Paper 2 – Local adaptation by alleles of small effect. Yeaman 2015 (American Naturalist)

Stats: 18 groups; 75+ (3 groups unreported)

**1. What kind of genomic architecture to expect to evolve under high gene flow?**

**FSU:**

* Many quantitative phenotypes involved in local adaptation, so having many small effect alleles prone to swamping and high turnover is probably common.

**WSU:**

* Better appreciations for possibilities but haven’t been able to develop rule set for genomic architecture.
* Haldane’s rule balancing selection with migration is best null hypothesis.

**Cal State:**

* High gene flow favors genomic architecture with fewer, larger, and tightly clustered alleles.
* Small mutations may occur but expect larger alleles to have greater effect.
* Genetic redundancy, rate and size of mutation, and allele effect size will affect ability of gene to persist.

**UMass Amherst:**

* Inversions are maintained and spread primarily due to suppression of recombination, and if recombination were to occur, it would be lethal to the individual.
* Migration/selection balance – number of loci captured by inversion was driving factor in determining fate of inversion.
* If they are such powerful drivers, why don’t we detect them more often? Technological capacity?

**Uchicago**:

* Small effect loci depends on genome size/complexity. Most of results (yeoman) based on number of loci and genetic redundancy of trait. Finding these out is difficult, but perhaps feasible using combo of GWAS and quantitative genetic based approaches.
* Allelic patterns of divergence might change over time during local adaptation, where allele effect size might be most important at beginning of local adaptation.
* Common challenge – if patterns of adaptation we observe now are due to historical evolutionary processes, can we use them accurately to make future predictions?
* Time scale over which spatially fluctuating selection pressures drive local adaptation is distinct than rate at which adaptation to rapidly changing environmental conditions occur.

**USC:**

* Strongly differentiated motifs can withstand gene flow, while moderate or weakly differentiated more likely to be swamped.
* Inversions expected to become fixed – increased migration increases fixation because recombination with immigrants in the ancestral haplotype lowers the frequency of adaptive alleles.

**Nicholls:**

* It depends and its complicated. If organism has genome sequenced, then forward genetics are possible with more informative markers. Non model may be limited to just reverse genomics.
* May miss signal of if only using outlier SNPs if there is high gene flow, especially when considering alleles of small effect.
* Finding candidate genes/pathways may be only way to identify local adaptation in this case.
* Using markers beyond SNPs is highly exciting but marker choice comes down to question – do you want to prove local adaptation? May be impossible, but useful for management/conservation.
* Getting bogged down in mechanism may be informative for basic science but may not be useful in application.
* Combining genomics with epigenetics, transcriptomics, or proteomics may help.

**Rutgers**:

* How likely is it for beneficial inversions to occur?
* No single genomic architecture is likely to evolve under high gene flow but what emerges is highly context specific depending on system, traits under selection, degree of genetic variation already present in the genome, etc. \

**UCDavis:**

* Echoing Haldane, locally favored allele would be lost when immigration rate of maladapted genotype exceeds strength of selection against it.
* Echoing Felsenstein, At higher migration rates, locally adapted allele will spend a larger proportion of its evolutionary time in environments wehre it is disfavored, and above a critical migration rate it may have lower fitness than intermediate.
* Yeaman, if migration between difrerent environments, might predict that stable maintenance of allelic polymorphism would be effectively prevented by swamping if all genetic variants are of small effect relative to migration rate.
* Migration homogenizes populations which is gene swamping.
* Without change in environment, would expect constant molecular clock, Kimura suggests that most mutations are neutral.
* Maynard Smith, real adaptation occurs in sequence space that is discrete. Number of possible sequences for a gene is limited. Adaptive walk with different local optima, with too much migration, there is no walk.

**ODU:**

* Genomic architecture = non random arrangement of genome and can be seen in chromosomes, gene inversions, loci, genes, or number of copies.
* High gene flow, alleles are migrating from one population to another bringing in both adaptive, maladaptive, and neutral alleles.
* Gene swamping will flod the locally adapted alleles of original populations under certain circumstances.
* Genome architecture would likely be similar in population experiencing high gene flow.
* One-off events could create barrier to gene flow, making genome architecture more likely to be different.

**Hal-Dames:**

* Any genomic architecture that creates post zygotic barrier and or prevents recombination could be fixed in a population despite high rates of gene flow.
* Inversion and chromosome duplication good examples of genomic architecture that allow maintenance of fitness despite influx of maladaptive alleles.
* Alleles with small effect that are numerous/redundant may be more adaptable to changing environments. Alleles constantly being swamped by other alleles of small effect, which allows fitness of individuals in population to vary slightly. May mean that locally adapted alleles never reach fixation.
* Very difficult to detect “small” genes – transient nature means that It would be difficult to capture the exact snapshot in the population’s history where this suite of alleles is adaptive.
* Chromosome inversions seem easier to detect especially given whole chromosome sequencing.

**Cornell**:

* Might inversions be less favored when there is more complex fitness landscape?

**Northeastern**:

* Didn’t test whether inversions tend to evolve in high migration scenario, so it is difficult to know if they are likely to evolve under high gene flow.
* However, if you think of these as alleles of large effect, it is possible to rationalize, but needs to be tested.
* Yeaman showed how polygenic traits comprised of many alleles could evolve depending on migration/mutation rate. Demonstrating that even transient alleles could influence the adaptive divergence of a population when there was sufficient genetic redundancy and mutation.
* Did not find compelling evidence that specific architecture could broadly expected.

**CSU Monterey:**

* Large effect sizes in single celled organisms enhances purifying selection to such an extent that it eliminates non coding junk DNA.
* This selection yields efficient genomes with different architectures in multicellular orgs.
* But marine species often have large effective sizes and high gene flow, which tends to unify local populations. Larger effective size might have less junk dna as a result, but yet to look into it.
* An inversion that captures 2+ beneficial alleles will spread faster given high gene flow is interesting and plausible.

**LSU:**

* Interesting delineation between genetic and genomic. Paper suggests that genomic architecture describes potential loci that could result in adaptive trait, while genetic architecture is representative of currently variable loci contributing to adaptive trait.

**2. How does genomic architecture constrain adaptation?**

**WSU:**

* Depends on what is meant by genomic architecture, constrain, and adaptation. Definitions are context specific. Depends what system and what you measure. If it is context dependent, is it worth pushing for a general definition?

**Cal State:**

* If allele effects are large, could swamp out newer alleles even if they are adaptive. (does not consider fitness aspect of the population).
* Populations are never “stable” as conditions constantly change.
* In perfectly stable environment, would anything change? Theory based on stagnant environment.
* Philosophical conundrum that our understanding is from selective pressures of the environment.

**USC:**

* Redundancy and migration can limit fixation of alleles and constrain adaptation
* Inversions can capture locally adapted alleles but may also capture deleterious alleles at other loci, which may prevent fixation
* Inversions may fix advantageous alleles, but if the environment changes, these organisms cannot recombine with those who lack the inversion to adapt to new conditions.
* Small effect alleles may be more likely to contribute to local adaptation on a short term scale, but may not persist due to swamping.

**Rutgers:**

* Pace of adaptation may differ depending on if trait of interest is governed by mainly large or small effect alleles. If large, adaptation should be fast with larger jumps in fitness as beneficial alleles move to fixation then plateauing. Small effect = slower adaptation because of weaker selection. Transient nature of adaptive genomic architecture with small alleles may further slow this pace.

**UCDavis:**

* Linkage: when strength of divergent selection on linked locus is large relative to recombination rate between them.
* Only large effect alleles will contribute to divergence while quantitative genetic models predict that divergence will evolve as long as genetic variation is maintained.
* Quantitative genetics: standing genetic variation is due to many alleles of small effect. Fst would not pick up differences in alleles in second scenario.
* As # of loci contributing to trait increases, relative contribution of fst at individual loci decreases, while among population covariatnce in allele effect size tends to contribute more.
* Kimura: mutations must be beneficial but also to escape accidental loss when rare
* Welch and Waxman: cost of complexity is that distance traveled to optimum by a benefical mutation is smaller in a complex than simple species. Complexity = number of characters.

**ODU:**

* Constraint is high gene flow bc will homogenize.
* Not necessarily less genetic diversity. Barrier to genetic recombination necessary to lead to local adaptation, whether they be inversions, linkages, etc.
* How often to large effect genes lead to adaptation vs. small effect genes?
* Larger areas of genome likely to be linked than originally thought, which could reduce local adaptation.
* Length of sequence is limited, so effect of mutation on a specific gene limited.

**Hal-Dames:**

* Inversions may make populations more rigid in face of climate change.
* Altered genomic architectures may not be able to take advantage of new alleles delivered by gene flow. These pops may need to rely on new mutations.

**Northeastern:**

* Question could be interpreted different ways depending on how you define constraint.
* Could reduce number of ways adaptation could occur, or limit the rate or likelihood of adaptive evolution.
* Low mutation rates, minimal standing genetic variation, decreased genetic redundancy in polygenic traits.
* Inversions could also constrain adaptation when new adaptive inversions rapidly rise to fixation. Inversions are well adapted but have limited variation.
* Potential from underdominance or maladaptation due to recombination between inverted and non-inverted chromosomes might serve to further limit variation, so if environment were to shift, population of newly fixed inversion may be limited in response.
* Larger effect size might improve efficiency of selection on adaptive allele.
* If inversions are considered alleles of large effect size, then could facilitate faster rate of adaptive evolution, however highly context dependent.
* With poly genic traits, if variation is limited, there is limited potential fro adaptation.

**CSU Monterey:**

* Stumped, but hox genes, which must be kept in same order on chromosome – inversion in this region would not be beneficial.

**LSU:**

* If no linkage or proximity, adaptation can be constrained.
* With inversions, potential for propagation of both positive and negative alleles in a population.
* Inversions can present meiotic incompatibilities resulting in reduced fitness further constraining adaptation and possibly leading to speciation.
* Location of mutations as well as mutational target size can also constrain.
* Different areas of genome have different likelihoods of mutations (CpG islands have higher mutation rates) and size of mutation can influence persistence.

**3. What are the implications of different genomic architectures for our ability to study adaptation using genomic data?**

**FSU:**

* Ability to use genomic data depends on of unknown locus of transcience and allele turnover rate relative to recent history of ecological causes of divergent selection on phenotypes.

**UGH/UNH:**

* Focus on few, large effect vs. many, small effect and how to detect causal loci. Experimental design (cmg, rt) affects the ability to pinpoint candidate genes.

**Virtual Group:**

* Large effect genes have gotten most focus, but this is unwarranted.
* Genomic architecture has huge influence on how well we identify local adaptation.
* Standard measures of differentiation (Fst and GEA) rely on loci of large effect with little/no redundancy but miss class of polygenic traits driven by small effect loci.
* Polygenic signal likely to be common in physiological adaptation.
* How can we id polygenic stuff in non model? GWAS? New approaches?

**Cal State:**

* Complex orgs evolve slower bc mutations tend to be more deleterious for less complex organisms. Is this bc there are more genomic redundancies?
* Interesting to see how different lineages evolve due to genomic architecture.
* Papers mention that changes in genome structure don’t always scale to phenotype
* Not sure of next steps – what should we target? If we want to assess if a population is subject to gene swamping from high gene flow, how would we assess? Impractical to assess karyotype or determine standing gen. variation in non-model organisms- what alternative techniques are available?

**UMass Amherst:**

* Need to look at genes with small but significant effects, not just Fst outliers.
* Should also be considering how we study polygenic traits with differing levels of genetic redundancy.

**Uchicago:**

* Wish to know more about prevalence of inversions in marine species – data is sparse.
* Likelihoods of inversions probably different across species, depending on genome size/complexity, or structure of genome around trait of interest.
* Are larger genomes more susceptible? Are polygenic traits more likely to be affected by inversion?
* Determining species specific inversion rates and genomic architecture are critical steps.

**USC:**

* If working in marine systems with high gene flow, large effect alleles will likely be the ones contributing to local adaptation.

**Rutgers:**

* May need several different techniques to study local adaptation – as not all architectures result in equally detectable signatures of selection/adaptation.
* Small effect alleles may often go undetected while large effect likely to be identified via fst outliers.
* How do we detect inversion? Look for linkage blocks or by comparing gene positions in two populations of closely related species?

**UCDavis:**

* Large alleles have higher probabilities of establishing. What is large allele? Is size dependent on phenotype? Can we define it as proportion of phenotypic variance it can explain?
* Simulations show that local adaptation can occur when individual alleles underlying a trait are prone to swamping, given enough genetic variation.
* Genetic variation is key. Adaptation under migration selection balance cannot always be predicted by deriving traditional population genetic models for the maintenance of polymorphisms and extrapolating to the whole genome. Rather, adaptation is quantitative genetic phenomenon.
* If high genetic redundancy and variation, there can be high turnover in loci that contribute to divergence even when individual alleles are highly swamp-resistent.
* Adaptation via swamping prone genes can occur when selection acts on traits that are quantitative, but unlikely in traits with simple genetic basis.
* Solution to combine popgen with quantitative genetics approach. GWAS to estimate genotype values by taking frequency-weighted sum of individual SNP effects on trait of interest (Berg and Coop 2014).

**ODU:**

* Difficult to study underlying genomic architecture for most phenotypes. Difficult to know what is driving local adaption via observing changing phenotypes.
* Effect of genome architecture could be better understood with better sequencing technology that can identify structural changes in chromosomes.

**Hal-Dames:**

* Genetic mechanism underlying local adaptation could influence how organism responses to changing environment (rigid vs. pliable) so might be important for predictions. Just don’t know how to detect.

**Cornell**:

* Different constellations of alleles at many loci that can produce optimum phenotype. When this occurs, detectable fst outliers may be few. GWAS approach by Berg and Coop was mentioned, but It requires that a trait be identifyied and a large sample size, and may be prone to false positives.

**Northeastern:**

* If we expect small allele genes to drive adaptive divergence, we lack power to detect them.
* Methods that evaluate each locus individually biased towards individual alleles of large effect, due to expectation that they are more strongly correlated with phenotype or environment.
* Many small alleles under weak selection may not have dominant frequencies that are highly differentiated or corrupted beyond what we’d expect with null model. (below threshold of detection).

**CSU Monterey:**

* Curious about inability to detect many small genes.
* Encouraged by idea that at higher migration rates, more alleles would be swamping prone, but any alleles large enough to resist swamping would be more readily distinguished from neutrally evolving loci.
* GWAS an option, alternatively could look for difference in mutation rates estimated over temporal range of molecular clock calibrations. Time dependence hypothesis – genes that show rate in calibration time are likely experiencing mild purifying selection.
* Marine species have shallower decline in mutation rate than terrestrial species, probably due to larger effective population sizes.

**LSU:**

* May be detection bias for alleles of large effect, and easier detection doesn’t make them more common.
* Identifying Fst outliers may not be sufficient for detecting alleles of small effect.
* Would only be able to see it if more than one locally adapted alleles are caught in the inversion.
* Absence of identification of alleles of small effect not enough to claim absence.