Managing for Genetic Variation: When, Why and How?

Oliver Ryder

San Diego Zoo Institute for Conservation Research

Managing for Genetic Variation: When, Why and How?

Processes, issues, and factors in genetic aspects of conservation management

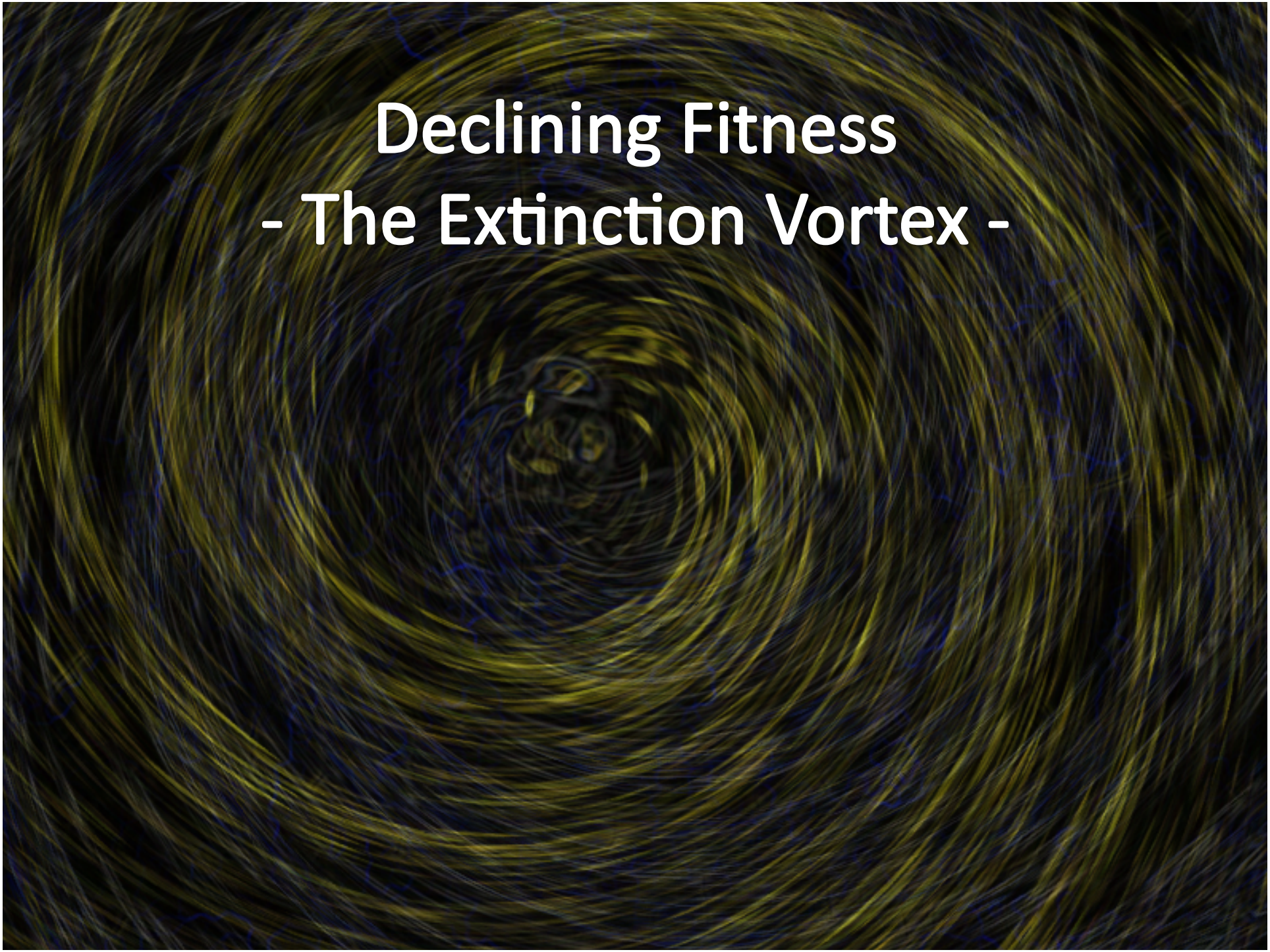
Conservation management:
Goals
Limitations

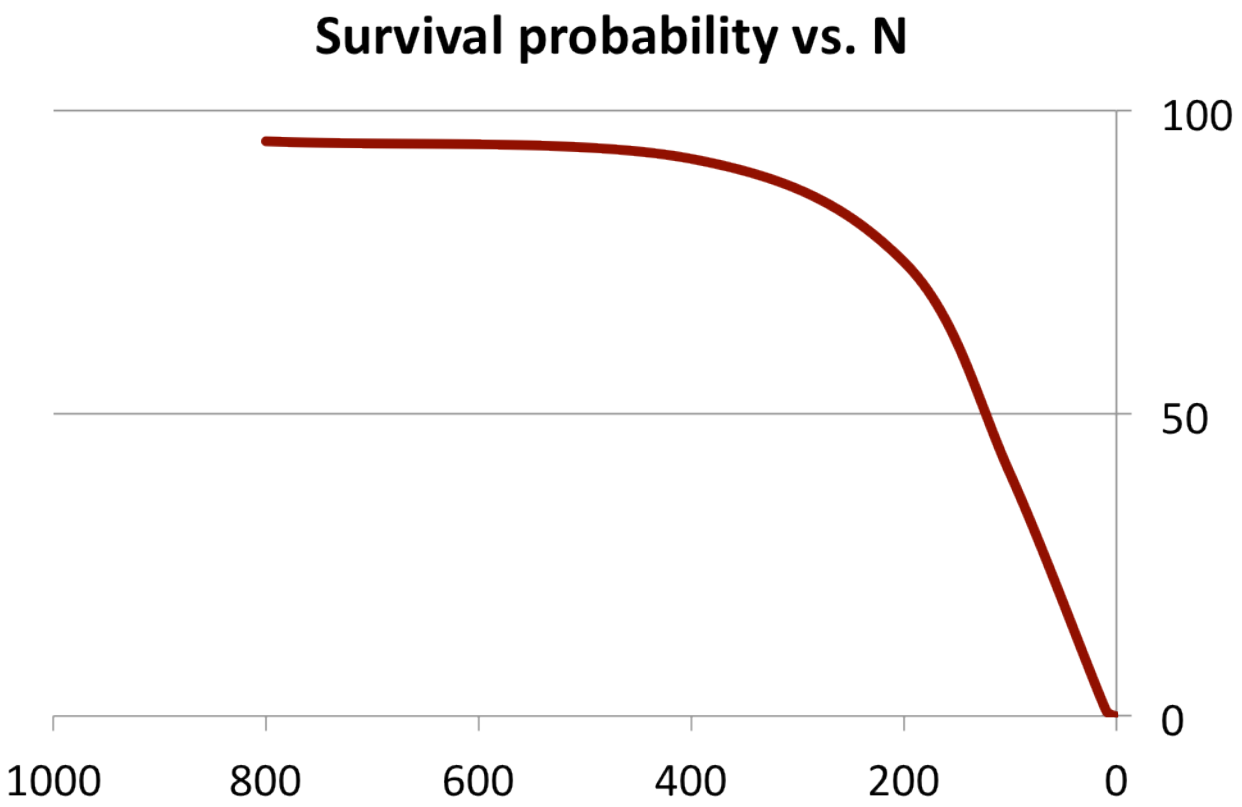
Managing for Genetic Variation: When, Why and How?

WHEN:

Extinction risk typically triggers management for non-domestic species.

But the level of threat required to trigger intervention is a matter of dispute. (And, we may wish to refine the definition of extinction.)


Declining Fitness
- The Extinction Vortex -


Survival probability vs. N
100
50
0
1000
800
600
400
200
0

Managing for Genetic Variation: When, Why and How?

WHEN:

Extinction risk typically triggers management for non-domestic species.

But the level of threat required to trigger intervention is a matter of dispute. (We may need to refine the definition of extinction.)

"When" may also depend on feasibility. Insufficient samples for a robust analysis is a chronic condition, *that can be addressed.*

Degrees of intensity of management

goals: population persistence

maintenance of ecological processes (?)

measurable assurance of recovery or lack of need to list

Intensive mangement:

pedigree vs. genetic markers

Intensive mangement:

- pedigree vs. genetic markers

Necessity has driven use of pedigree management

- robustness
- it works
- results can be compared to goals

However, assumptions are violated in nature

Is direct analysis of genetic variation a better tool for management?

Managing for Genetic Variation: When, Why and How?

WHEN:

Extinction risk typically triggers management for non-domestic species.

But the level of threat required to trigger intervention is a matter of dispute. (We may need to refine the definition of extinction.)

"When" may also depend on feasibility. Insufficient samples for a robust analysis is a chronic condition, *that can be addressed.*

For now, whenever one can. There are too few model systems. With the advance of potential applications for analysis of genetic data (notably genomic data), many (most) previous studies are vulnerable to challenge.

WHY IS THAT?

Managing for Genetic Variation: When, Why and How?

Why are so many studies going to come to look inadequate?

Pedigrees are not available

Too few markers.

Poor sampling regime.

Low statistical power.

Problems inherent with rapidly evolving neutral markers, including microsatellites and mitochondrial haplotypes.

Managing for Genetic Variation: When, Why and How?

Problems with neutral markers, including microsatellites and mitochondrial haplotypes.

Microsatellites: mode of mutation uncertainty (we are not highly confident about their mode of evolution). Rapid mutation rate.

Mitochondrial DNA: small effective population size. Matrilineal inheritance. High mutation rate.

These factors, in combination with founder effect and genetic drift, can imply or demonstrate genetic isolation, but for how long and to what functional consequence?

Managing for Genetic Variation: When, Why and How?

Problems with neutral markers, including microsatellites and mitochondrial haplotypes.

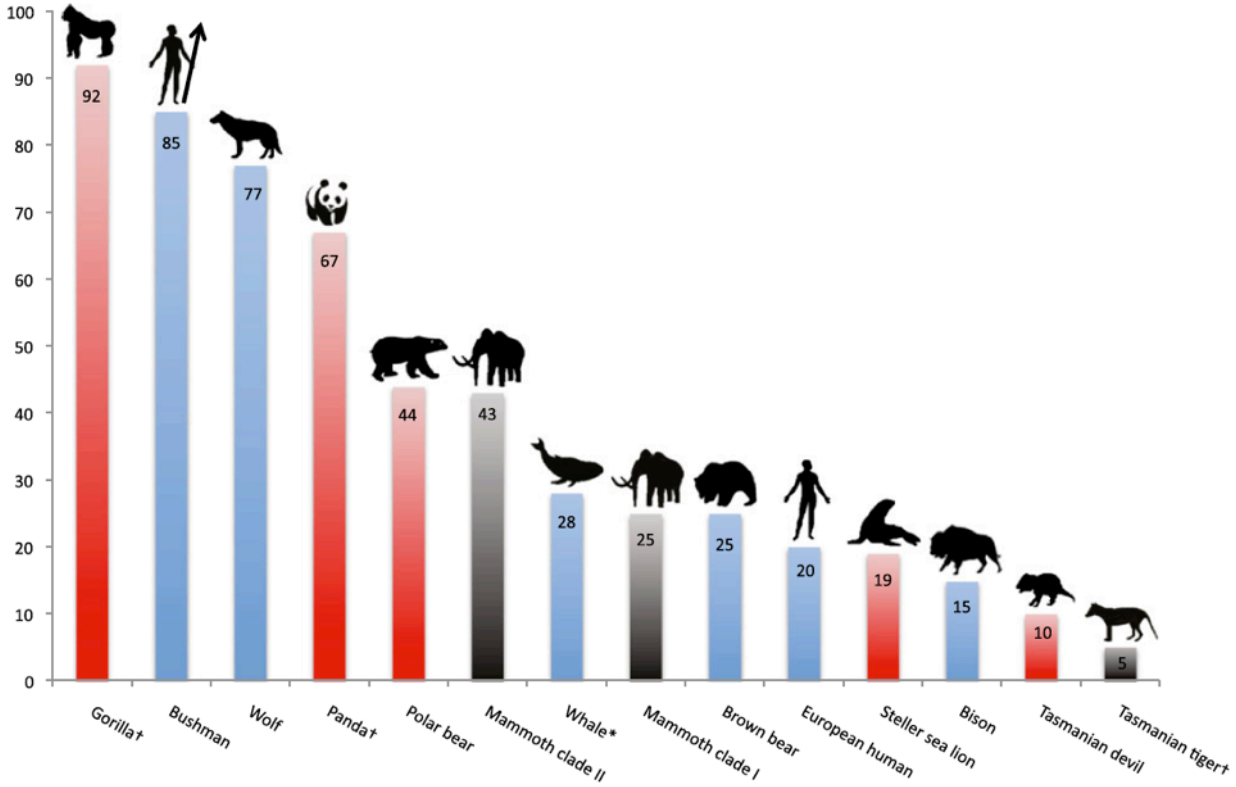
Microsatellites: mode of mutation uncertainty (we are not highly confident about their mode of evolution). Rapid mutation rate.

Mitochondrial DNA: small effective population size. Matrilineal inheritance. High mutation rate.

These factors, in combination with founder effect and genetic drift, can imply or demonstrate genetic isolation, but for how long and to what functional consequence?

What about neutral markers? Why did they get used, if they are not the wanted tool? Why not change, if there is something better?

Species vary in genetic diversity



Average numbers of mitochondrial genome differences between pairs of individuals, ignoring hypervariable regions. Species designated by the 2008 IUCN Red List of Threatened Species as “endangered” or “critically endangered” are indicated in red, and extinct species are in black. Species and populations in blue are thriving. †Species represented by only two sequences. *Whales are averaged over five species. Woolly mammoths are divided into two mitochondrial clades (30). The gorillas may be from separate subspecies, Gorilla gorilla and Gorilla beringei. It is apparent that mitochondrial diversity is not the only factor affecting species endangerment; habitat loss and other factors are often critical.

Miller et al. PNAS 2011

Pacific pocket mouse
Perognathus longimembris pacificus

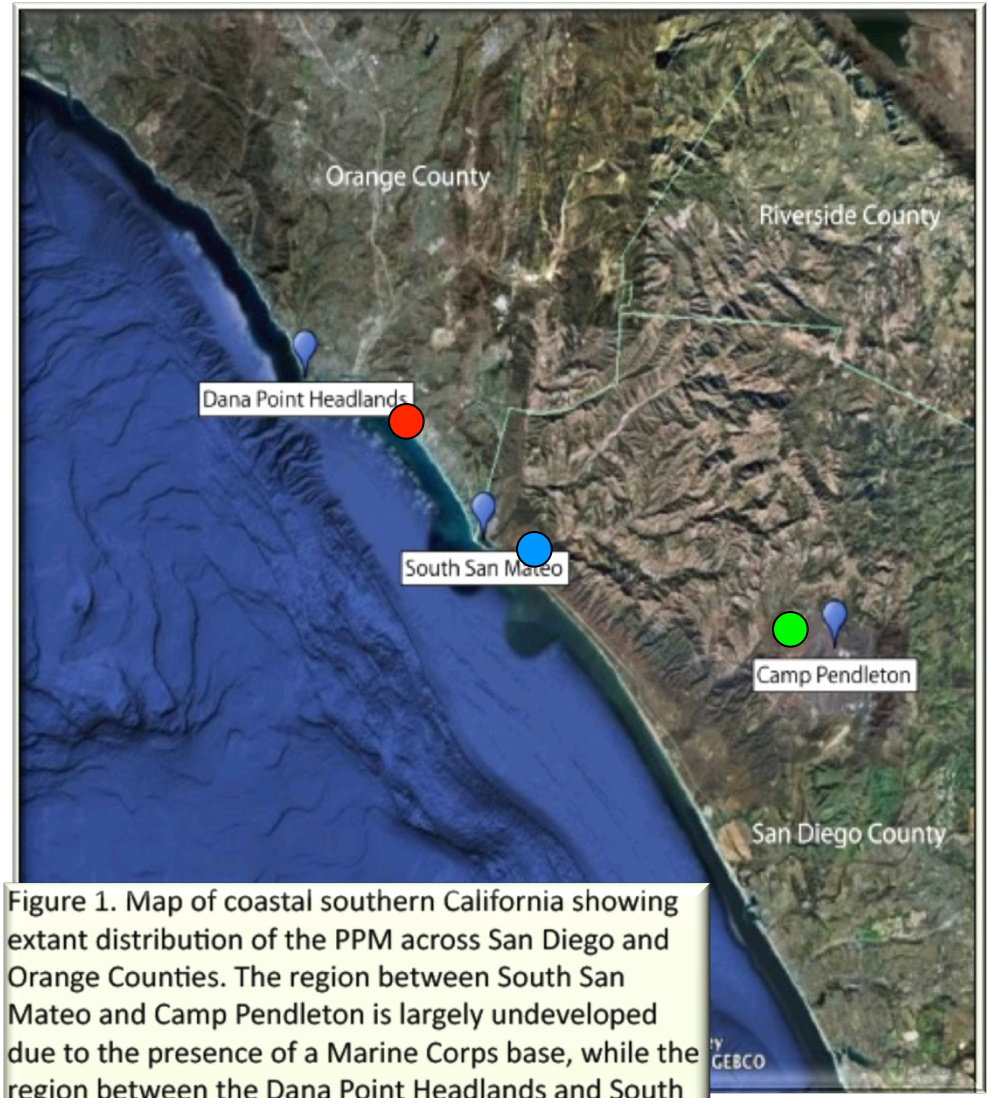


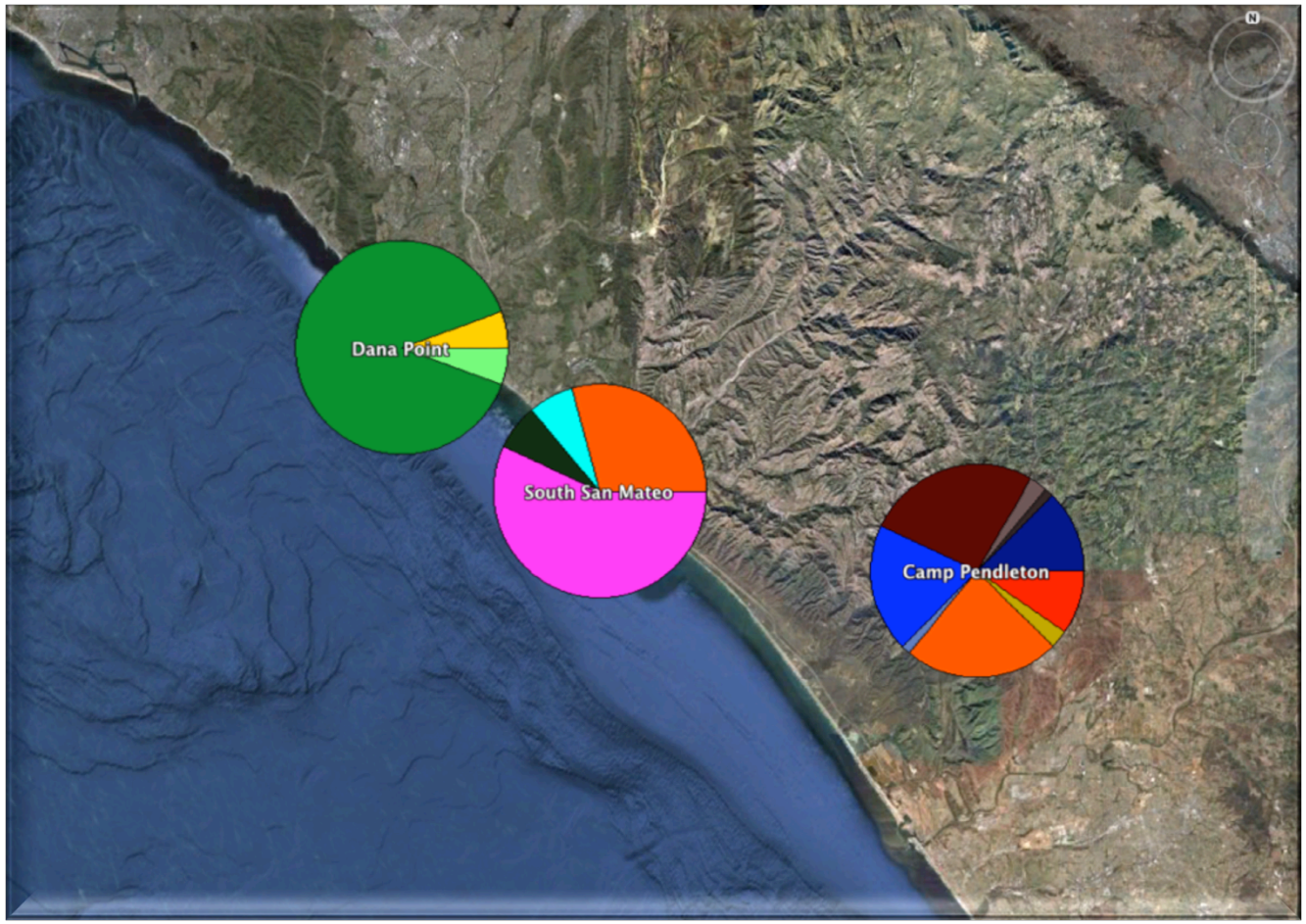
Figure 1. Map of coastal southern California showing extant distribution of the PPM across San Diego and Orange Counties. The region between South San Mateo and Camp Pendleton is largely undeveloped due to the presence of a Marine Corps base, while the region between the Dana Point Headlands and South San Mateo sites is almost completely urbanized, making the Dana Point population extremely isolated. The historic range of the PPM extended approximately 60 miles north and 70 miles south of that pictured here.

Location	N	Avg # alleles per locus	H_e	Probability of ID (sib)
Dana Point	12	3.00	0.41	2.54E-04
South San Mateo	9	3.42	0.50	3.63E-05
Camp Pendleton	23	7.11	0.75	4.00E-08

Steven Thomas, Asako Navarro & Debra Shire

PPM mtDNA haplotype distribution

Limited haplotype sharing (almost reciprocally monophyletic)



Steven Thomas

Pacific pocket mouse
Perognathus longimembris pacificus

STRUCTURE *analysis is suggestive of separate species under PSC*

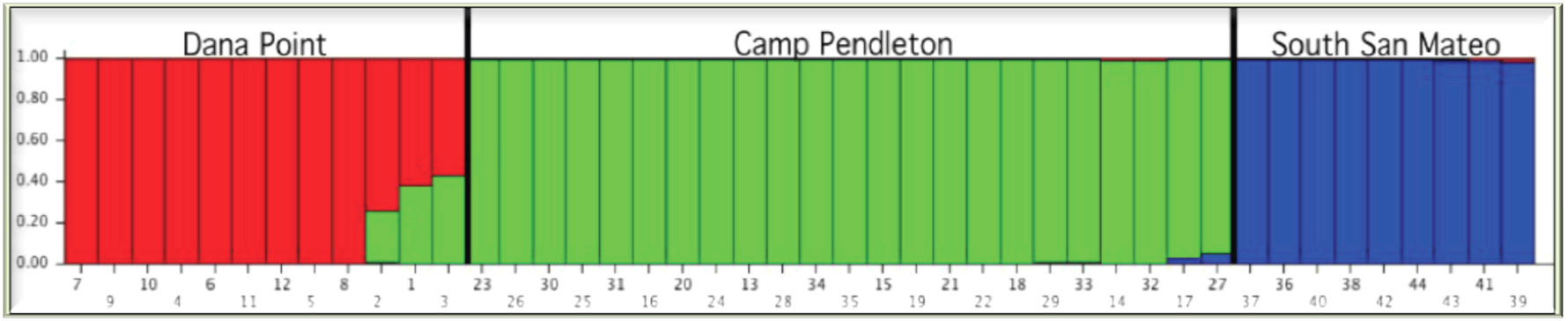


Figure 2. Likelihood values from STRUCTURE indicate that the data are best explained by a three-population sub-structuring of the PPM, corresponding to the three sampling sites. The y-axis indicates the proportional membership of 44 individuals (x-axis) in each of the three inferred clusters. With the exception of three individuals from Dana Point that exhibit mixed genetic ancestry, all individuals could be assigned to the sampling site from which they originated with nearly 100% proportional membership.

Steven Thomas

Managing for Genetic Variation: When, Why and How?

Why are so many studies going to come to look inadequate?

Too few markers.

Poor sampling regime.

Statistical power.

Problems with neutral markers, including microsatellites and mitochondrial haplotypes.

PPM example demonstrates some concerns. SPECIES CONCEPTS impact conservation management operations.

Managing for Genetic Variation: When, Why and How?

PPM example demonstrates some concerns. SPECIES CONCEPTS impact conservation management operations.

Phylogenetic species concept: operational (emphasizes ability to diagnose). But, may overdiagnose, due to genetic drift and rapid marker evolution.

For genetically diverged populations: protect divergence when it involves adaptive differences, but counter it when it threatens populations.

Managing for Genetic Variation: When, Why and How?

PPM example demonstrates some concerns. SPECIES CONCEPTS impact conservation management operations.

Phylogenetic species concept: operational (emphasizes ability to diagnose). But, may overdiagnose, due to genetic drift and rapid marker evolution.

For genetically diverged populations: protect divergence when it involves adaptive differences, but countered when it threatens populations.

So, we would really like to know more about adaptive differences! Maybe, we would want to manage for them to contribute to sustainability.

Managing for Genetic Variation: When, Why and How?

So, we would really like to know more about adaptive differences! Maybe, we would want to manage for them to contribute to sustainability.

How would we identify adaptive differences and how would this information be applied?

- measure components of fitness and associate with genetic locus
- evaluate mutations at and across loci
- threatened status limits direct experimental investigations

Genomics

There are basic, unresolved, questions about biology and evolution that genomics can address: recombination, role of types of genetic variation, mutation, life history attributes, selection. Enhanced knowledge in these areas impacts many conservation applications.

Conservation applications that genomics can inform:
conservation units, hybridization, resolving power for identifying systematics, population genetics, demographic questions

Look for case-by-case approaches as the field develops.

The risk of gene flow between isolated populations involves declines in fitness resulting from genetic incompatibilities, i.e., outbreeding depression

Chromosomal divergence can lead to outbreeding depression and should routinely be evaluated

Madoqua kirki - Kirk’s dik-dik

image: robertwinslowphoto.com

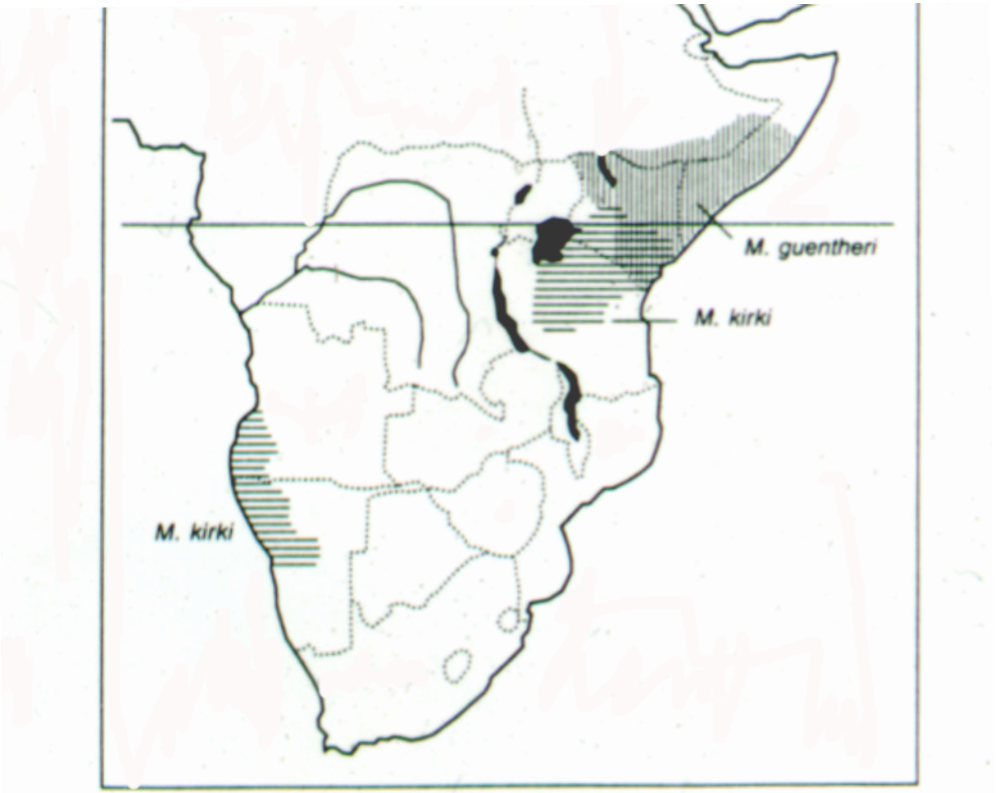
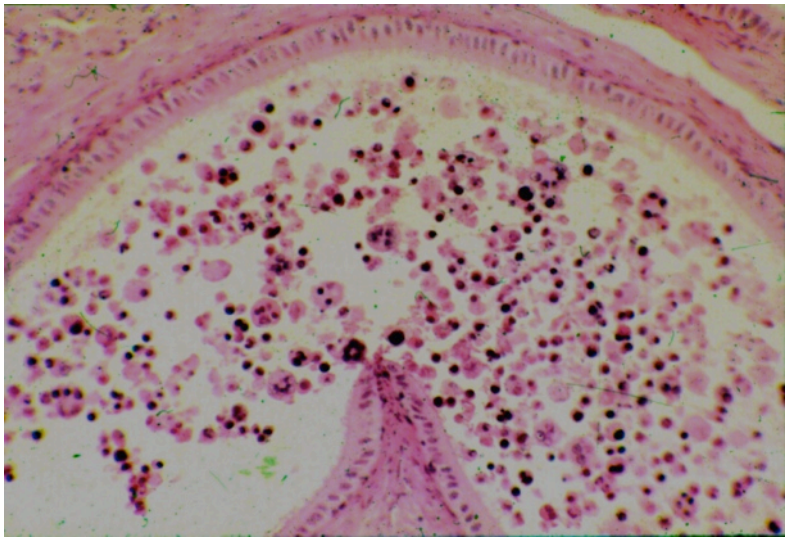
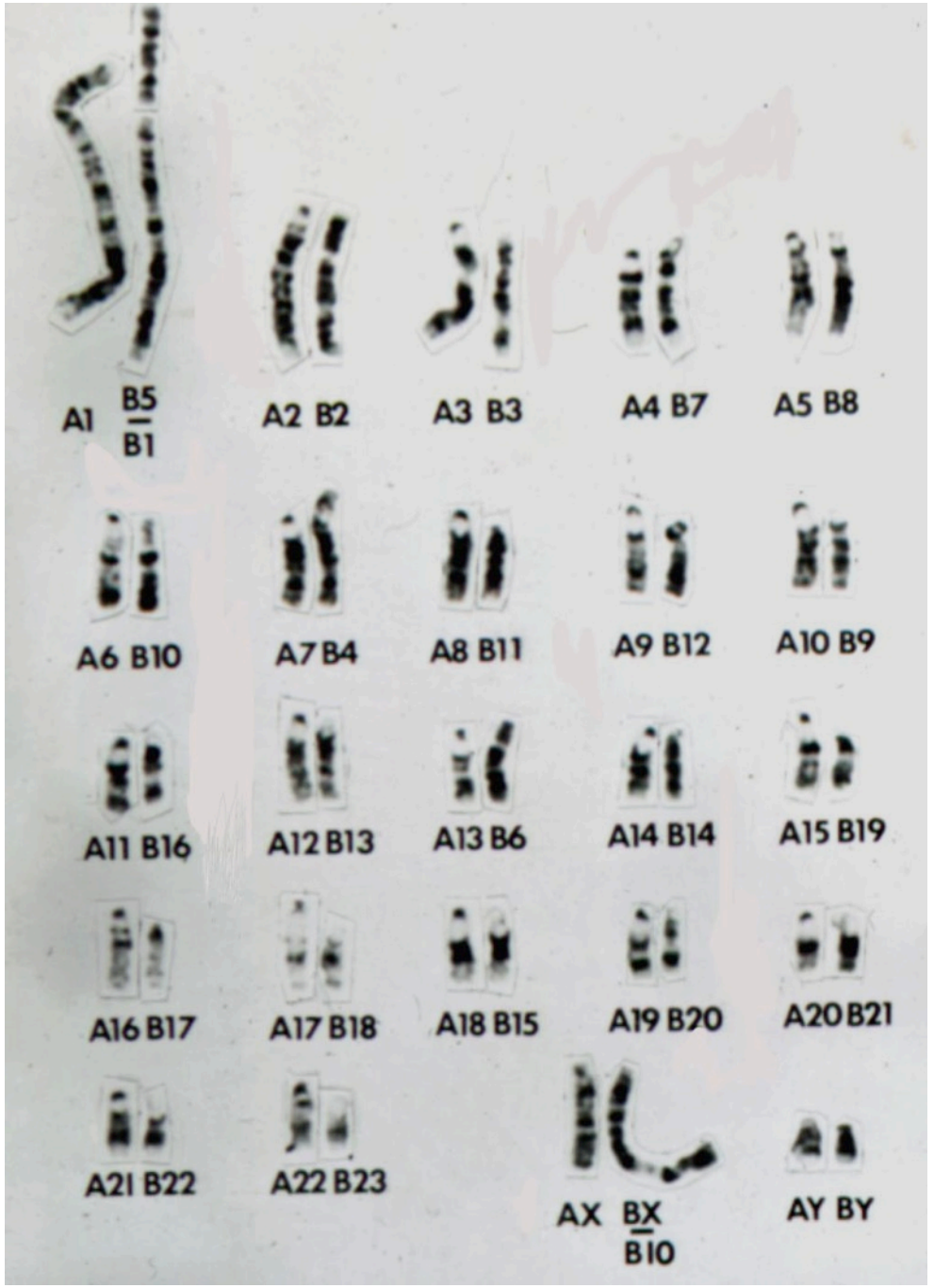


FIGURE 1. African distribution of *Madoqua kirki* and *M. guentheri*. After Kingdon (1982) for East Africa and Haltenorth and Diller (1980) for southwest Africa.

Hybridization of Kirk's dik-dik cytotypes produce sterile males



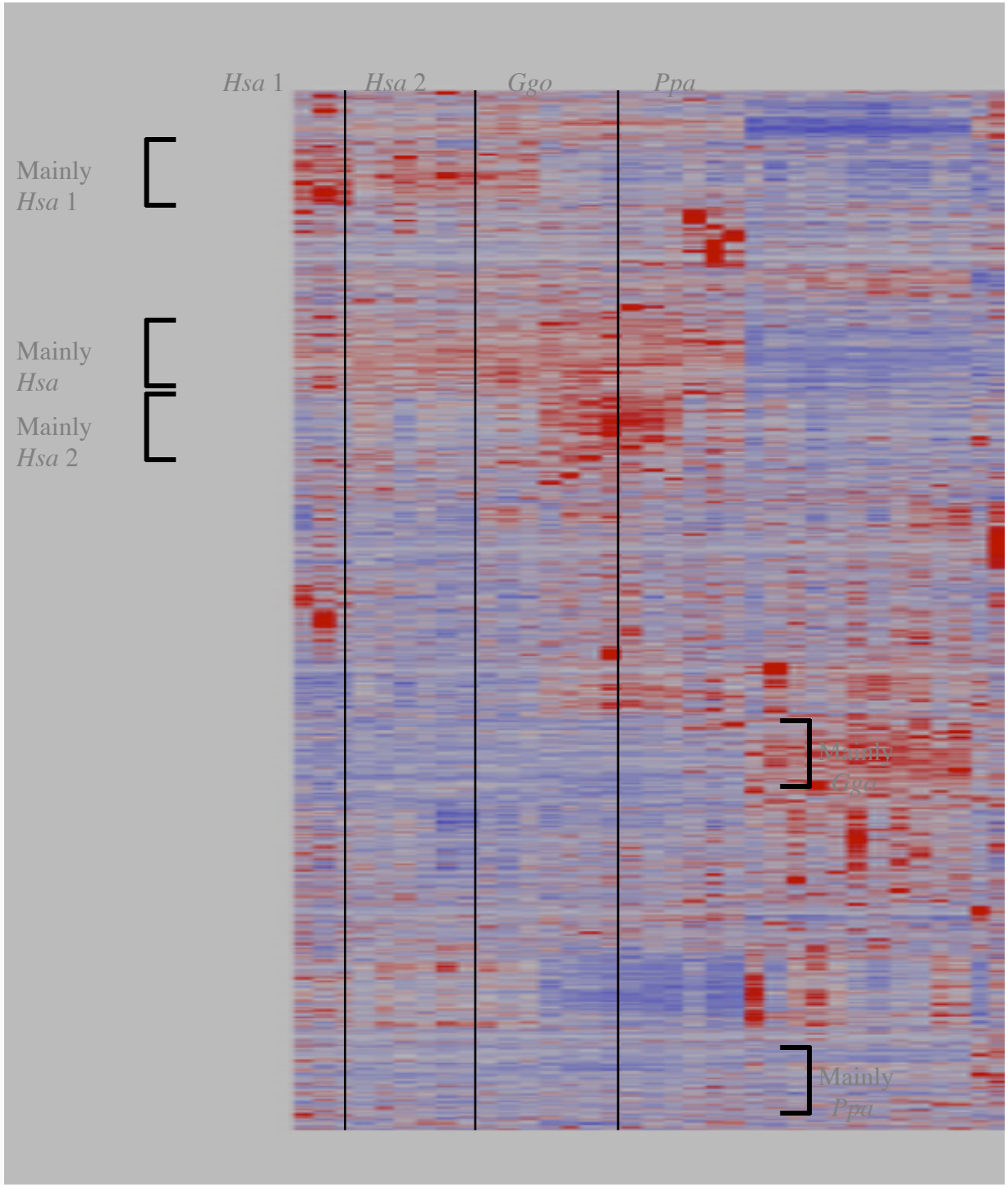


Assessing *functional* genetic divergence:

types of mutations can imply functional changes

dN/dS ratios

changes in gene expression can imply functional changes



Relative Gene Expression in Human and Ape Fibroblasts

Karaman, et al.
2003
Genome Research

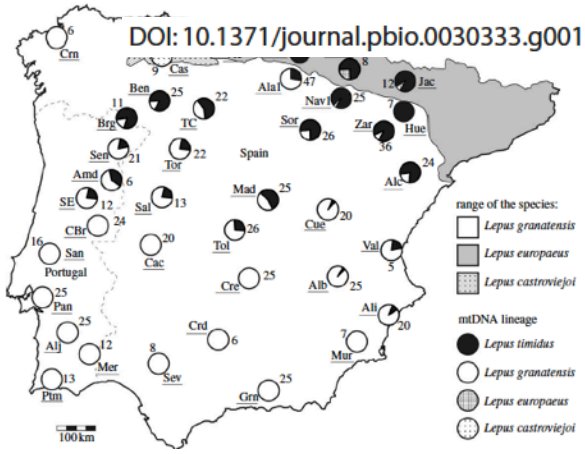
Hacia Lab
Ryder Lab

Gene flow happens!

We are at the early stages of discovering how often and when introgressive gene flow occurs following reproductive isolation

Gene flow: natural, managed, restorative, adaptive, and maligned

Figure 1. Current species ranges of *L. europaeus* and *L. timidus* in Eurasia according to Flux & Angermann (1990) and Mitchell-Jones *et al.* (1999). The dashed box depicts the Iberian Peninsula. (See figure 2 for the ranges of hare species in this region.)



Two quick examples of current studies in measuring genetic diversity in endangered species.

These studies are anticipated to assist in long-term conservation management.

Great apes

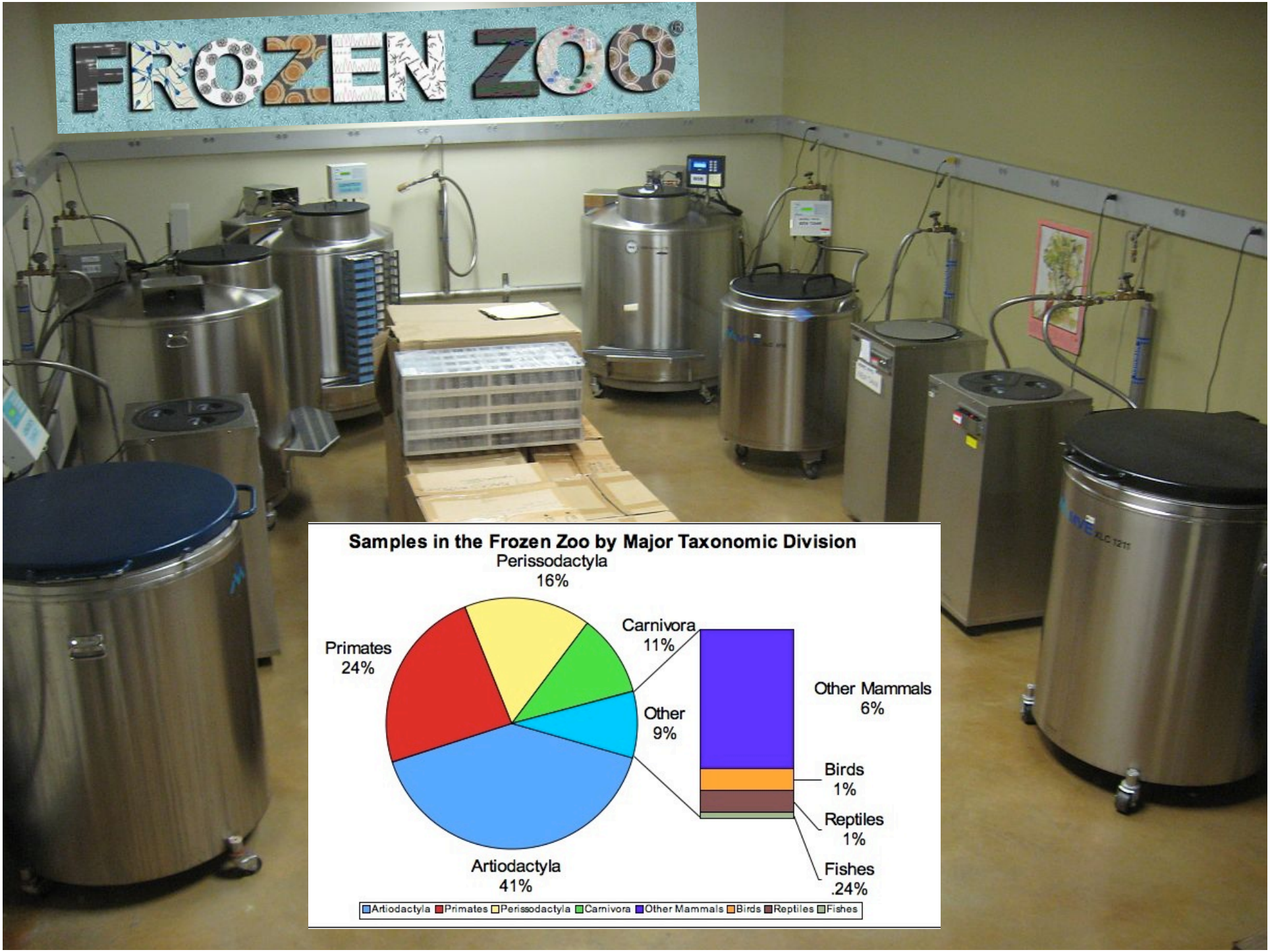
California condor

And, another plug for banking samples. It’s worth will exceed your expectations.

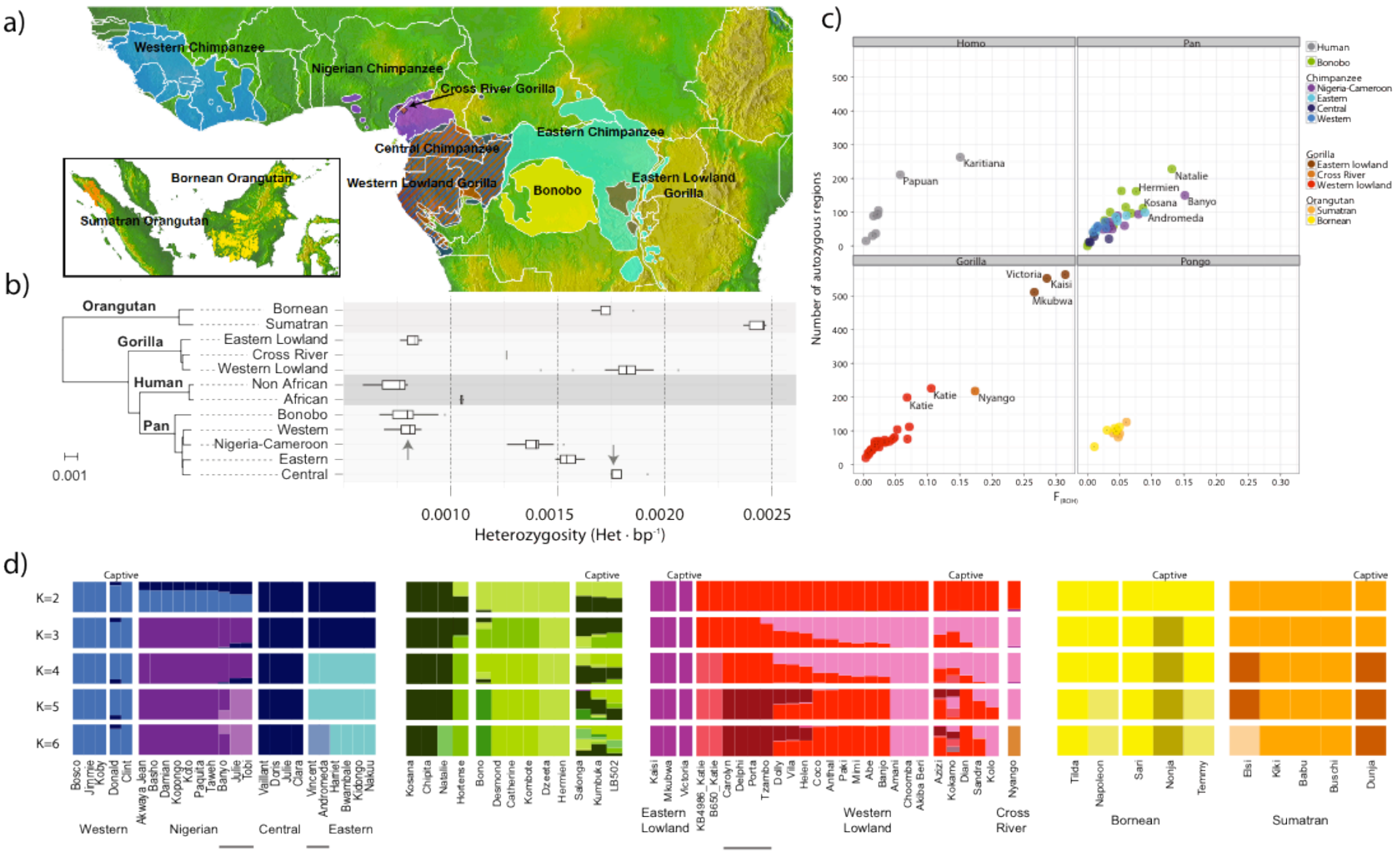
The Frozen Zoo®

Mission of the Frozen Zoo

To help preserve the legacy of life on Earth for future generations by establishing and maintaining genetic resources in support of worldwide efforts in research and conservation.


FROZEN ZOO®
Samples in the Frozen Zoo by Major Taxonomic Division
Perissodactyla
16%
Carnivora
11%
Primates
24%
Other
9%
Other Mammals
6%
Birds
1%
Reptiles
1%
Fishes
.24%
Artiodactyla
41%
Artiodactyla Primates Perissodactyla Carnivora Other Mammals Birds Reptiles Fishes

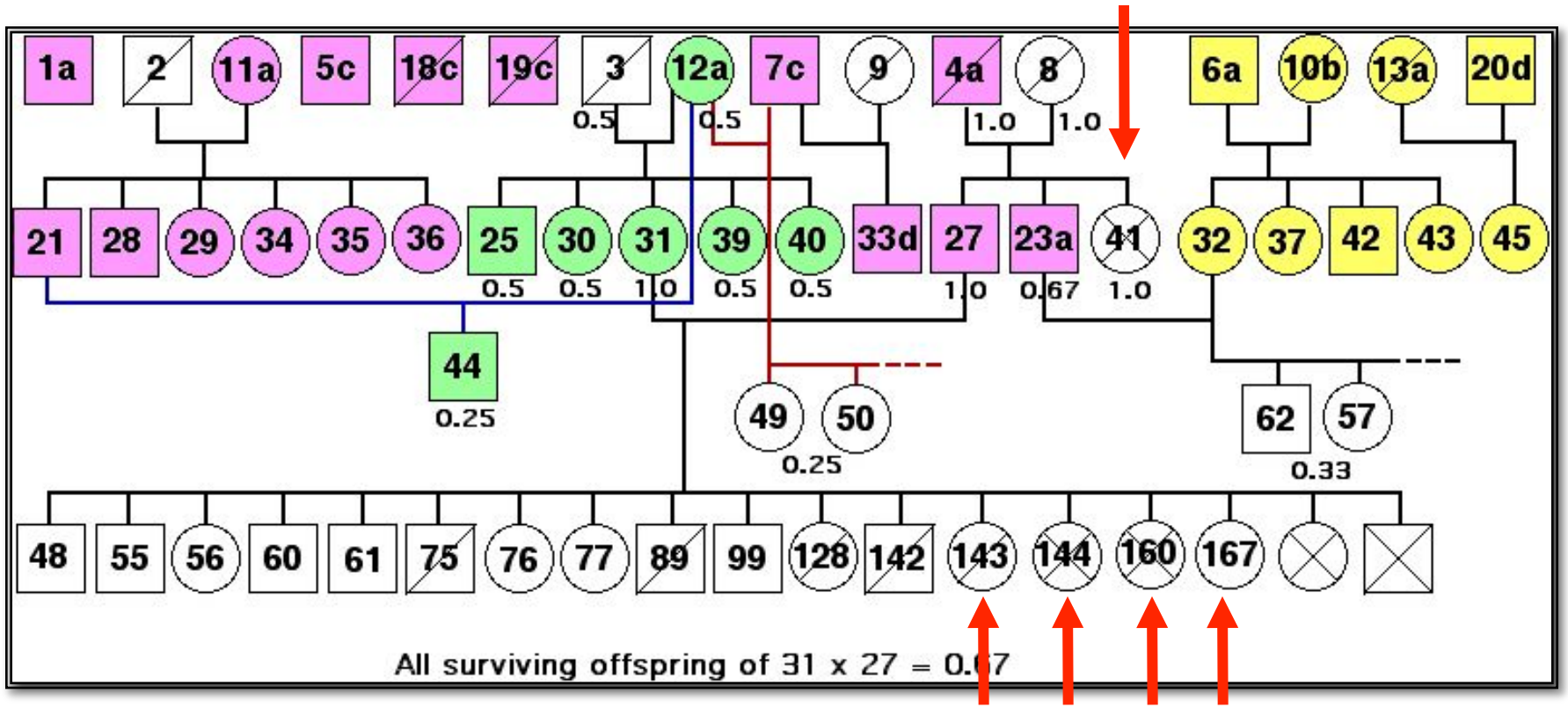
Prado-Martinez, et al. *Nature* (2013)



California condors

Partial pedigree of expanding California condor population

SAN DIEGO ZOO INSTITUTE FOR CONSERVATION RESEARCH



OPEN ACCESS Freely available online

PLoS one

Double Digest RADseq: An Inexpensive Method for *De Novo* SNP Discovery and Genotyping in Model and Non-Model Species

Brant K. Peterson*, Jesse N. Weber, Emily H. Kay, Heidi S. Fisher, Hopi E. Hoekstra

Department of Organismic & Evolutionary Biology, Department of Molecular & Cellular Biology, Museum of Comparative Zoology, Harvard University, Cambridge, Massachusetts, United States of America

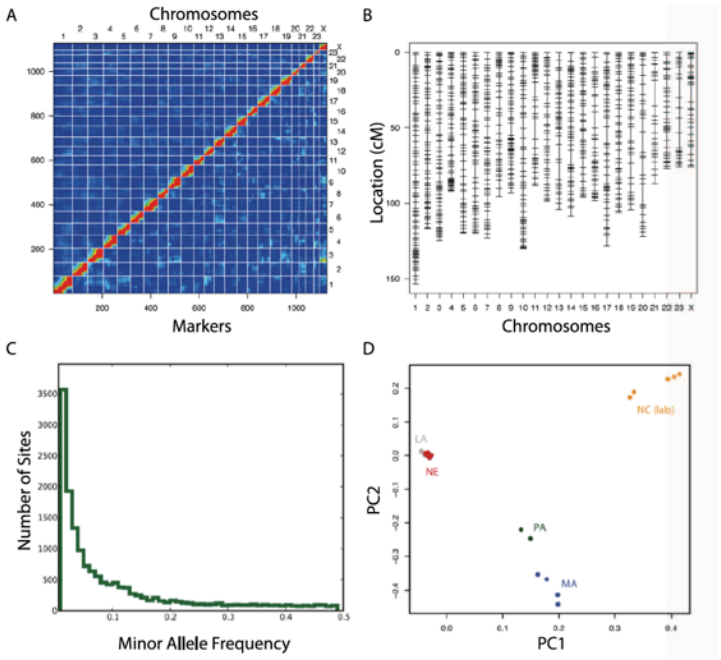


Figure 5. Discovery and genotyping of ddRADseq markers in a laboratory cross and wild populations without a reference genome. ddRADseq was used to identify SNPs between two *Peromyscus* species, neither of which had a genome sequence available, that were crossed as part of a QTL experiment. This yielded 1158 unique markers that were fixed within, but different between, the parental species. By calculating the fraction of recombinant genotypes and LOD of linkage between markers, we generated (A) 24 groups of strongly linked markers, heatmap colors represent

Ecosystem Ark

Acknowledgments

Past and present staff of Genetics Division, including Suellen Charter, Cynthia Steiner, Steven Thomas, Leona Chemnick, Asako Navarro, Heidi Davis, Marlys Houck, Christie Otten, Paquita Hoeck, Arlene Kumamoto.

SDZGlobal: Jamie Ivy, Andrea Putnam

Penn State: Webb Miller, Stephan Schuster

Species concepts in conservation group: Dick Frankham, Katherine Ralls, Bob Lacy, Jon Ballou, Michele Dudash, Mark Eldridge, Charles Fenster, Joe Mendelson, Ingrid Porton

Funding: NIH award to Evan Eichler; John and Beverley Stauffer Foundation, Seaver Institute, IMLS, USFWS, Caesar Kleberg Wildlife Conservation Foundation