



# Factors affecting phasing quality in a commercial layer population

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- Inferring points and number of recombination
- Imputation of low frequency variants
- Study of haplotype structure
  - genetic diversity and
  - accuracy in genomic selection
- Computational approaches with **phasing software**
  - sample size, marker density
  - genotype accuracy
  - relatedness in the sample



- Aim: Assessing **haplotype phasing quality** for a highly-related laying hen population using different phasing software
  - FImpute v2.2 (with and without pedigree information)  
*(Sargolzaei et al., 2014)*
  - Beagle v3.3 (without pedigree information)  
*(Browning and Browning, 2007)*
  - Beagle v4.1  
*(Browning and Browning, 2007)*



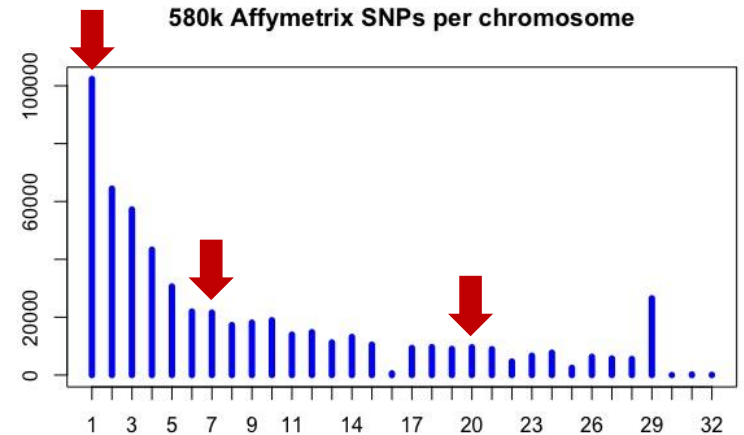


- Real SNP data from a purebred line of brown layers
- A pedigree of 53'882 individuals across 13 generations
- 918 genotyped individuals (belonging to gen. 7 to 12)
- SNPs from the 580k Affymetrix Axiom<sup>®</sup> Genome-Wide Chicken Array





- Editing was done with Plink (*Purcell et al., 2007*)
  - Individuals with a call rate < 90%,
  - monomorphic SNPs and
  - SNPs not in HWE with  $p < 10^{-8}$were removed.
- 888 individuals remained in the dataset.
- We used chromosomes 1, 7 and 20. (77'910, 16'059 and 7'004 SNPs)

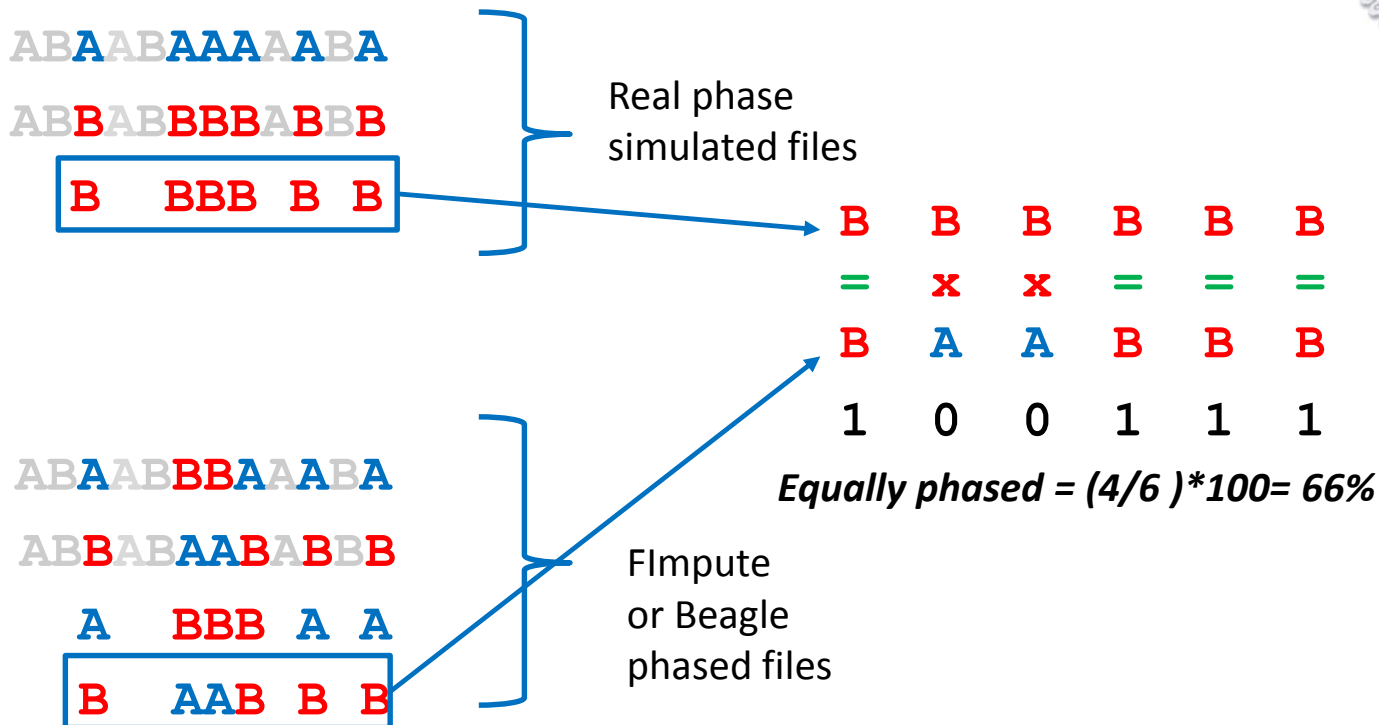




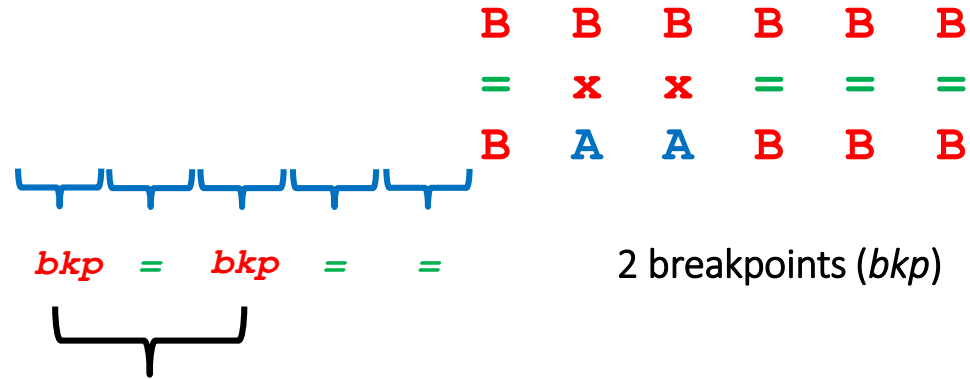
- We performed a simulation in order to have known phases from real SNP data.
- Simulation in three steps:
  1. From the 888 individuals' genotypes, haplotypes were derived in-silico to create a **library of haplotypes**.
  2. 2'000 randomly sampled from the library and **assigned to the founders** of the pedigree.
  3. Founders' haplotypes were **dropped through the pedigree** assuming random crossing-over events but no mutations.



- Phasing with four approaches:
  - FImpute 2.2 (with pedigree information)
  - FImpute 2.2 (without pedigree information)
  - Beagle v 3.3
  - Beagle v 4.1
- Comparison of true simulated and in-silico phased haplotypes:
  - Proportion of equally phased heterozygous SNPs
  - Number of breakpoints (change of phase)
  - Segment size between breakpoints







Distance between  
breakpoints

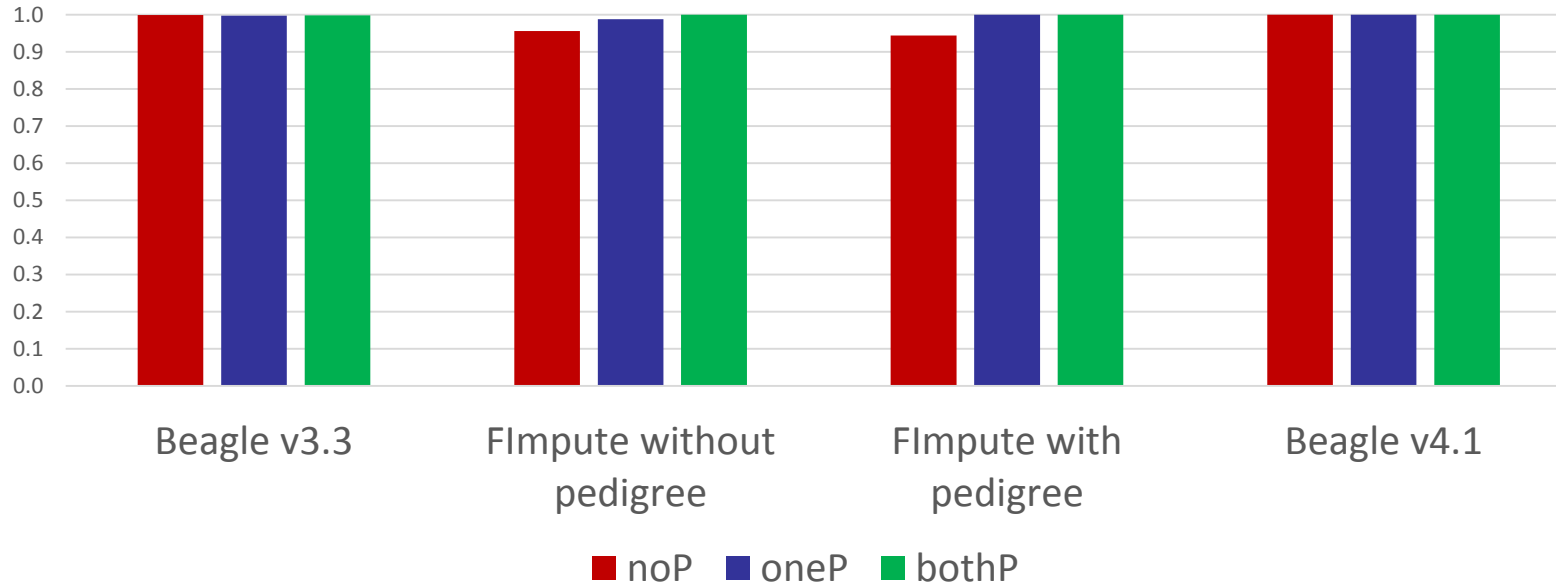


- Statistics were obtained for three subsets in order to analyze the effect of genotyped parents:
  - **noP**: 231 individuals with no genotyped parents
  - **oneP**: 606 individuals with one genotyped parent
  - **bothP**: 51 individuals with both parents genotyped



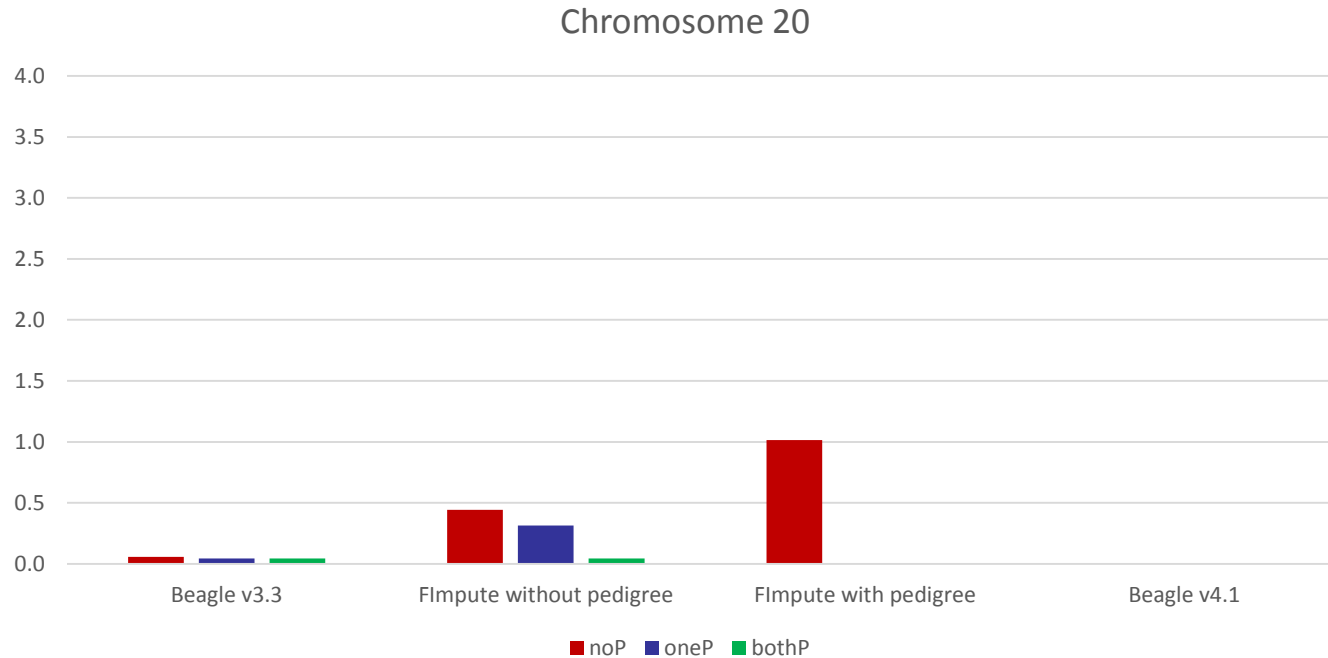
## *Median values of proportion of correctly phased SNPs*

Chromosome 20



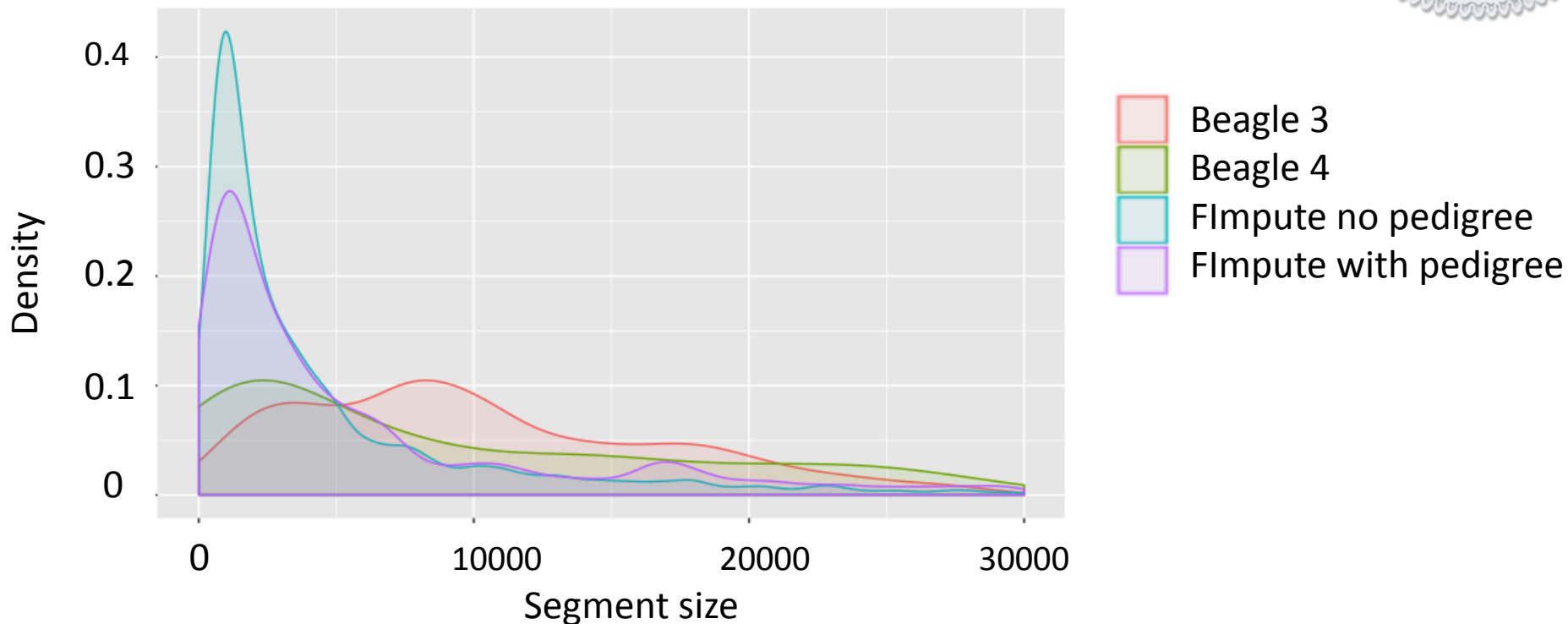


- *Number of breakpoints per 1000 SNPs*





## *Density plots of segments (kB) between breakpoints for Chr. 7*





- Phasing quality was in general better with Beagle v4.1
- With at least one parent genotyped, FImpute with pedigree information reached similar levels of phasing quality
- Number of breakpoints and segments' size between breakpoints varied among the alternatives studied
- FImpute recovered haplotypes with a larger amount of short inverted segments
- FImpute computation time was approx. 1/3 in relation to Beagle 4.1



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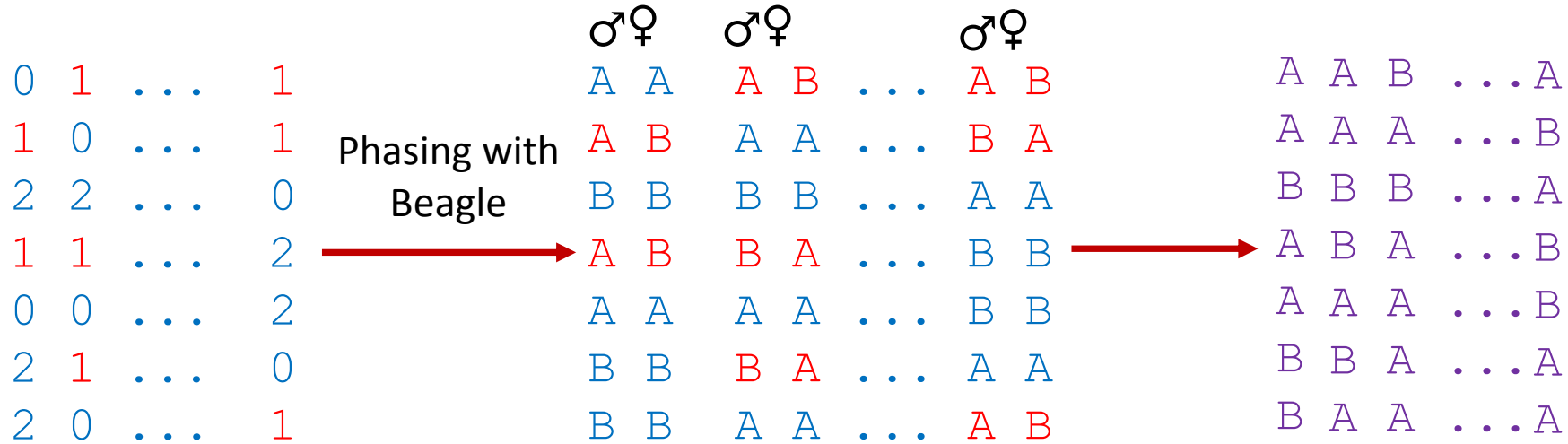
We thank Lohmann Tierzucht GmbH for providing the data.

Thanks for your attention!





## Real data



Population of 888  
individuals

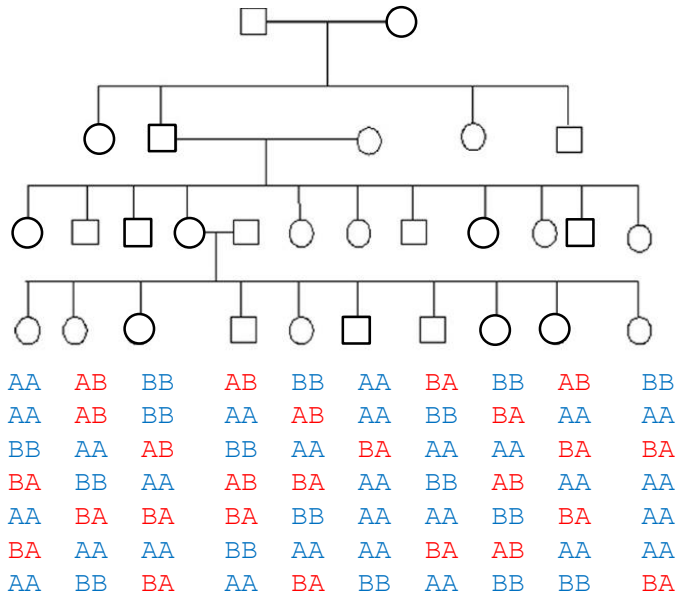
888 phased diplotypes  
(1776 haplotypes)

2000 haplotypes  
randomly chosen  
for the simulation process





A B	A A
A A	A B
B B	A A
B A	B B
A A	A B
B A	A A
A A	A A

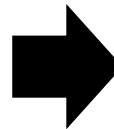


True simulated diplotypes

Assign random haplotypes to founders

Drop through real pedigree

- no mutations
- random crossing overs  
(Poisson-distribution recombination, uniform distribution)



0	1	...	2
0	1	...	0
2	0	...	1
1	2	...	0
0	1	...	0
1	0	...	0
0	2	...	1

Phasing with

- FImpute v2.2(w or w/out Pedigree)
- Beagle v3.3
- Beagle v4.1

Simulated genotypes

# Results Chr. 1



Phasing software	Window Subset	Equally phased			Breakpoints			Correctly phased [%]	Switched segment size			
		100	200	400	100	200	400		SNP		Bases	
		Mean	Median	Mean	Median							
FImpute	None-P	96.22	94.87	92.96	1.99	3.99	7.97	0.15	121.29	18.09	0.66	0.18
	One-P	99.63	99.40	99.21	0.13	0.26	0.52	72.92	86.22	63.30	0.57	0.43
	Both-P	99.85	99.79	99.77	0.12	0.23	0.46	88.04	25.15	11.75	0.20	0.12
	Total	98.81	98.30	97.66	0.56	1.13	2.25	54.63	108.01	57.42	0.66	0.40
FImpute no pedigree	None-P	97.35	95.60	92.84	0.62	1.25	2.50	0.21	191.55	17.75	1.05	0.19
	One-P	97.67	96.53	94.99	0.88	1.77	3.54	8.11	65.14	13.01	0.42	0.12
	Both-P	99.78	99.56	99.41	0.06	0.12	0.24	78.63	43.71	24.09	0.44	0.32
	Total	97.58	96.29	94.45	0.83	1.67	3.34	6.16	102.23	17.18	0.61	0.15
Beagle 3	None-P	98.97	98.14	96.52	0.11	0.22	0.44	11.60	1742.95	1285.82	9.39	7.44
	One-P	99.06	98.25	96.66	0.06	0.12	0.23	11.70	1929.92	1490.39	10.46	8.59
	Both-P	99.06	98.21	96.63	0.05	0.10	0.20	11.18	1965.24	1533.07	10.85	9.00
	Total	99.04	98.24	96.65	0.07	0.14	0.28	12.08	1911.22	1470.92	10.33	8.45
Beagle 4	None-P	99.85	99.62	99.23	0.04	0.08	0.17	88.45	1830.57	1545.96	9.70	8.28
	One-P	99.97	99.83	99.56	0.01	0.02	0.05	96.64	2006.97	1803.10	10.80	9.75
	Both-P	99.99	99.90	99.70	0.01	0.01	0.02	98.82	2094.93	2011.04	11.67	11.26
	Total	99.94	99.79	99.49	0.02	0.04	0.07	94.93	1946.97	1719.76	10.44	9.28

# Results Chr. 7



Phasing software	Window Subset	Equally phased			Breakpoints			Correctly phased [%]	Switched segment size			
		100	200	400	100	200	400		SNP		Bases	
		Mean	Median	Mean	Median							
FImpute	None-P	95.73	94.16	92.05	2.15	4.32	8.64	4.54	98.30	69.59	3.62	2.44
	One-P	99.56	99.35	99.10	0.12	0.24	0.48	75.46	23.70	21.48	2.92	2.68
	Both-P	99.83	99.81	99.78	0.09	0.18	0.36	88.82	5.70	4.91	1.17	1.05
	Total	98.64	98.09	97.36	0.59	1.18	2.36	57.70	45.05	35.96	3.39	2.72
FImpute no pedigree	None-P	94.35	91.95	88.71	2.62	5.30	10.64	10.46	60.00	41.89	2.85	1.87
	One-P	95.60	93.90	91.66	2.13	4.31	8.63	25.91	41.45	29.01	2.25	1.54
	Both-P	99.23	98.83	98.31	0.26	0.52	1.01	67.65	42.60	37.04	3.98	3.56
	Total	95.34	93.49	91.02	2.23	4.50	9.03	22.49	45.97	32.07	2.41	1.63
Beagle 3	None-P	98.88	98.04	96.22	0.11	0.22	0.44	24.12	444.42	432.80	23.04	22.37
	One-P	99.02	98.27	96.58	0.06	0.12	0.23	27.37	449.92	440.99	26.72	26.26
	Both-P	99.03	98.35	96.70	0.05	0.10	0.20	24.90	439.99	435.21	27.53	27.31
	Total	99.00	98.23	96.52	0.07	0.14	0.28	26.98	447.07	437.71	25.96	25.45
Beagle 4	None-P	99.70	99.53	99.09	0.04	0.08	0.16	76.91	40.42	37.20	8.43	7.73
	One-P	99.84	99.75	99.52	0.01	0.02	0.05	85.84	21.85	21.32	8.62	8.39
	Both-P	99.89	99.86	99.71	0.01	0.01	0.02	89.41	1.80	1.82	1.92	1.92
	Total	99.81	99.70	99.43	0.02	0.04	0.07	84.09	25.55	24.44	8.50	8.11

# Results Chr. 20



Phasing software	Window Subset	Equally phased			Breakpoints			Correctly phased [%]	Switched segment size			
		100	200	400	100	200	400		SNP		Bases	
		Mean	Median	Mean	Median							
FImpute	None-P	96.03	94.47	92.32	1.91	3.88	7.98	27.84	81.52	62.54	5.70	4.63
	One-P	99.57	99.40	99.20	0.11	0.22	0.44	84.25	50.16	44.68	3.51	3.22
	Both-P	99.83	99.78	99.75	0.07	0.16	0.33	93.12	11.42	9.82	0.50	0.44
	Total	98.75	98.24	97.57	0.52	1.05	2.15	70.55	70.89	57.91	4.93	4.23
FImpute no pedigree	None-P	96.17	94.45	92.20	1.51	3.03	6.06	41.91	83.80	63.17	5.95	4.69
	One-P	97.31	96.11	94.52	1.03	2.06	4.13	52.60	91.44	71.79	6.36	5.22
	Both-P	99.00	98.45	97.90	0.26	0.53	1.05	72.30	74.81	62.19	5.66	4.87
	Total	97.10	95.79	94.08	1.12	2.24	4.48	50.57	90.36	70.61	6.31	5.16
Beagle 3	None-P	99.18	98.49	97.09	0.10	0.19	0.39	64.74	316.55	306.15	22.37	21.77
	One-P	99.33	98.66	97.41	0.05	0.10	0.19	66.61	309.11	302.72	23.96	23.56
	Both-P	99.38	98.70	97.59	0.04	0.07	0.14	69.74	307.13	306.06	25.87	25.82
	Total	99.30	98.63	97.35	0.06	0.12	0.24	66.35	311.58	303.97	23.64	23.18
Beagle 4	None-P	99.73	99.52	99.15	0.04	0.07	0.15	87.68	122.67	113.62	9.69	9.26
	One-P	99.85	99.72	99.47	0.01	0.03	0.05	92.27	136.08	129.12	8.71	8.33
	Both-P	99.89	99.79	99.60	0.01	0.01	0.03	93.91	50.46	50.46	3.79	3.79
	Total	99.83	99.68	99.41	0.02	0.04	0.07	91.37	128.57	120.96	8.90	8.51