

Quantification of non-additive genetic effects in Nile tilapia using both pedigree and genomic information

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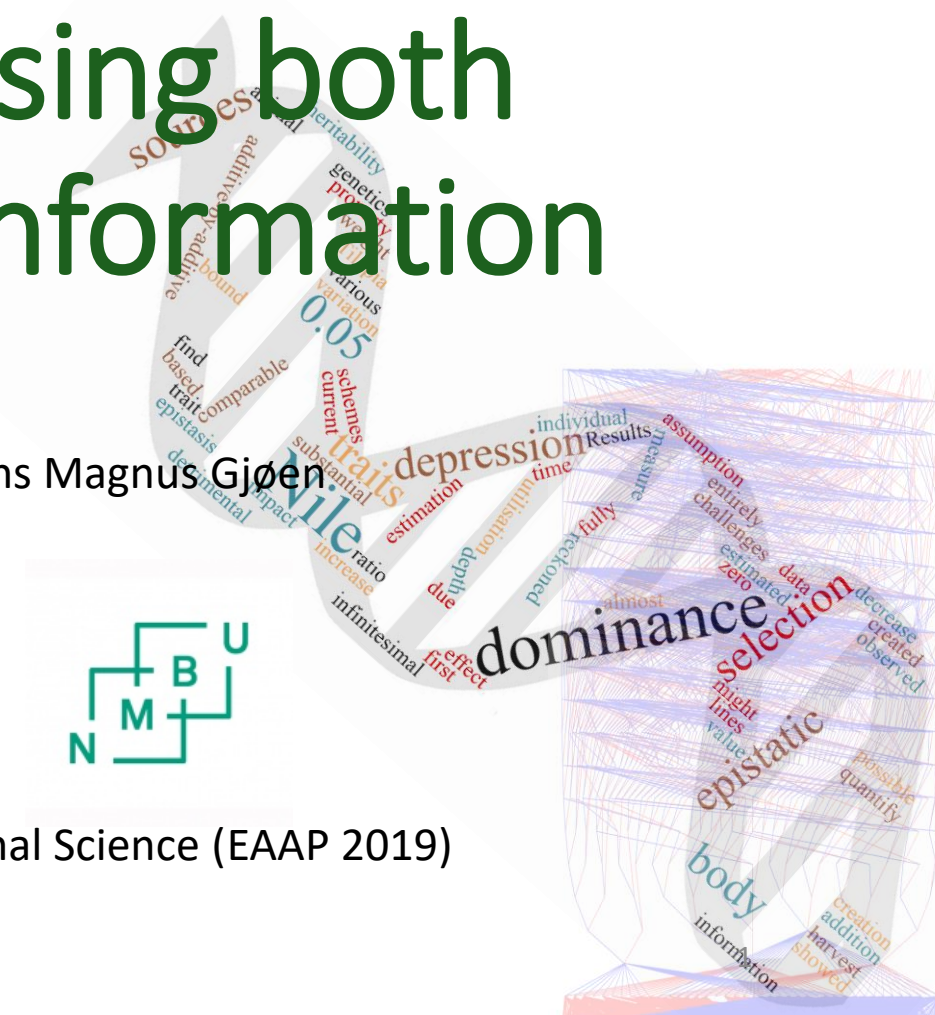


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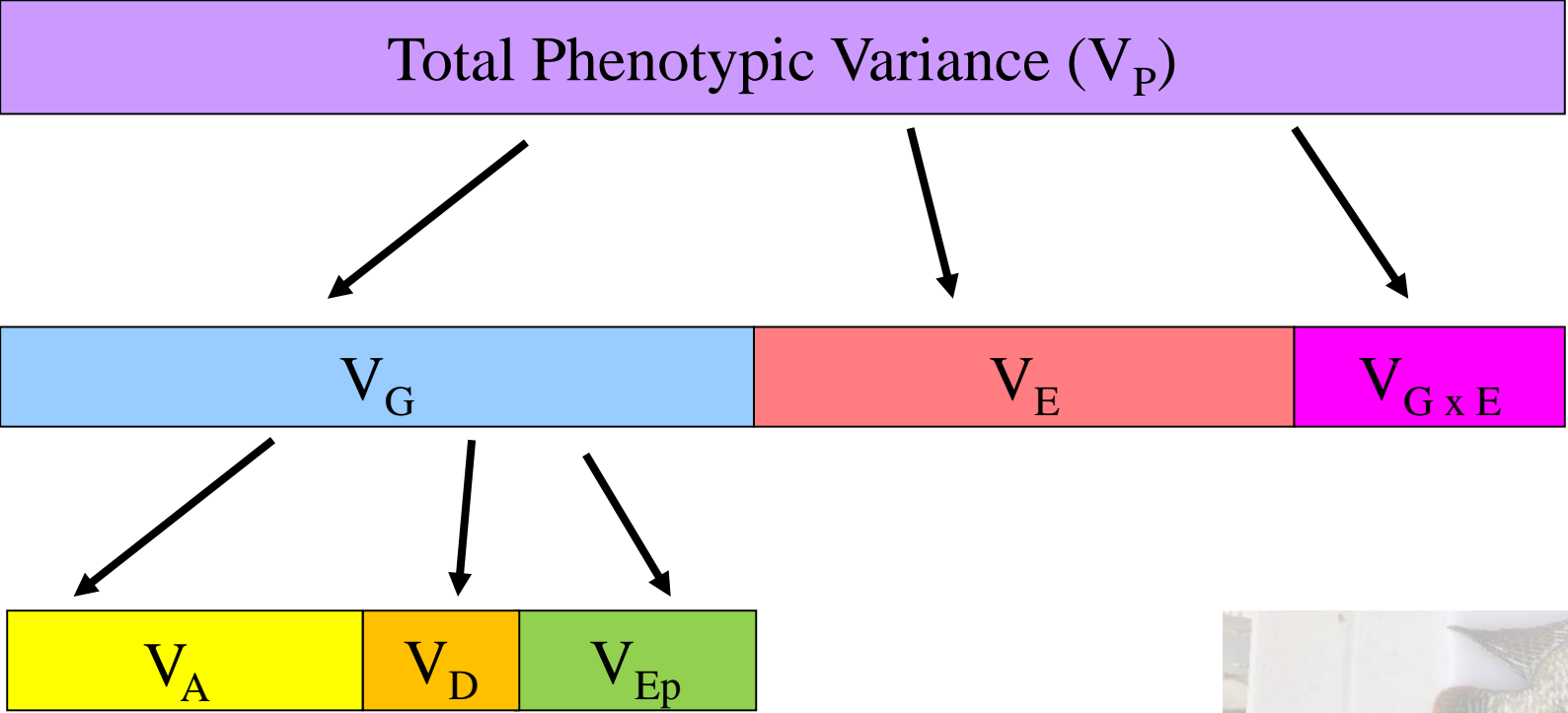
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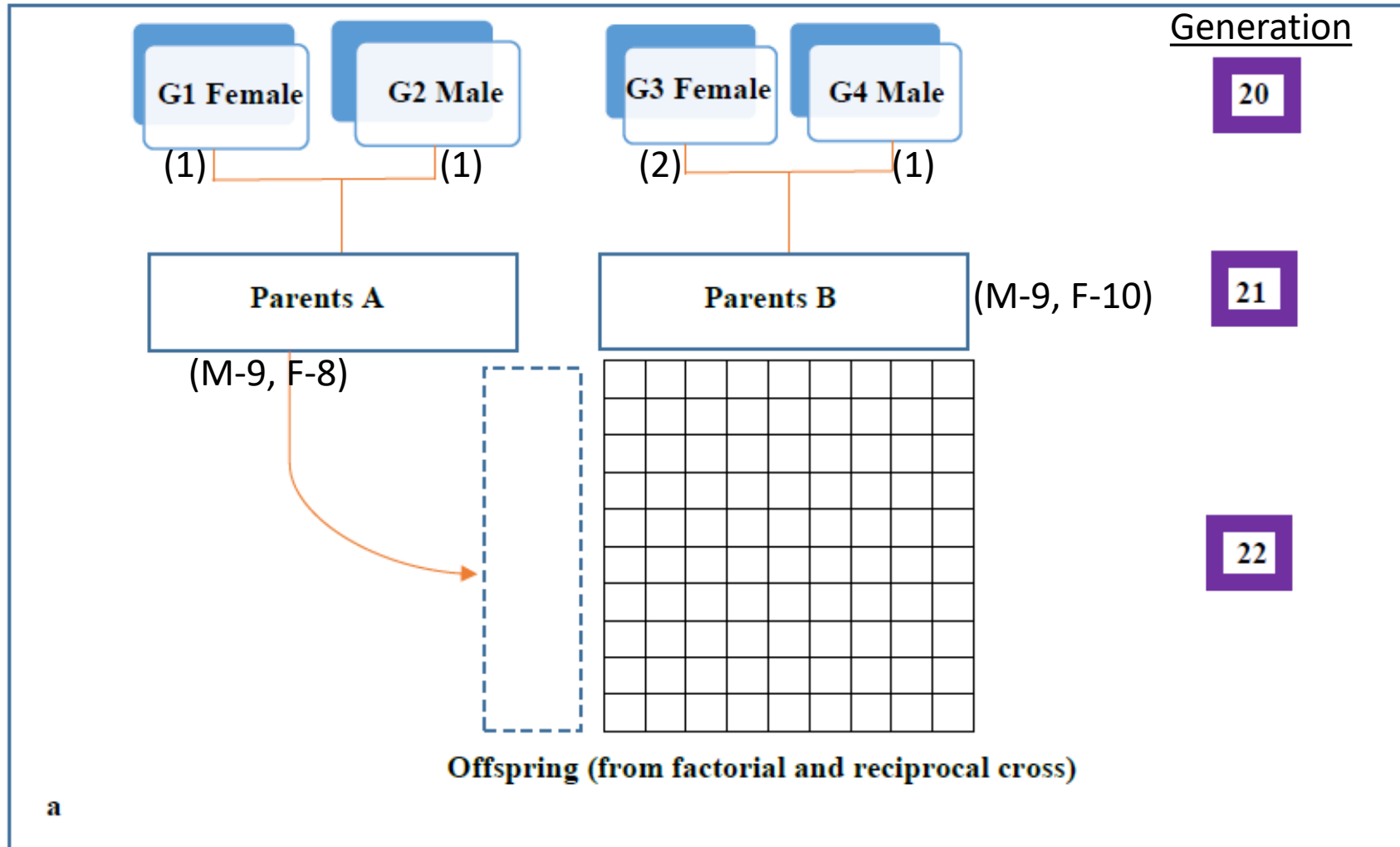


Introduction

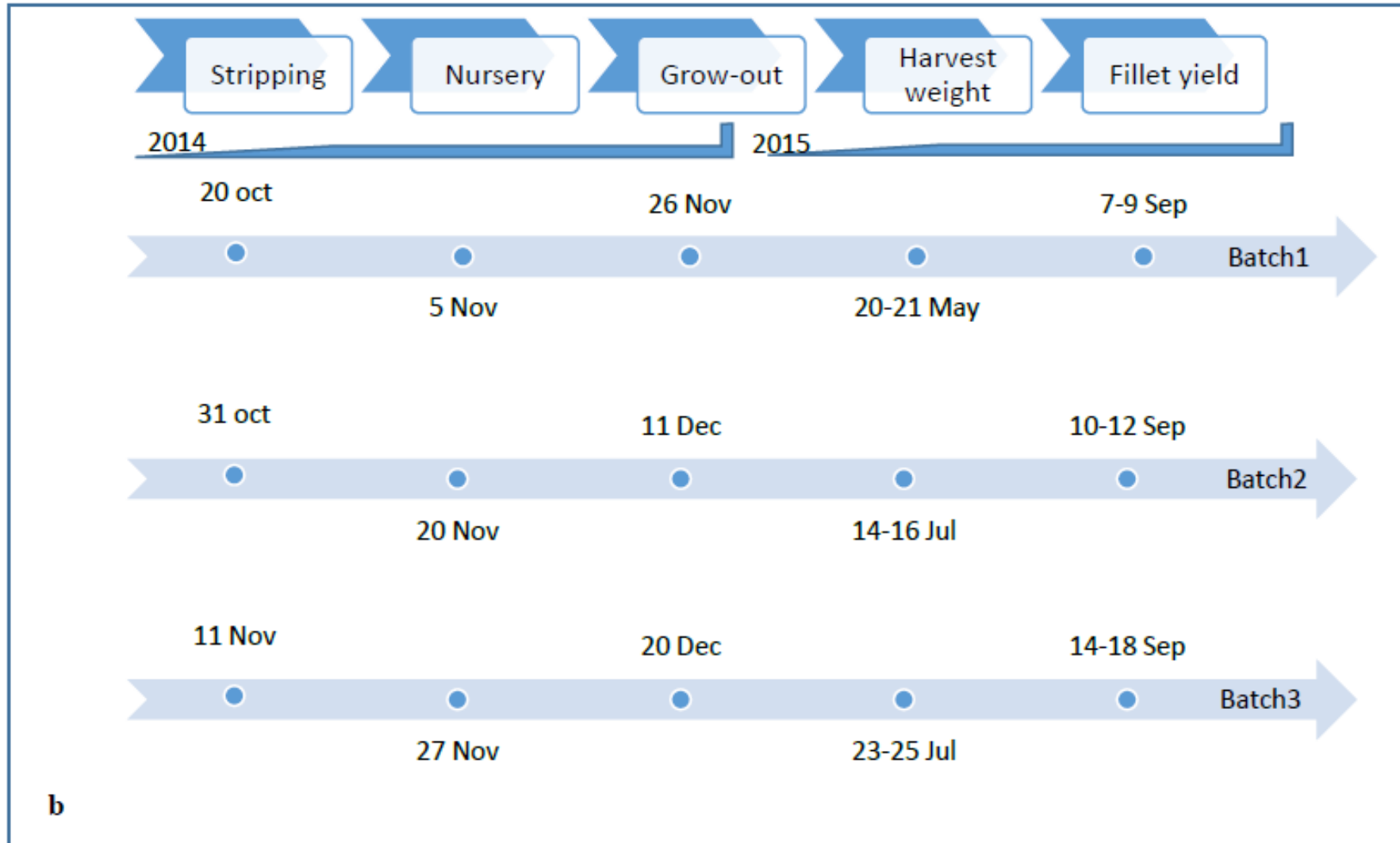
- 2nd most important aquaculture spp in terms of global production (7.4%)
- Commercial and farmed Nile tilapia strains derived from GIFT
- Despite having large full-sib families- non-additive genetic effects have been ignored in commercial structures
- Huge difference in profit between breeding programs that utilise non-additive vs. additive genetic effects



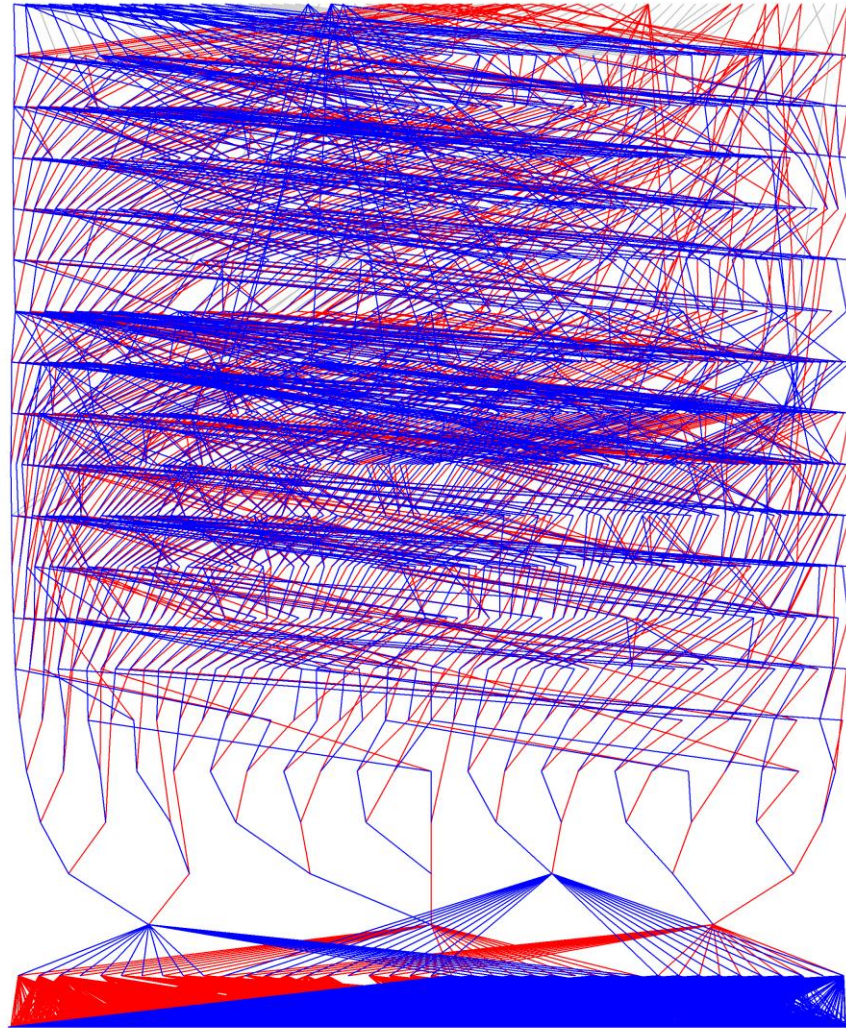
Experimental design



Experimental design.....



Experimental design.....



- **Observations:**
2524 (1318 A x B & 1206 B x A)
- **Fs-family:**
55 (Avg: 16.3)

Experimental design.....



Modification to the regular commercial Nile tilapia aquaculture practices

maternal effects in factorial crosses
are free from effects other than
maternal

Regular	Modifications
Hierarchical mating	Factorial design with reciprocal cross

Experimental design.....



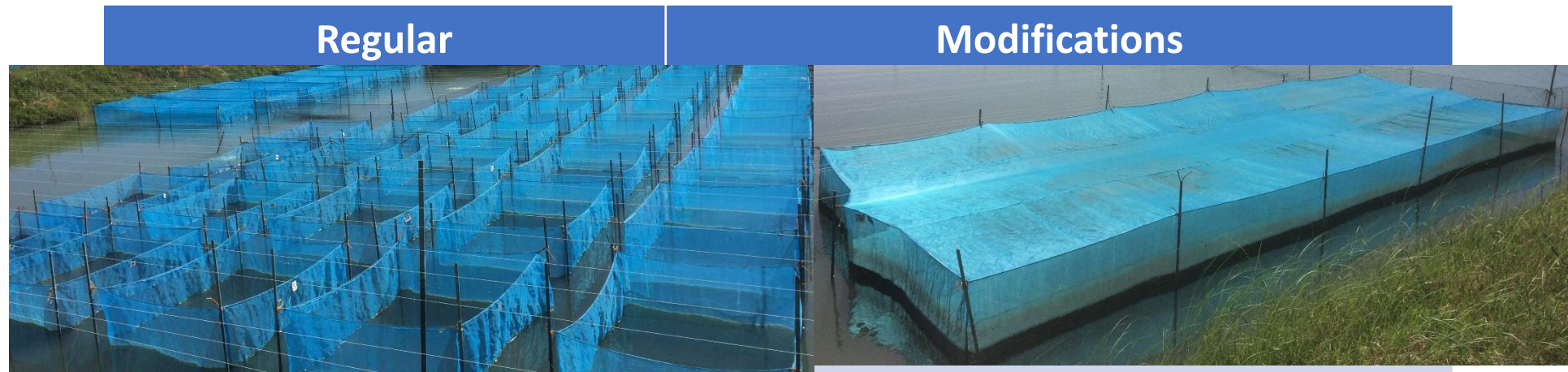
Modification to the regular commercial Nile tilapia aquaculture practices

Confounds fs-family
and maternal effects

Regular	Modifications
Hierarchical mating	Factorial design with reciprocal cross
Natural mating and mouth brooding	Artificial breeding

Experimental design.....

Modification to the regular commercial Nile tilapia aquaculture practices



Regular

Modifications

Confounds tank, fs-family and maternal effects

Statistical model

ADM Model

$$y = Xb + Z_1a + Z_2d + Z_3m + e$$

BD BL
BT
BWH
FW
FY



Statistical model



ADM Model

$$\mathbf{y} = \mathbf{Xb} + \mathbf{Z}_1\mathbf{a} + \mathbf{Z}_2\mathbf{d} + \mathbf{Z}_3\mathbf{m} + \mathbf{e}$$

BD BL
BT
BWH
FW
FY

Reciprocal cross
batch
day of harvest /
day of filleting
filleter

A- Numerator relⁿ
matrix- pedigree

$$\text{Var} \begin{bmatrix} a \\ d \\ m \\ e \end{bmatrix} = \begin{bmatrix} \mathbf{A}\sigma_A^2 & 0 & 0 & 0 \\ 0 & \mathbf{D}\sigma_D^2 & 0 & 0 \\ 0 & 0 & \mathbf{I}\sigma_M^2 & 0 \\ 0 & 0 & 0 & \mathbf{I}\sigma_E^2 \end{bmatrix}$$

D- matrix of coefficients of fraternity

R package 'nadiv' (Wolak, 2012)

- $h^2 = \sigma_A^2 / \sigma_P^2$, $d^2 = \sigma_D^2 / \sigma_P^2$, $m^2 = \sigma_M^2 / \sigma_P^2$.
- A, AM, AD models
- LRT - goodness of fit

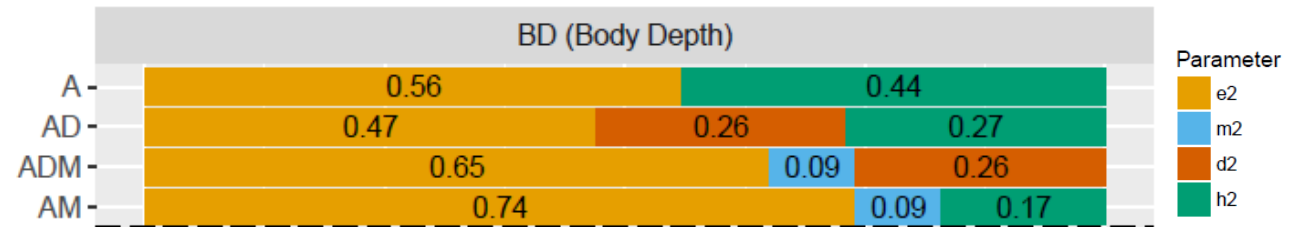
Results: Goodness of fit



- BL and FY - no evidence of maternal and dominance effects
- BT and FW - evidence of maternal effects
- BWH and BD - significant maternal and dominance effects

Estimates of heritabilities....

- Simple model
high h^2
- Inclusion of dominance
 $\downarrow h^2$
- Maternal effect
 $\downarrow h^2$ considerably



Traits	ADM models		
	h^2	d^2	m^2
BD	0 (0)	0.26 (0.09)	0.09 (0.04)
BWH	0 (0)	0.22 (0.08)	0.09 (0.04)
BT	0.11 (0.06)	—	0.03 (0.02)
FW	0.10 (0.05)	—	0.11 (0.05)
BL	0.29 (0.08)	—	—
FY	0.24 (0.07)	—	—

Genomics

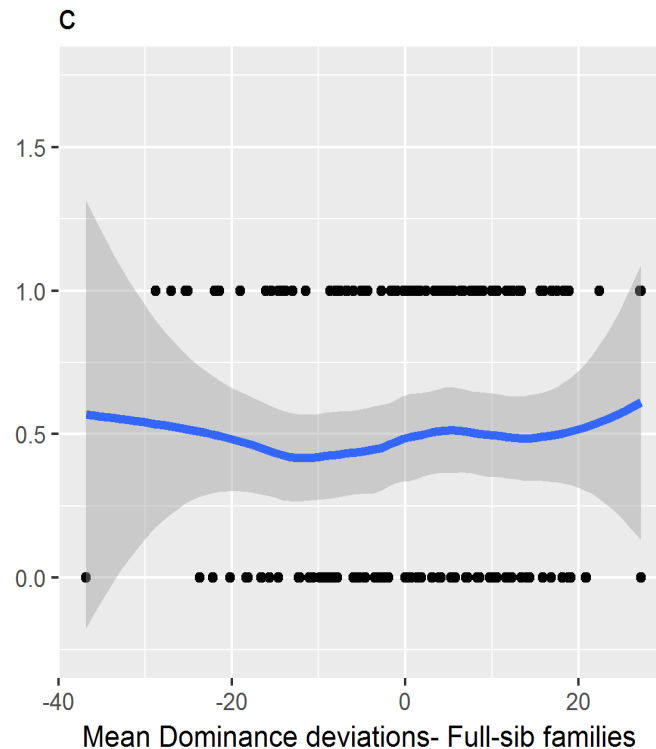


- Phenotypes and genotypes from 1119 individuals in 74 full-sib families (average of 15.1 offspring per family)
- SNP filtration:
 1. PolyHighResolution
(formation of 3 clusters with good resolution)
 2. NoMinorHom
(formation of two clusters with no samples of one homozygous genotype) → 74% SNPs
 3. $MAF \geq 0.05$ → 68.3%
- Individual homozygosity was calculated as the proportion of homozygous loci per individual as a measure of directional dominance

Comparison with pedigree approach

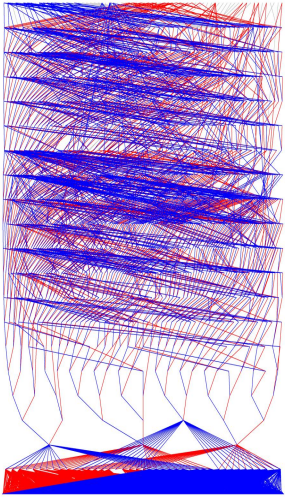


- Data used in genomic study: a subset of pedigree data, with some evidence of non-randomness in the sampling



The selected individuals were coded as 1 and the non-selected individuals were coded as 0

Statistical analysis



ADM model- Pedigree

$$\mathbf{y} = \mathbf{X}\mathbf{b} + \mathbf{Z}_1\mathbf{a} + \mathbf{Z}_2\mathbf{d} + \mathbf{Z}_3\mathbf{m} + \mathbf{e}$$

$$\text{Var} \begin{bmatrix} a \\ d \\ m \\ e \end{bmatrix} = \begin{bmatrix} A\sigma_A^2 & 0 & 0 & 0 \\ 0 & D\sigma_D^2 & 0 & 0 \\ 0 & 0 & I\sigma_M^2 & 0 \\ 0 & 0 & 0 & I\sigma_E^2 \end{bmatrix}$$

A, AM, AD models

ADME model- Genomics

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{h}\mathbf{b} + \mathbf{Z}_1\mathbf{a} + \mathbf{Z}_2\mathbf{d} + \mathbf{Z}_3\mathbf{e}_{aa} + \mathbf{Z}_4\mathbf{m} + \mathbf{e}$$

$$\text{Var} \begin{bmatrix} a \\ d \\ e_{aa} \\ m \\ e \end{bmatrix} = \begin{bmatrix} \mathbf{G}\sigma_A^2 & 0 & 0 & 0 & 0 \\ 0 & \mathbf{D}\sigma_D^2 & 0 & 0 & 0 \\ 0 & 0 & k(\mathbf{G}\#\mathbf{G})\sigma_{E_{aa}}^2 & 0 & 0 \\ 0 & 0 & 0 & \mathbf{I}\sigma_M^2 & 0 \\ 0 & 0 & 0 & 0 & \mathbf{I}\sigma_E^2 \end{bmatrix}$$

A, AM, AD, ADE, ADME, ADM, AME, AE models

is the hadamard product- element by element multiplication

Construction of RMs

NOIA approach

relaxes the assumption of HWE

$$\mathbf{G} = \frac{\mathbf{Z}\mathbf{Z}'}{2 * \sum_{i=1}^m p_i(1-p_i)}$$

\mathbf{Z} is the centered $(-2p_i)$ matrix, p_i is the allele frequency of the second allele

$$\mathbf{D} = \frac{\mathbf{H}_d \mathbf{H}_d'}{\text{tr}(\mathbf{H}_d \mathbf{H}_d')/n}$$

\mathbf{H}_d contains dominance coefficients (h_d)

$$h_d = \begin{cases} -\frac{2p_{AB} p_{BB}}{p_{AA} + p_{BB} - (p_{AA} - p_{BB})^2} \\ \frac{4p_{AA} p_{BB}}{p_{AA} + p_{BB} - (p_{AA} - p_{BB})^2} \\ -\frac{2p_{AA} p_{AB}}{p_{AA} + p_{BB} - (p_{AA} - p_{BB})^2} \end{cases} \text{ for genotypes } \begin{cases} AA \\ AB \\ BB \end{cases}$$

$$k(\mathbf{G}\#\mathbf{G}), k = \frac{1}{\text{tr}(\mathbf{G}\#\mathbf{G})/n}$$

Results

1. Genetic Architecture

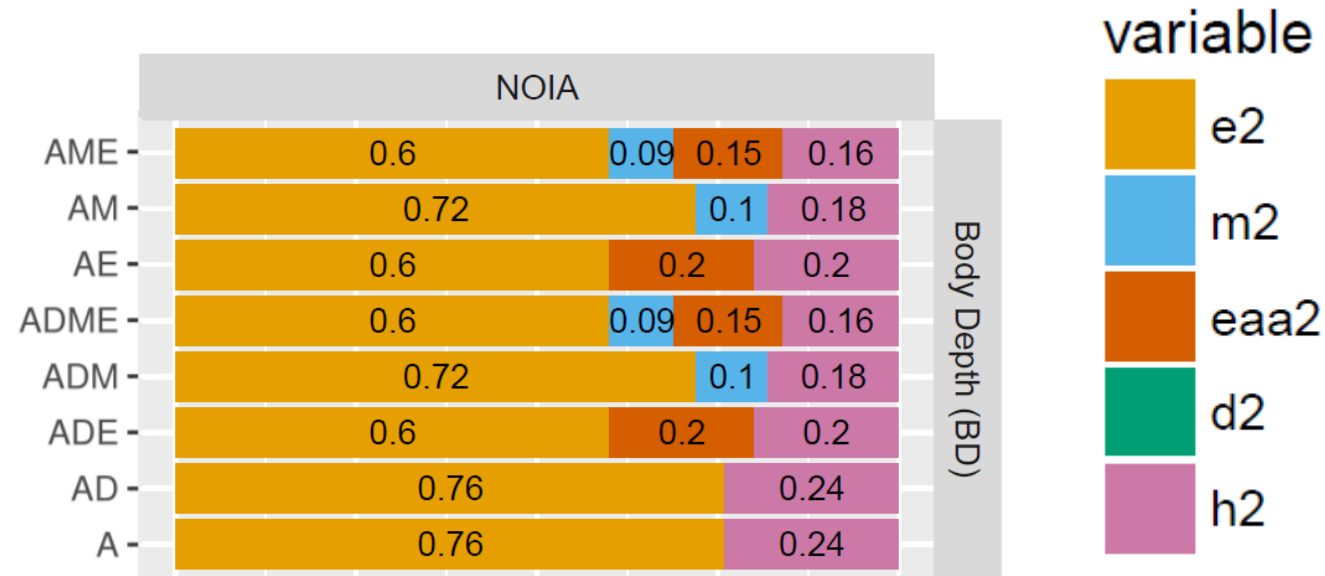
	Genomics
no evidence of maternal and non-additive genetic effects	BT and FY
evidence of maternal effects	BL and FW
significant maternal and non-additive genetic effects	BD and BWH

Results

1. Genetic Architecture

	Genomics	Pedigree
no evidence of maternal and non-additive genetic effects	BT and FY	BL and FY
evidence of maternal effects	BL and FW	BT and FW
significant maternal and non-additive genetic effects	BD and BWH	BD and BWH

Decomposition of variance components



- simple A model - higher σ^2_A & h^2 across all the traits
- Genomic: addⁿ of Dominance – no effect to σ^2_A , but Epistasis \downarrow σ^2_A
- Maternal effect \downarrow h^2 considerably
- BT and FY: no effects

Trait	Model	σ^2_A	σ^2_{Eaa}	σ^2_m	σ^2_e	σ^2_p	h^2	H^2	m^2	e_{aa}^2
NOIA										
BD	AME	0.086 (0.024)	0.080 (0.049)	0.047 (0.032)	0.328 (0.044)	0.541 (0.039)	0.158 (0.042)	0.307 (0.090)	0.087 (0.055)	0.148 (0.091)
BWH	AME	699 (268)	1183 (680)	635 (418)	4540 (618)	7059 (498)	0.099 (0.037)	0.266 (0.093)	0.090 (0.054)	0.167 (0.096)
BL	AM	0.284 (0.107)		0.257 (0.162)	2.803 (0.136)	3.345 (0.209)	0.085 (0.031)		0.076 (0.045)	
FW	AM	118 (42)		99 (63)	1009 (50)	1227 (79)	0.096 (0.033)		0.080 (0.047)	
BT	A	1.695 (0.441)			8.015 (0.411)	9.710 (0.458)	0.174 (0.041)			
FY	A	1.758 (0.406)			7.461 (0.378)	9.220 (0.435)	0.190 (0.039)			

Inbreeding depression



regression coeff on individual homozygosity

	BD	BWH	BL	FW	BT	FY
b	-3.27** (1.19)	-371** (137)	-7.57* (2.95)	-156** (56)	-7.08 (5.05)	-6.90 (4.93)
D	0.37	0.91	0.34	1.08	0.17	0.21
Unit	cm	g	cm	g	mm	%

% decrease in the trait value per 1% increase in the individual homozygosity due to inbreeding depression

Conclusions

- The estimates of the additive by additive epistatic ratio ($P < 0.05$) was found to be 0.15 and 0.17 in the current breeding population using genomic data.
- maternal variance ($P < 0.05$) for BD, BWH, BL and FW explaining approximately 10% of the observed phenotypic variance.
- negative effects of inbreeding, with 1.1%, 0.9%, 0.4% and 0.3% decrease in the trait value with 1% increase in the individual homozygosity for FW, BWH, BD and BL, respectively.