Session 15

Age-dependent quantitative trait loci (QTL) affecting growth in sheep

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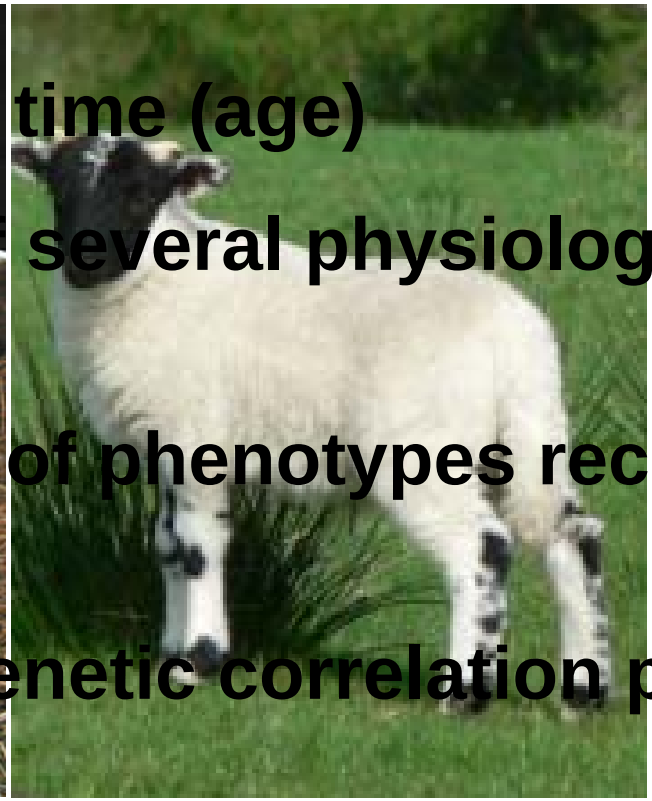
Background

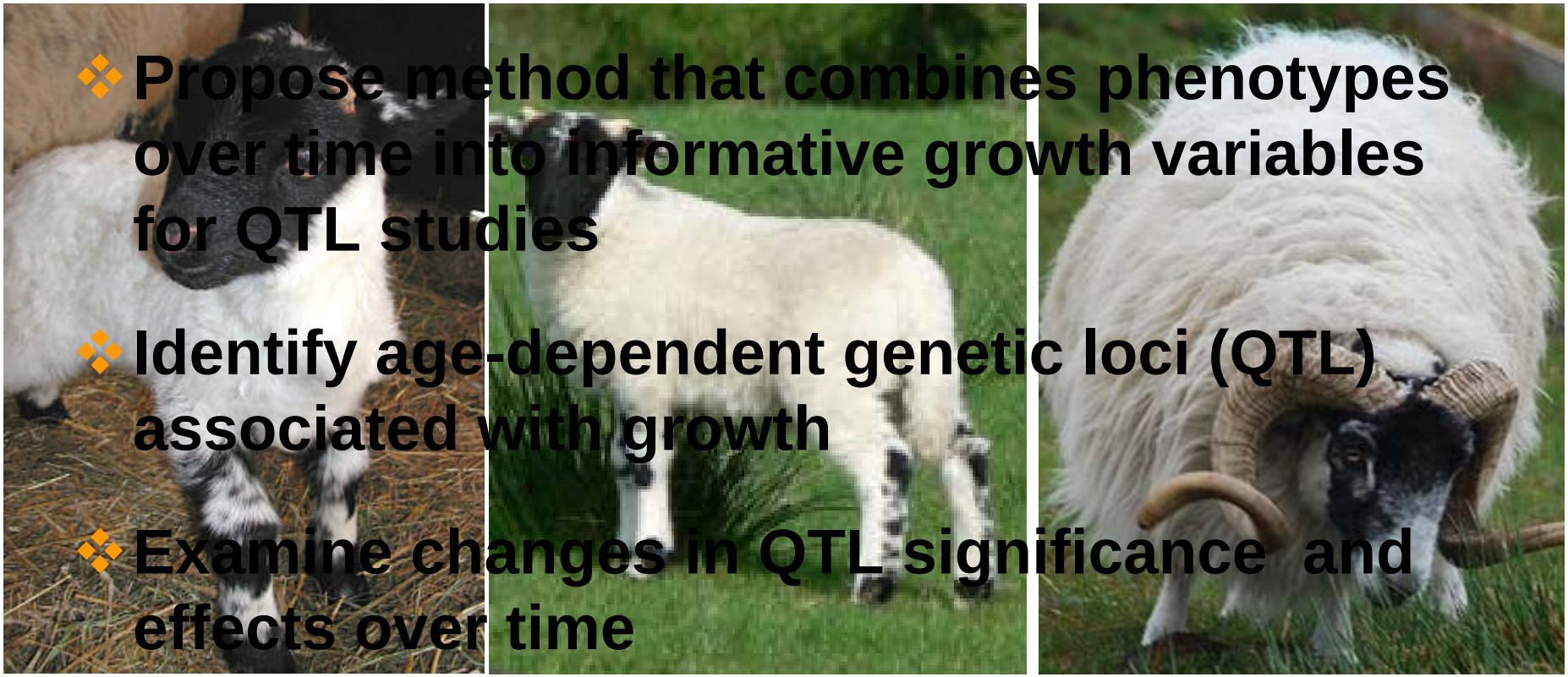
Background

Growth: longitudinal trait



- Varies with time (age)
- Function of several physiological processes
- Composite of phenotypes recorded over time
- Complex genetic correlation patterns

Objectives



- Propose method that combines phenotypes over time into informative growth variables for QTL studies
- Identify age-dependent genetic loci (QTL) associated with growth
- Examine changes in QTL significance and effects over time

Research Process

Dataset:

788 Scottish Blackface lambs, 9 half-sib families

- **Live weights at 4-week intervals (birth-24 weeks)**
- **Marker information (8 chromosomes)**

A) Fit growth models to live weights

- **Derive growth descriptors from model**

B) Map QTL for growth components

- **Describe QTL significance over time**

Research Process

A) Growth Model: Longitudinal model for a longitudinal trait

Gompertz Model

$$Y(t)=Ae^{\{-e^{[Be(C-t)/A]}\}}$$

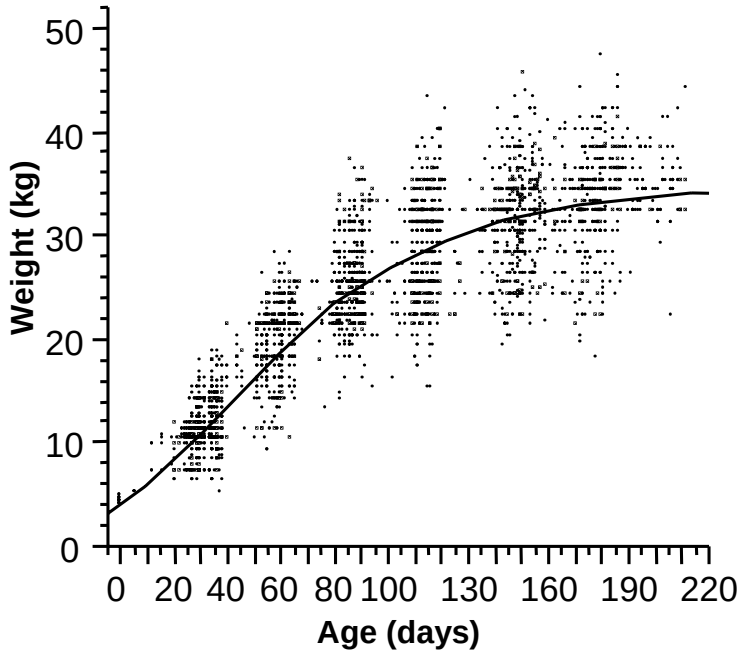
Y: live weight at time t

A: final body weight (kg)

B: max. growth rate (kg/d)

C: age at max. growth rate (d)

dY(t)/dt: growth rate at time t



Research Process

A) Growth Model: Longitudinal model for a longitudinal trait

Outcomes

- **Estimated Gompetz model parameters (A, B, C)**
- **Predicted growth rates and live weights**

"Univariate" Traits Encompassing Longitudinal Growth Information

Research Process

A) Growth Model: Longitudinal model for a longitudinal trait

Output Summary: More informative and biologically relevant growth descriptors for QTL Analyses

Observed weights at 4-week intervals	Final body weight (A) Max. growth rate (B) Age at max. growth rate (C)	Predicted growth rates and weights at weekly intervals

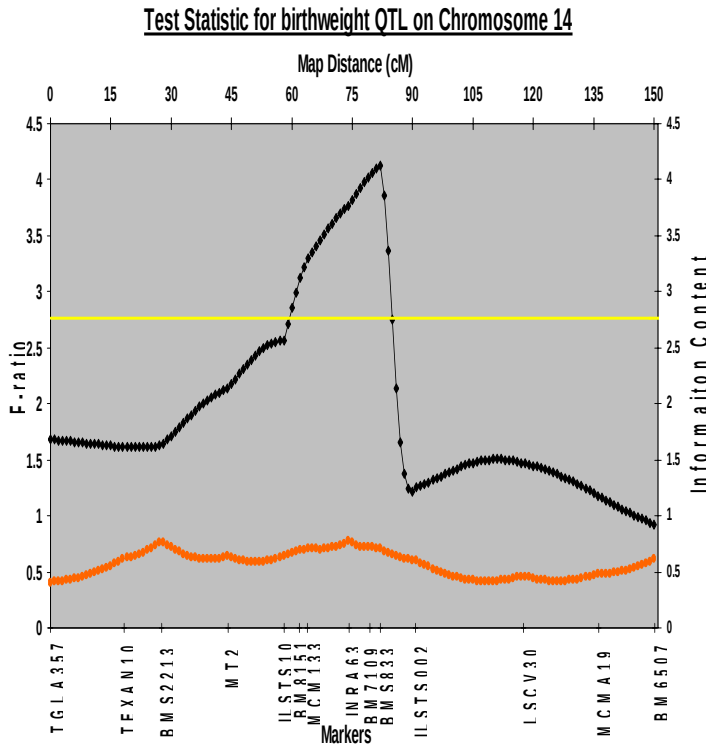
For Each Lamb

Research Process

B) Growth QTL Mapping: Univariate approach for a longitudinal trait

- Interval QTL mapping
  - Half-sib regression*
  - OAR 1-3, 5,14,18, 20, 21
- QTL significance and effects over time for predicted growth descriptors

*(Knott *et al.* 1996)



Results: Observed Live Weight QTL

Trait	OAR	QTL Position (cM)	F-statistic*
Birth Wt (kg)	14	82	4.13 (2.76, 3.38)
8wk Wt (kg)	14	110	2.8 (2.47, 3.00)
16wk Wt (kg)	20	61	2.53 (2.47, 3.03)

*Chromosome-wide thresholds (P<0.05; P<0.01) determined via permutation testing (Churchill & Doerge 1994)

Results: Growth Model Parameter QTL

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Max. Growth Rate (B) (kg/d)	**20**	**60**	**2.92 (2.41, 2.92)**

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Results: Growth Model Parameter QTL

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Birt			.38)
8wk			.00)
16w			.03)
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Growth QTL detected:

- for observed weights
- for growth model parameters
- at specific time points

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Results: Growth Model Parameter QTL

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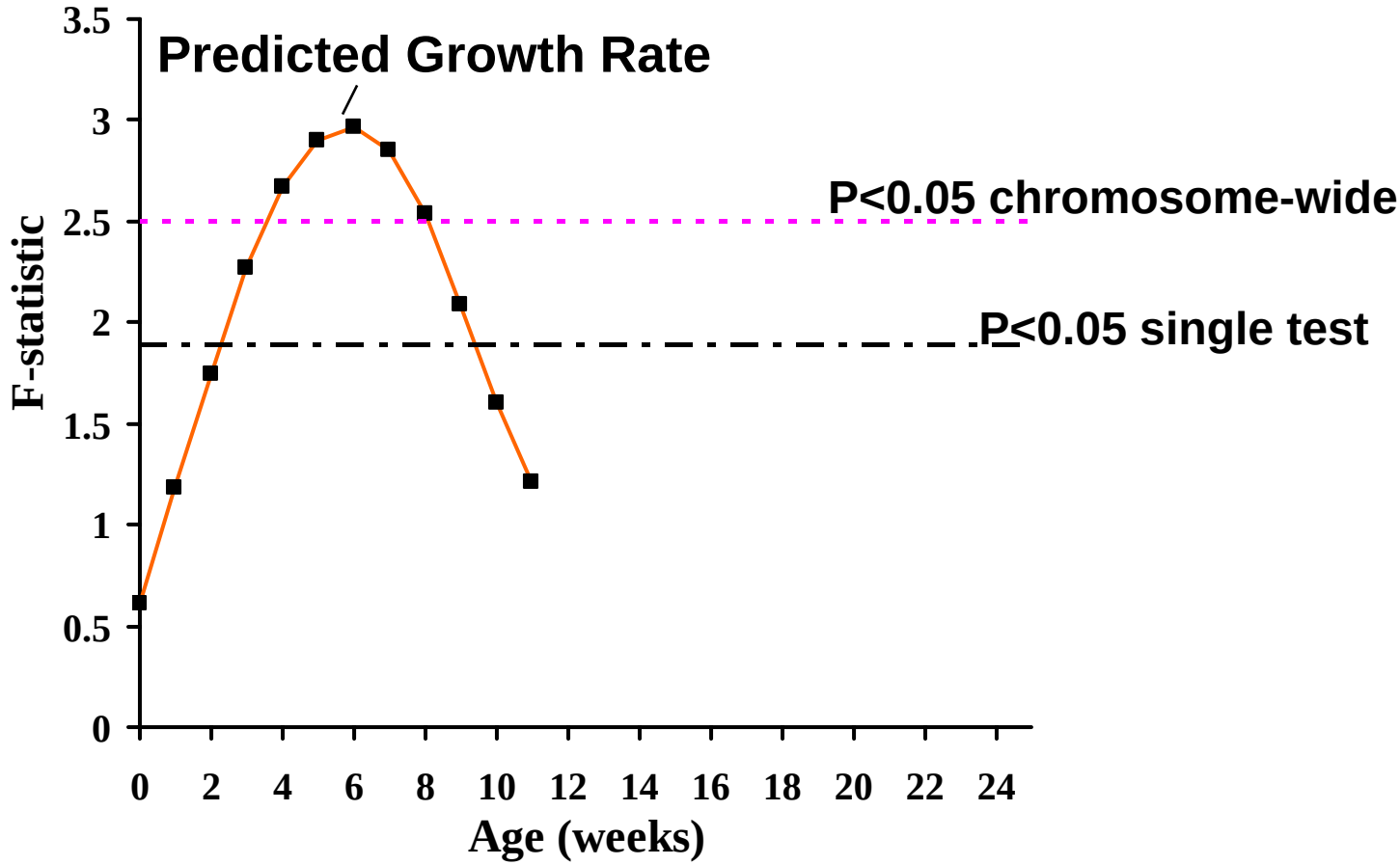
Are these (or other) QTL age-dependent?

*Chromosome-wide thresholds (P<0.05; P<0.01) determined via permutation testing (Churchill & Doerge 1994)

Results: Age-dependent Growth QTL

Chromosome 20, QTL at 60 cM



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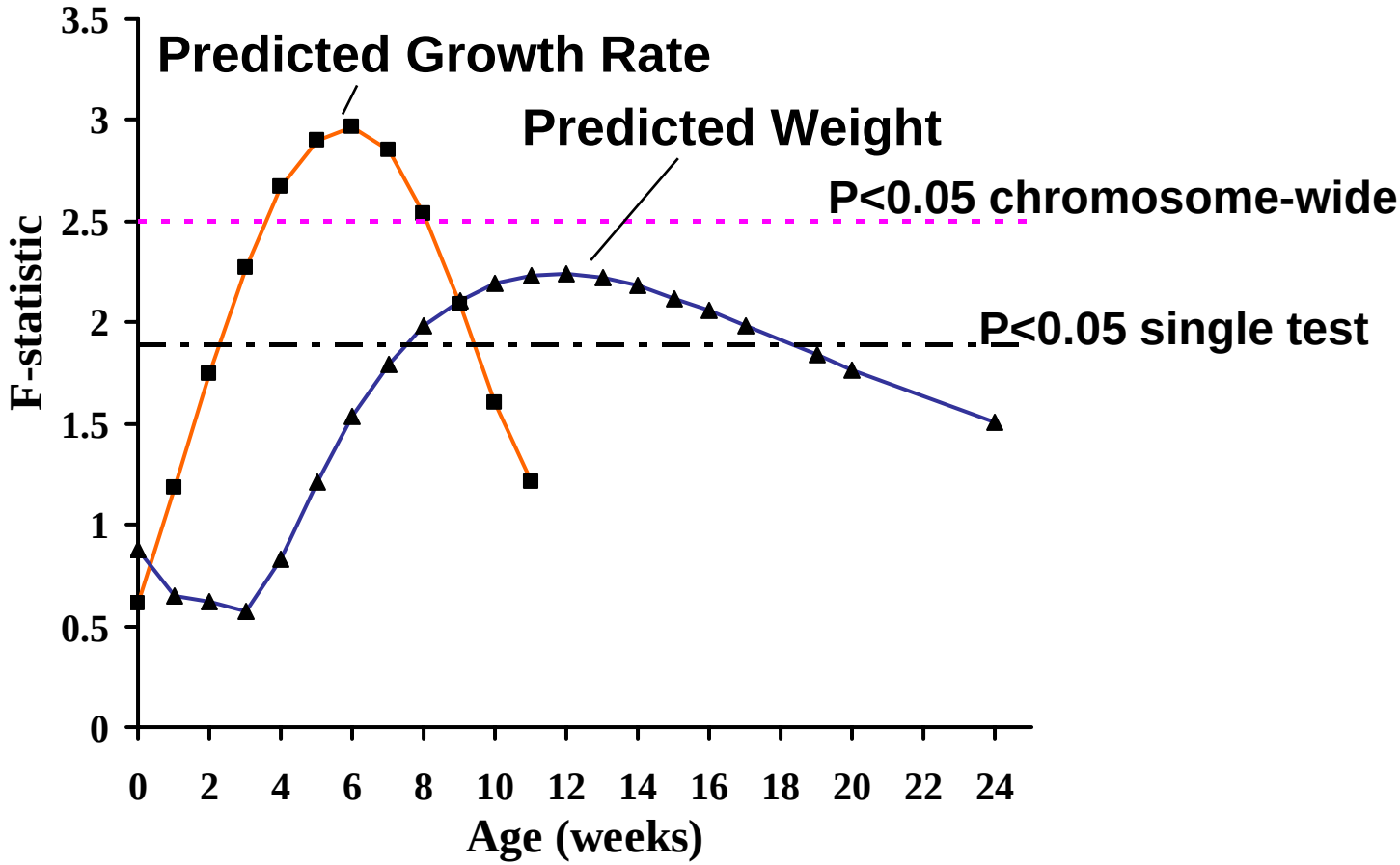

Results: Age-dependent Growth QTL

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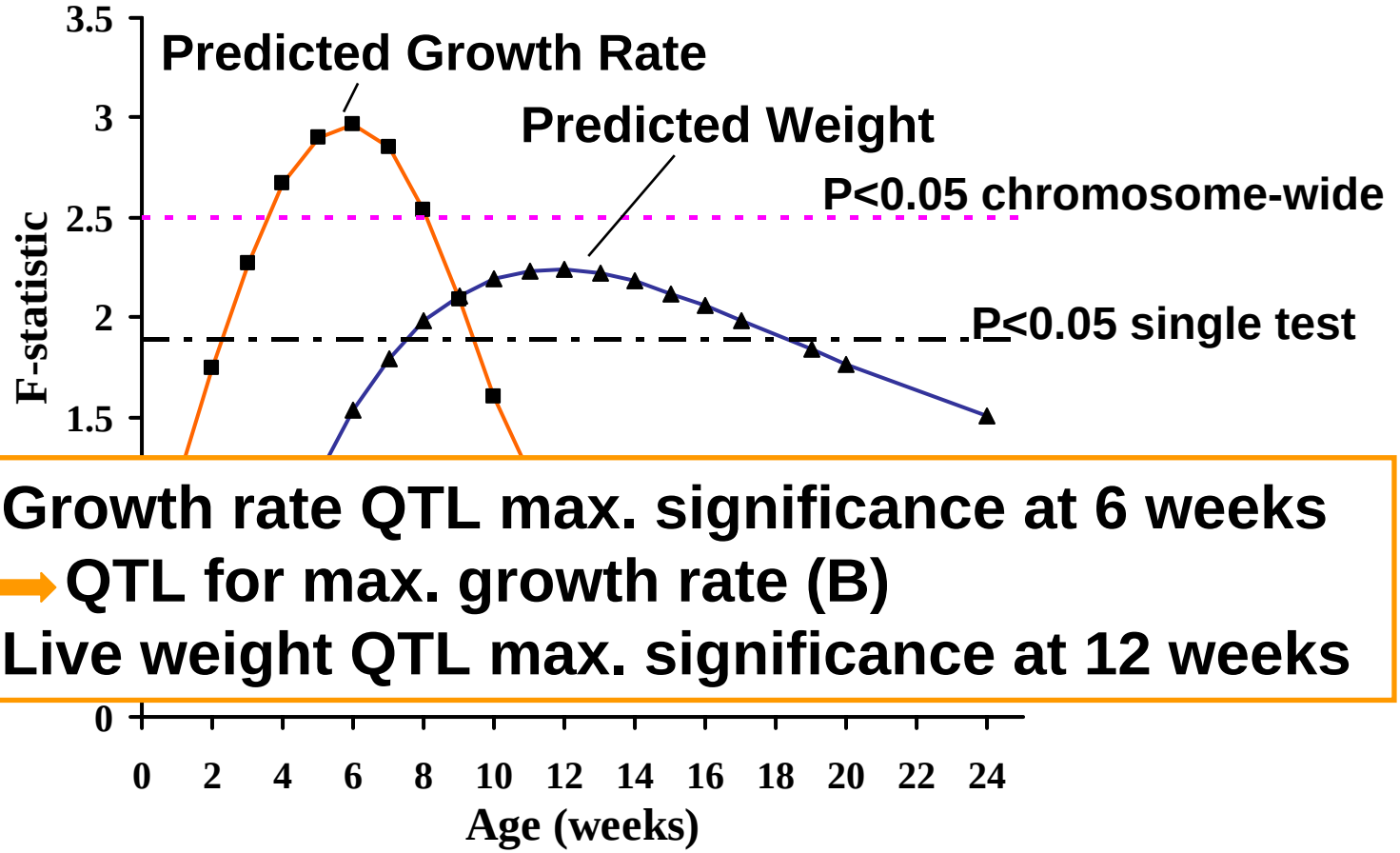
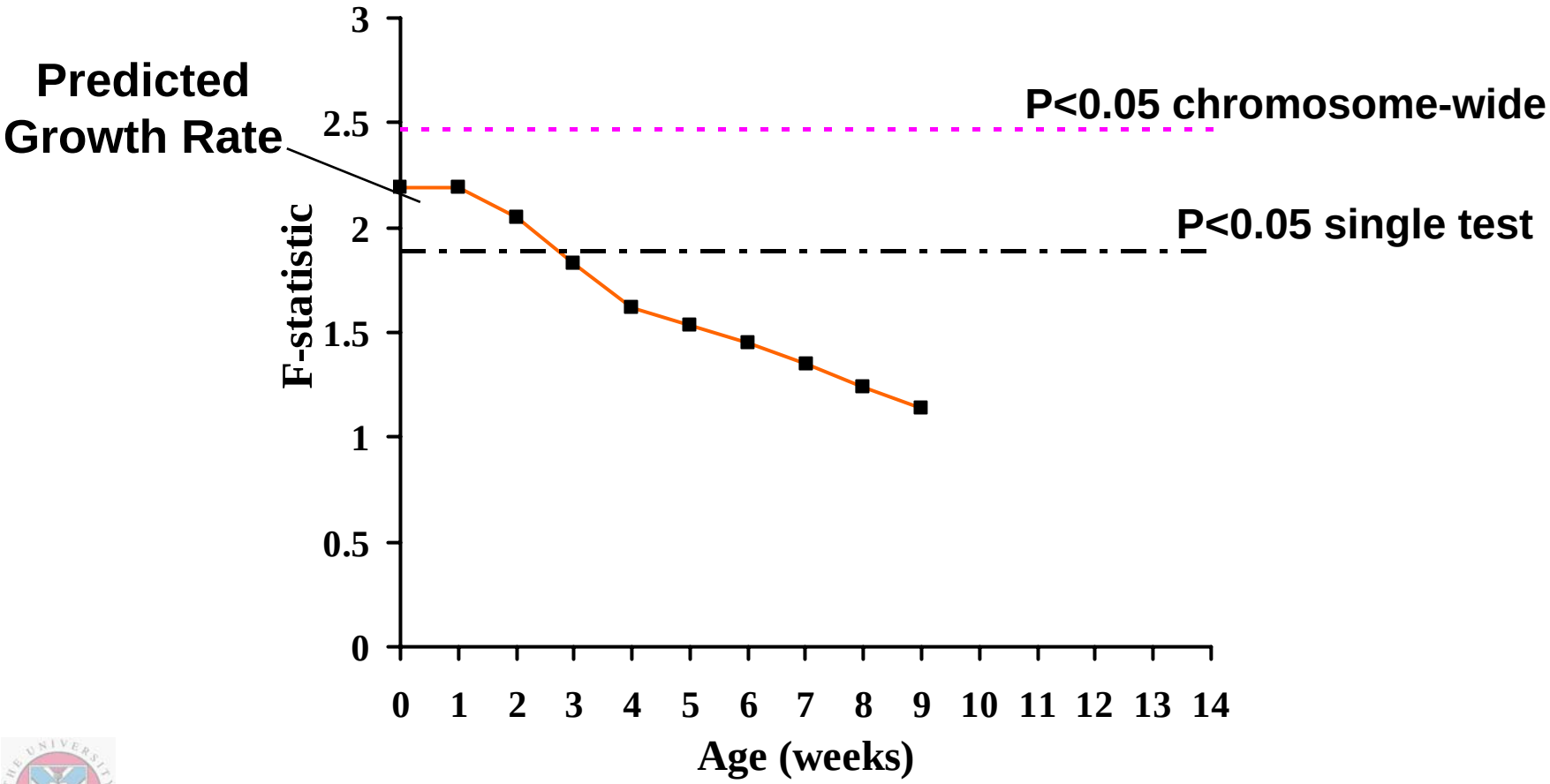


- Growth rate QTL max. significance at 6 weeks
  - ➡ QTL for max. growth rate (B)
- Live weight QTL max. significance at 12 weeks

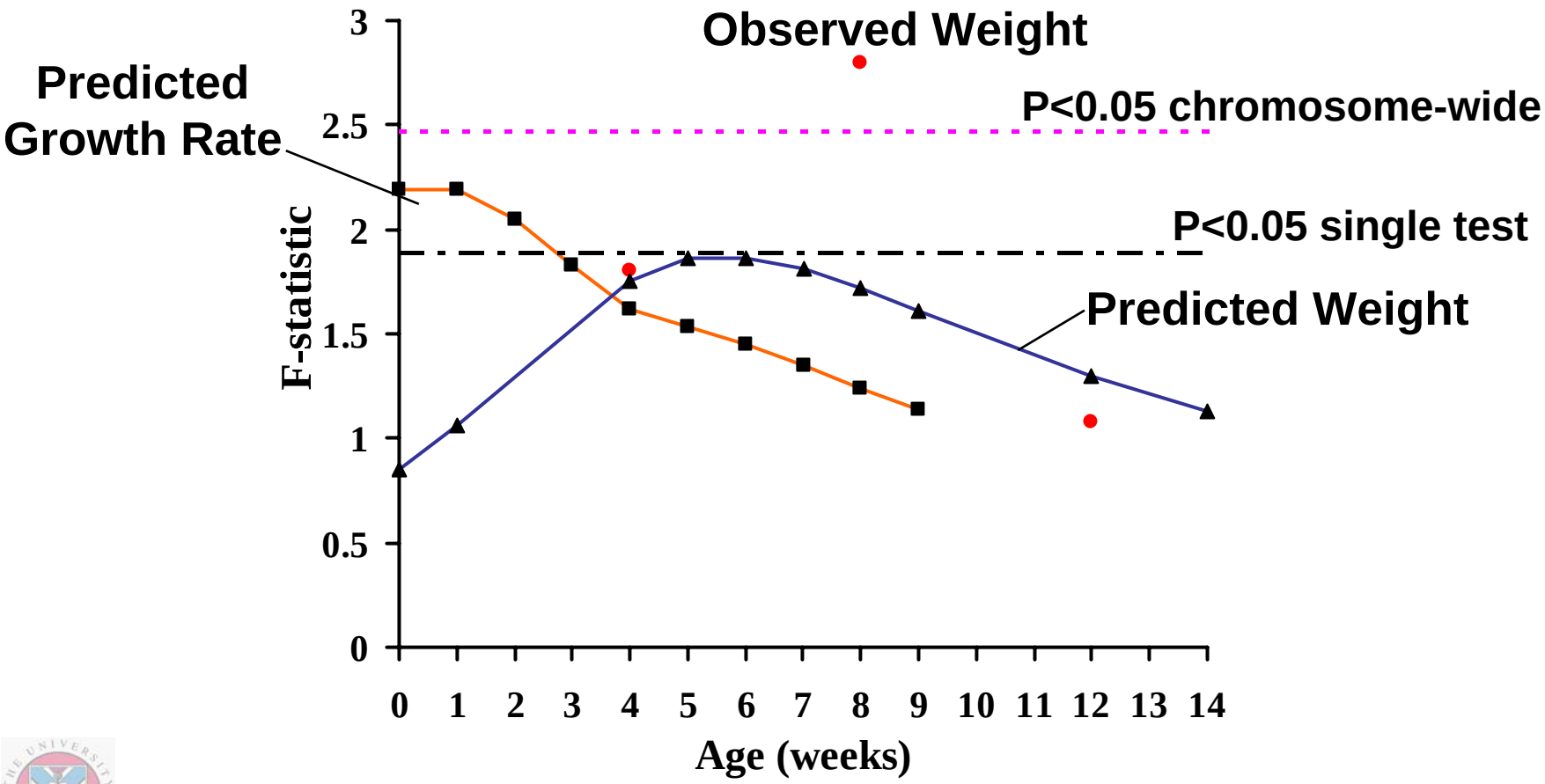
Results: Age-dependent Growth QTL

Chromosome 14, QTL at 105 cM



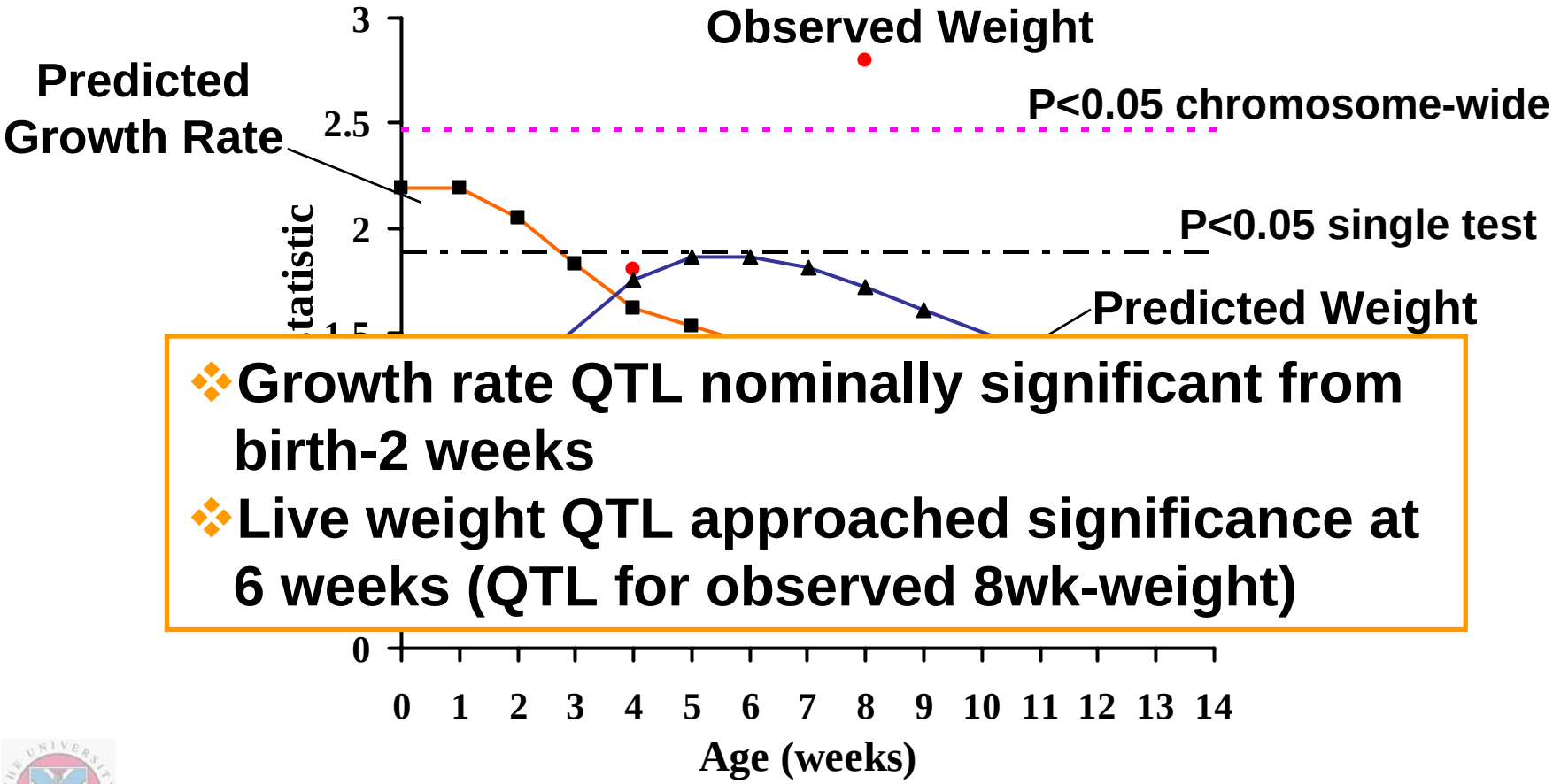
Results: Age-dependent Growth QTL

Chromosome 14, QTL at 105 cM



Results: Age-dependent Growth QTL

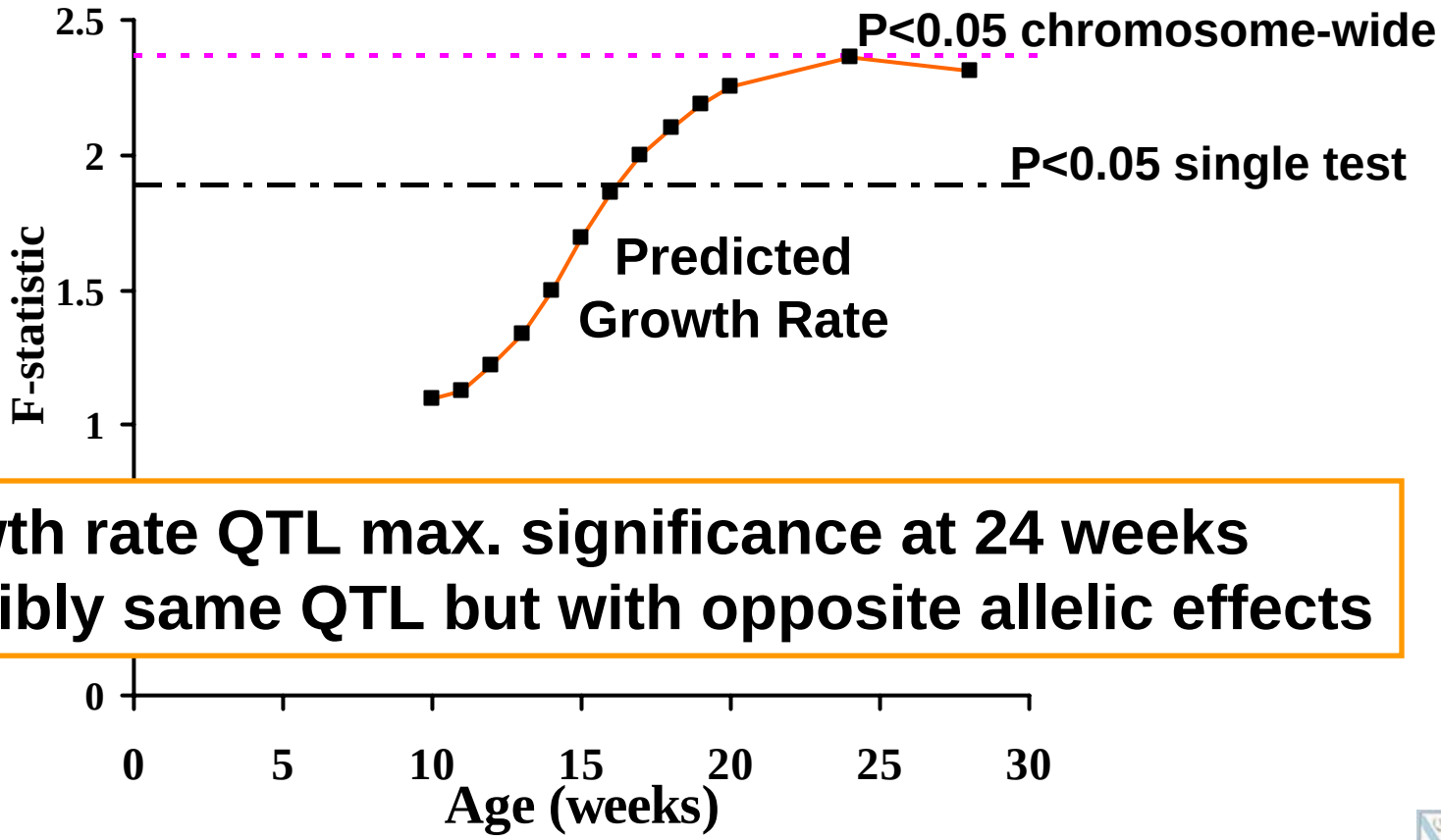
Chromosome 14, QTL at 105 cM



- Growth rate QTL nominally significant from birth-2 weeks
- Live weight QTL approached significance at 6 weeks (QTL for observed 8wk-weight)

Results: Age-dependent Growth QTL

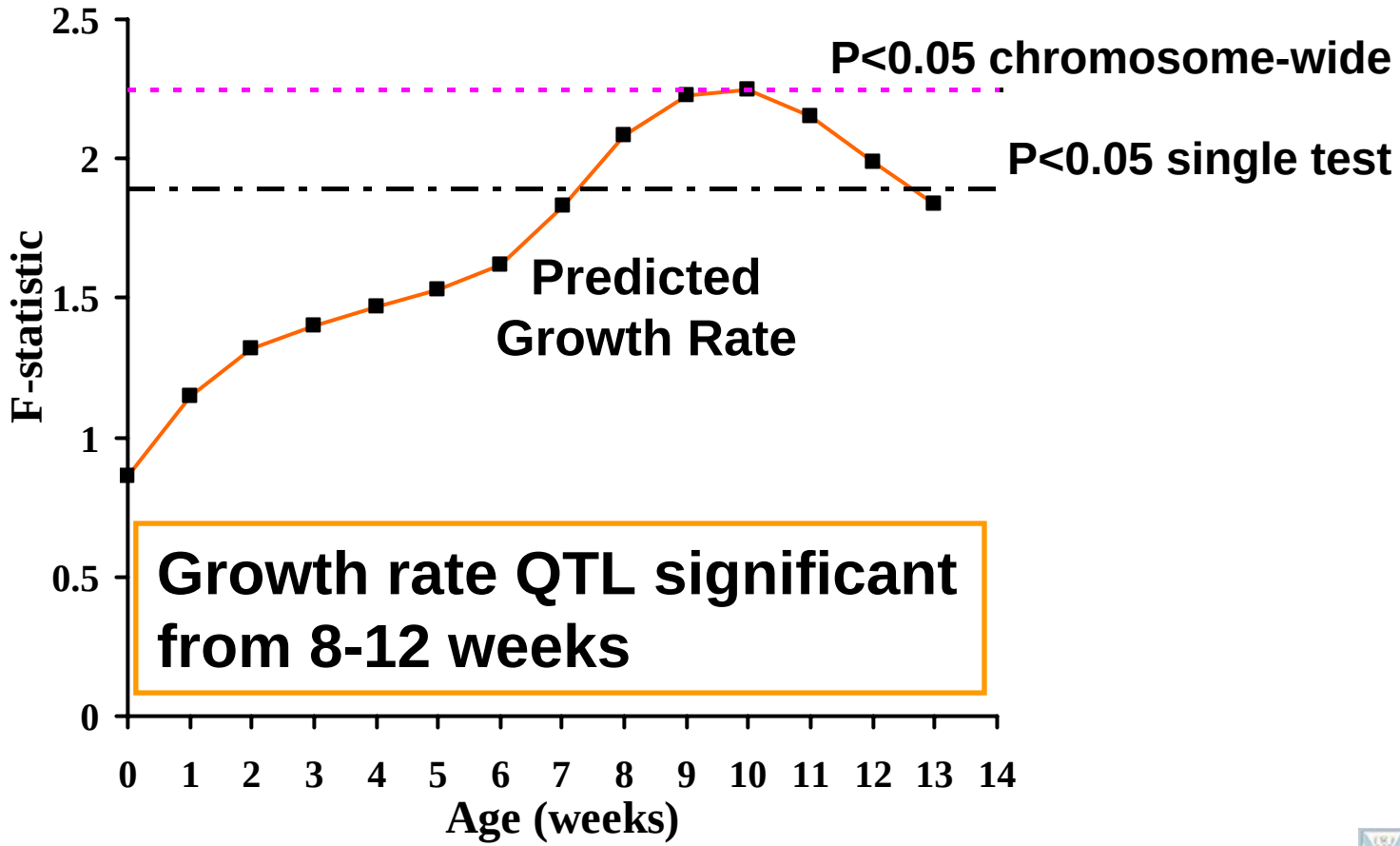
Chromosome 14, QTL at 99 cM



- Growth rate QTL max. significance at 24 weeks
- Possibly same QTL but with opposite allelic effects

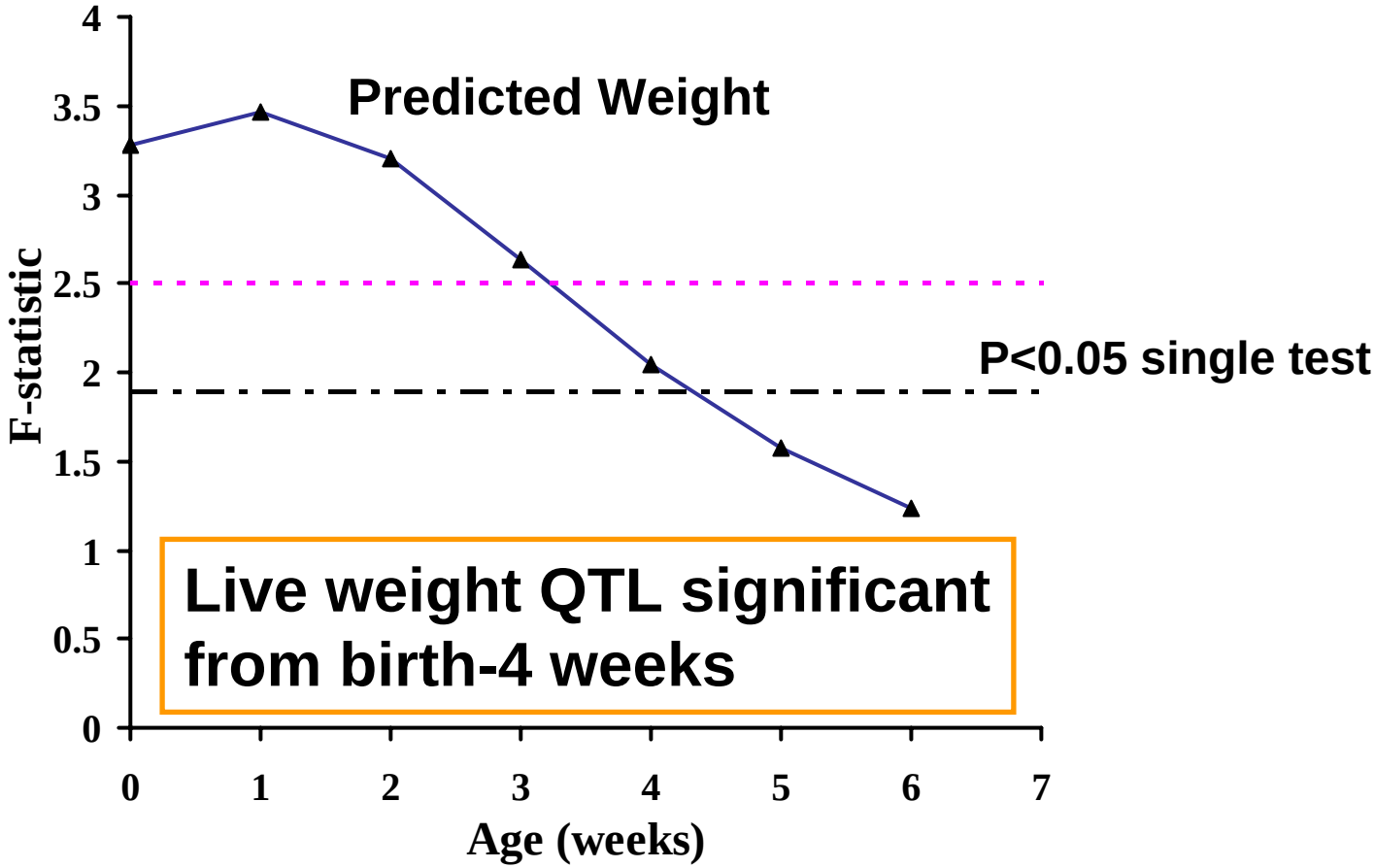
Results: Age-dependent Growth QTL

Chromosome 18, QTL at 59 cM



Results: Age-dependent Growth QTL

Chromosome 3, QTL at 213 cM



Conclusions

- Growth model fitting is a multivariate method for:
  - extracting more phenotypic information from longitudinal growth data
  - decomposing data into more informative growth variables for QTL analyses
- Growth model predictors resulted in increased ability to detect time-dependent growth QTL

Conclusions

- Growth QTL significance varied with age, as depicted by QTL F-ratio trajectories across time (age)
- QTL for growth rate occurred earlier than equivalent ones for live weight
- QTL on different chromosomes associate with distinct growth stages

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