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Novel milk phenotypes based on a biological model of lactation – a synthesis

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67th EAAP Annual Meeting, Belfast, UK

Introduction

- Lactation models have tried to use the underlying biology of the animal to describe the lactation curve (Dijkstra et al, 1997; Pollott, 2000)
- The use of such models may provide more information on which to base selection or management decisions than the methods currently used
- Can we measure components of the lactation curve from milk samples?
- Synthesis of work from 3 JDS papers and 2 EAAP presentations plus one ‘in press’ publication

Biology of lactation

Milk yield is the result of three major biological processes

- Mammary cell production and differentiation
- Milk secretion rate per cell
- Cell death rate

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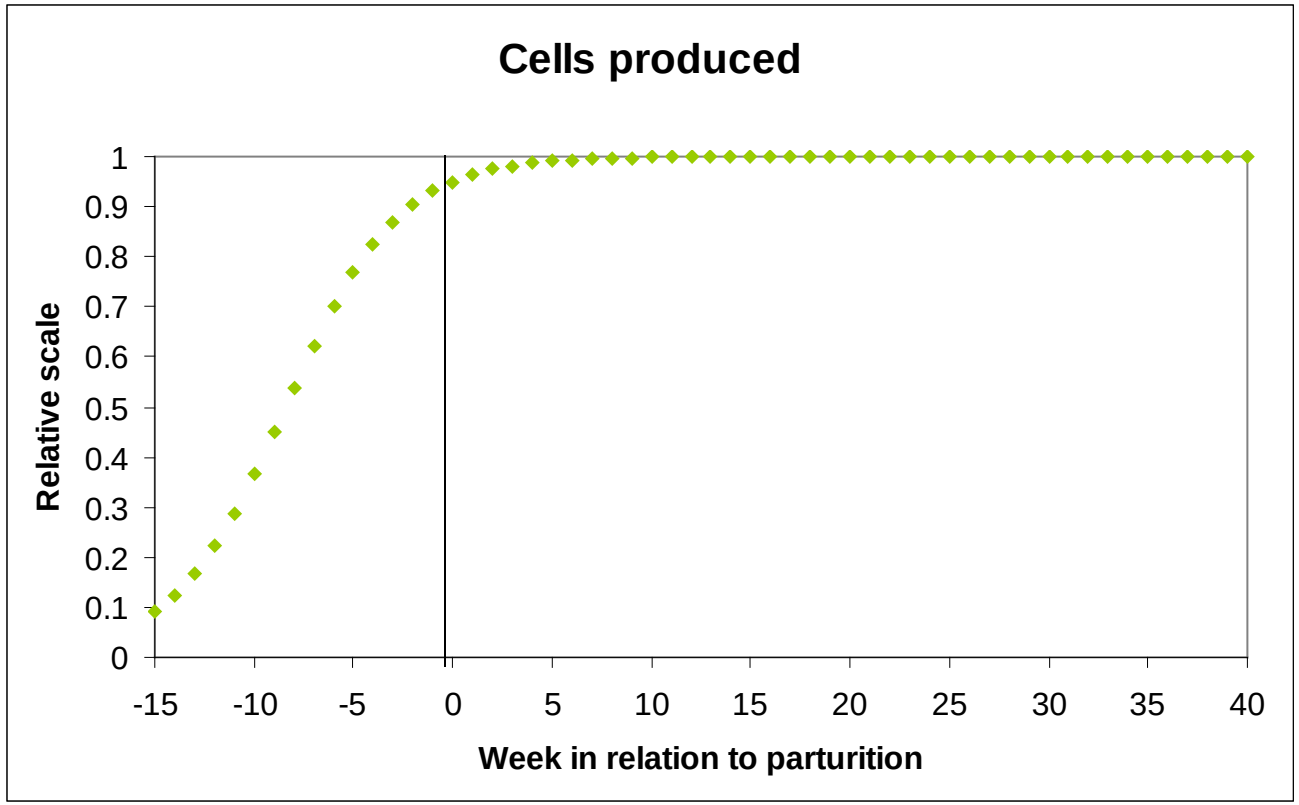
Biology of lactation 1



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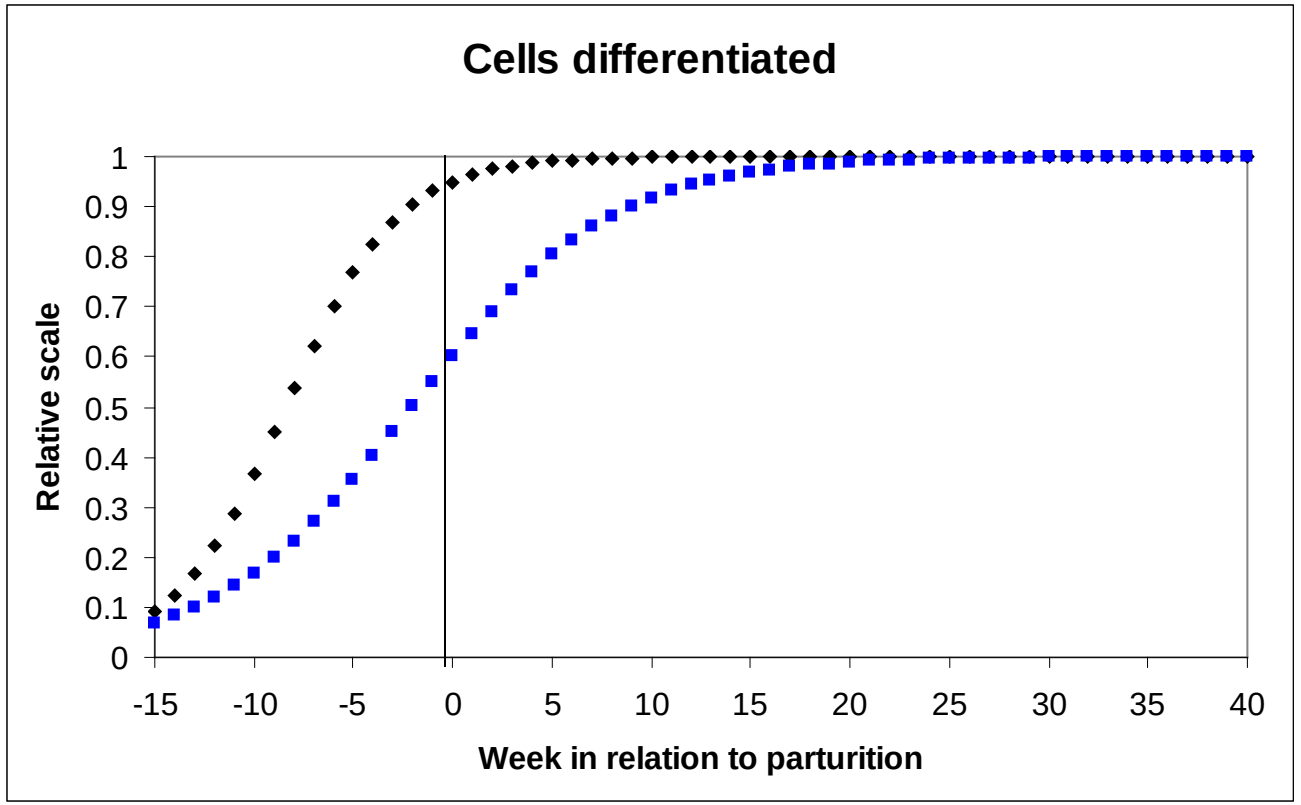
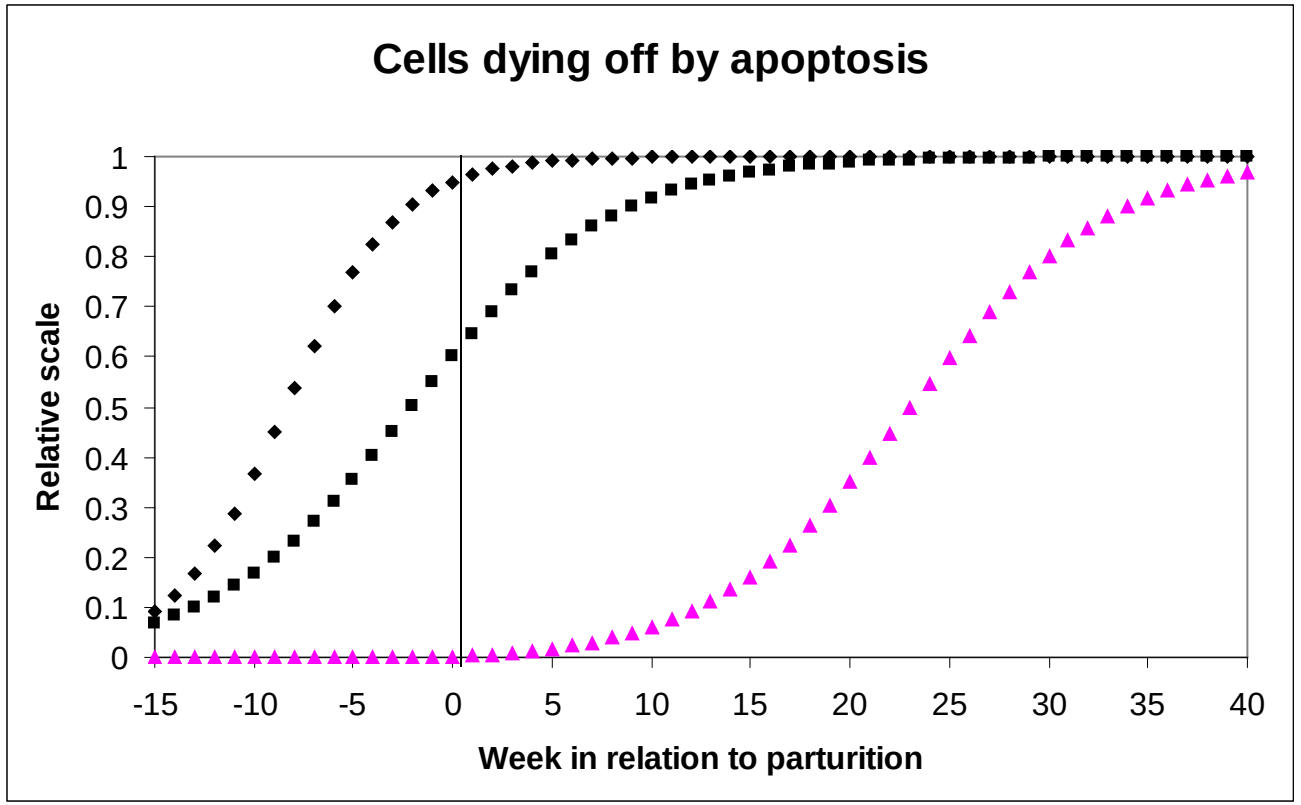
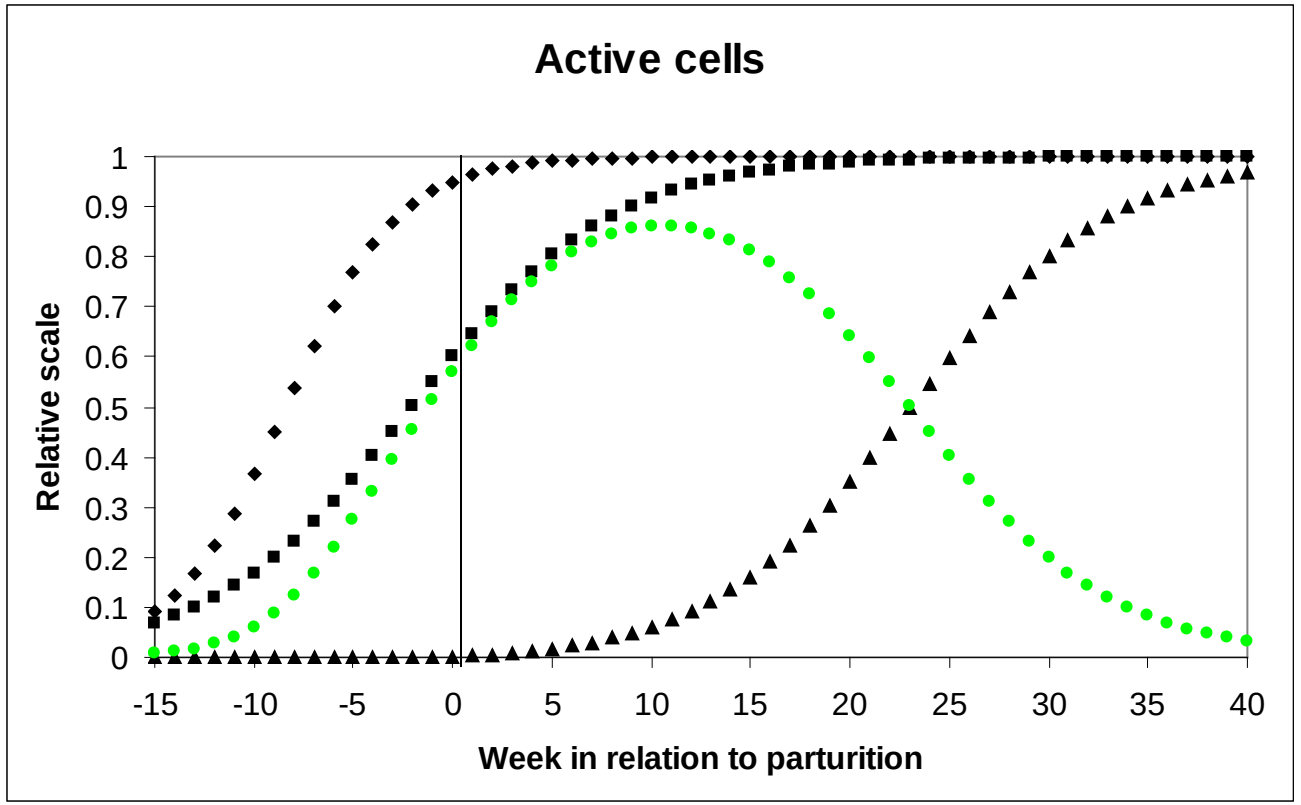
Biology of lactation 2



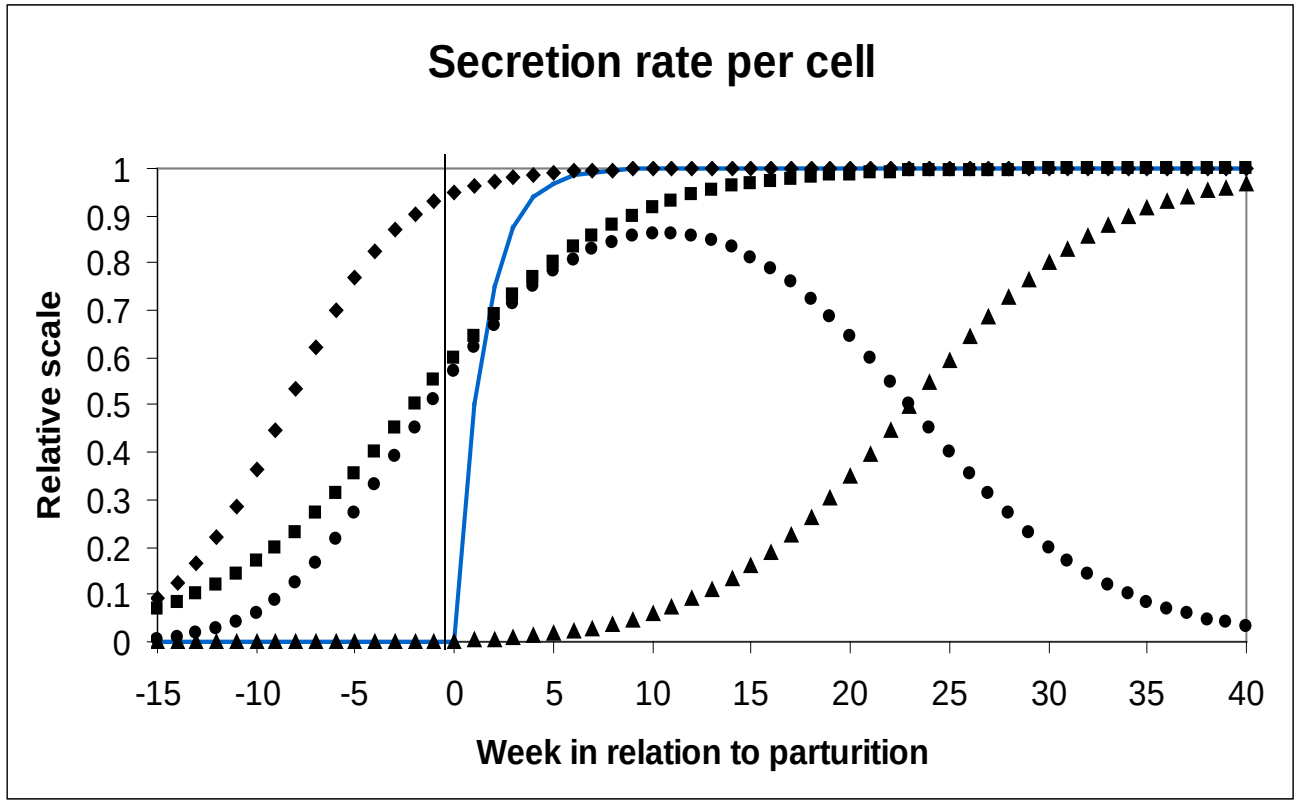
Biology of lactation 3



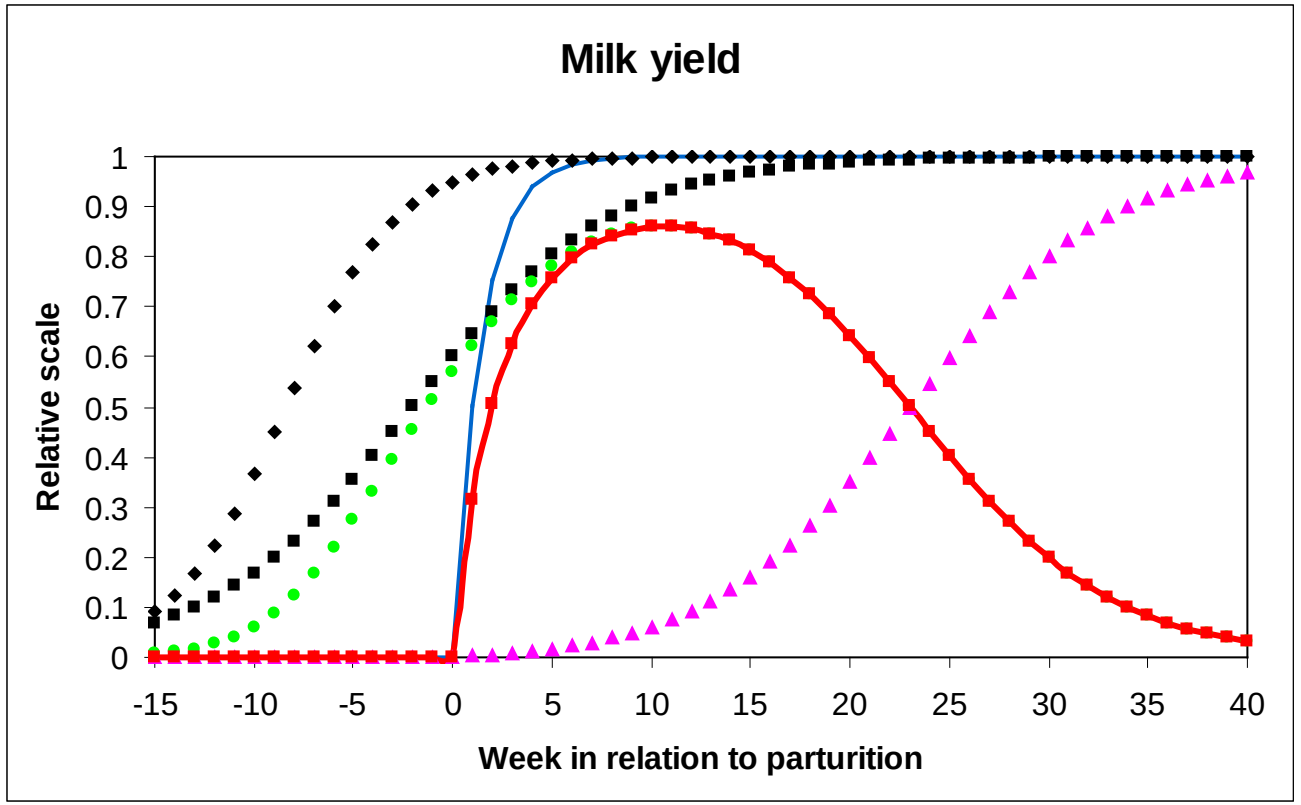
Biology of lactation 4



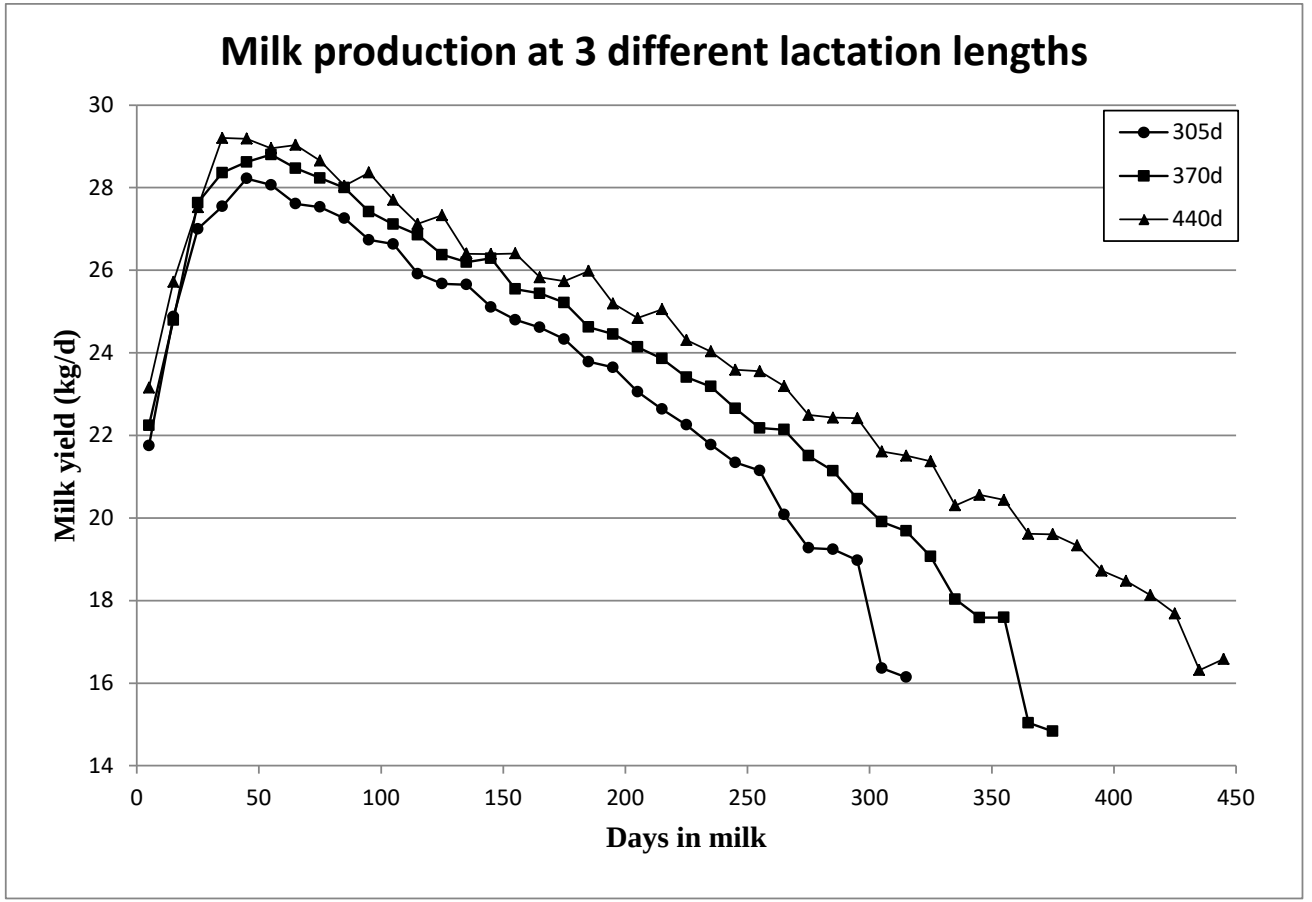
Biology of lactation 5



Biology of lactation 6



Lactation curve



Daily milk yield

Milk yield (M) on day t of lactation is:

Number of differentiated parenchyma cells (NDPC)

minus

Number of differentiated cells dying ($NDCD_t$)

multiplied by

Cell secretion/offtake rate (S_t)

$$M_t = (NDPC - NDCD_t)\ S_{Mt}$$

If we could measure one or more of the these processes then we may be able to gain more control over milk production

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$M_t = (NDPC - NDCD_t)\ S_{Mt}$

$NDPC = (M_t / S_{Mt}) + NDCD_t$

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Estimating NDCD

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Number of cells dying

- Apoptosis likely to be cause of decline in milk production in late lactation
- Commonly measured as persistency
- Extracellular vesicles (EV) formed by apoptosis
- Can we measure EV in milk to estimate apoptosis rate?

Extracellular vesicles

- EV - membrane-bound vesicles of less than 1µm diameter released from many different cell types
- Formed by blebbing of the parent cell membrane
- During cell membrane blebbing and EV formation phospholipids become exposed on the outer leaflet of the plasma membrane and the outer surface of the microparticle
- Presence of these normally hidden molecules allow the detection of microparticles by binding to specific markers (annexin V (AV) and merocyanin 540 (MC))

Correlations between persistency and the regression slope of the 4 microparticle densities on DIM for each cow (n = 12)

	Persistency	Total	Both^{+}	AV^{+}
Total	**-0.65**			
Both^{+}	-0.32	0.37		
AV^{+}	**-0.50**	0.69	0.85	
MC^{+}	**-0.49**	0.76	0.71	0.74

Correlations which were > 2 SE shown in bold
AV^{+} = Annexin-V positive microparticles; MC^{+} = MC540 positive microparticles;
Both^{+} = microparticles positive for both Annexin-V and MC540; Total = all microparticles.

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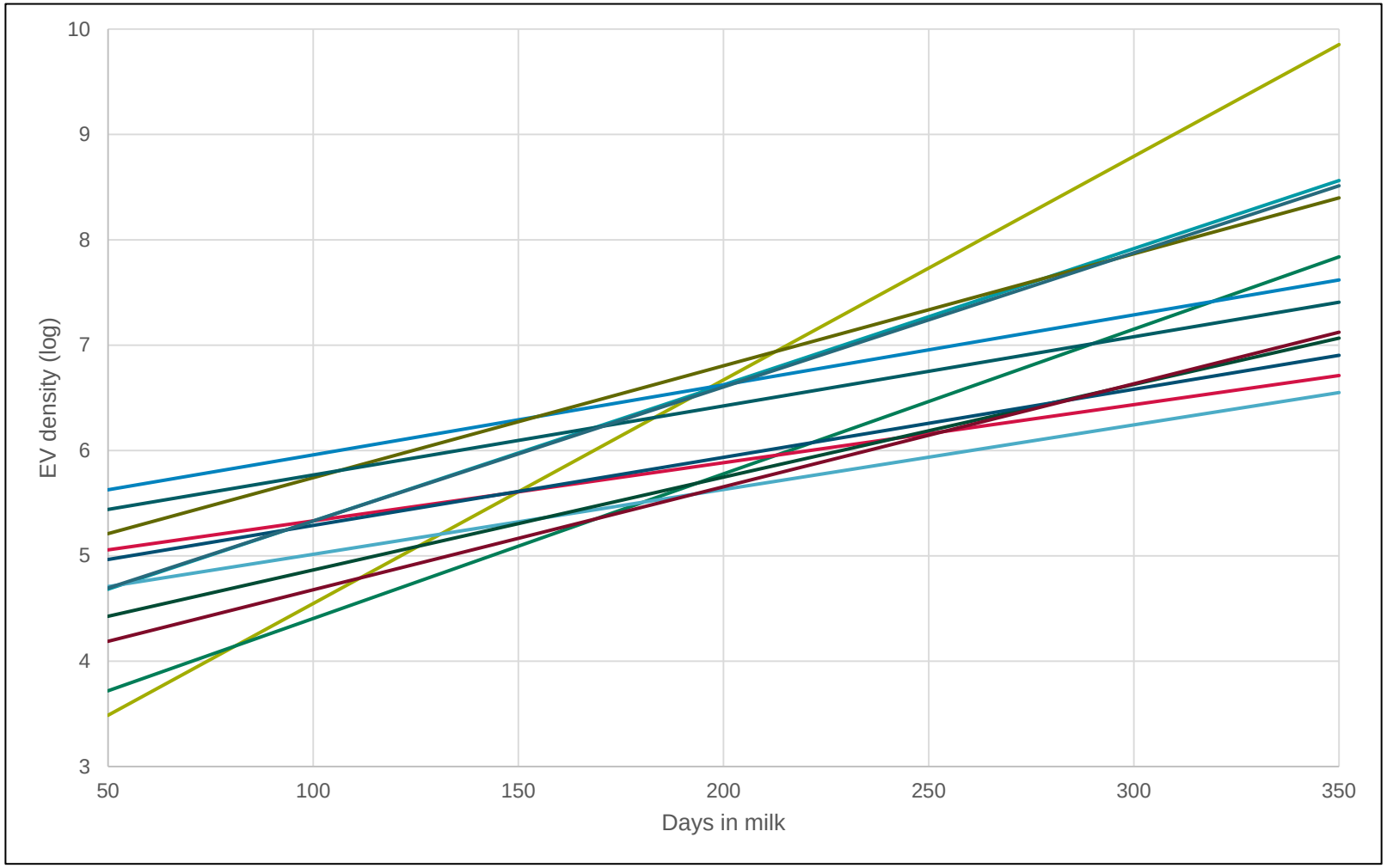
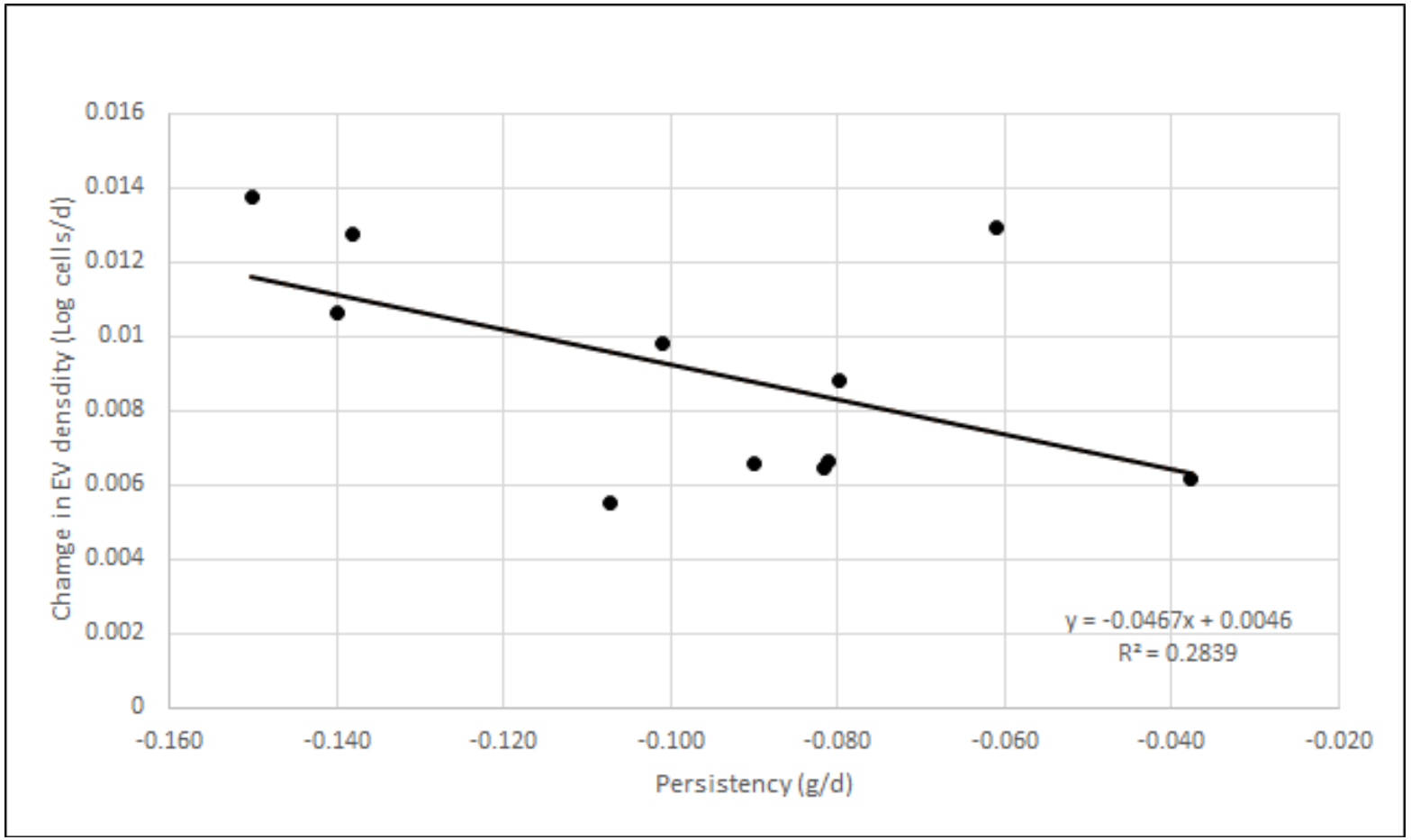
Cow EV densities by days in milk



EV density and persistency



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Number of differentiated cells dying

- Persistency related to EV in milk
- Relationship between EV and ‘apoptosis’ parameter needs defining
- Also the factors which affect it or cause variation need investigating

Estimating milk secretion rate per cell

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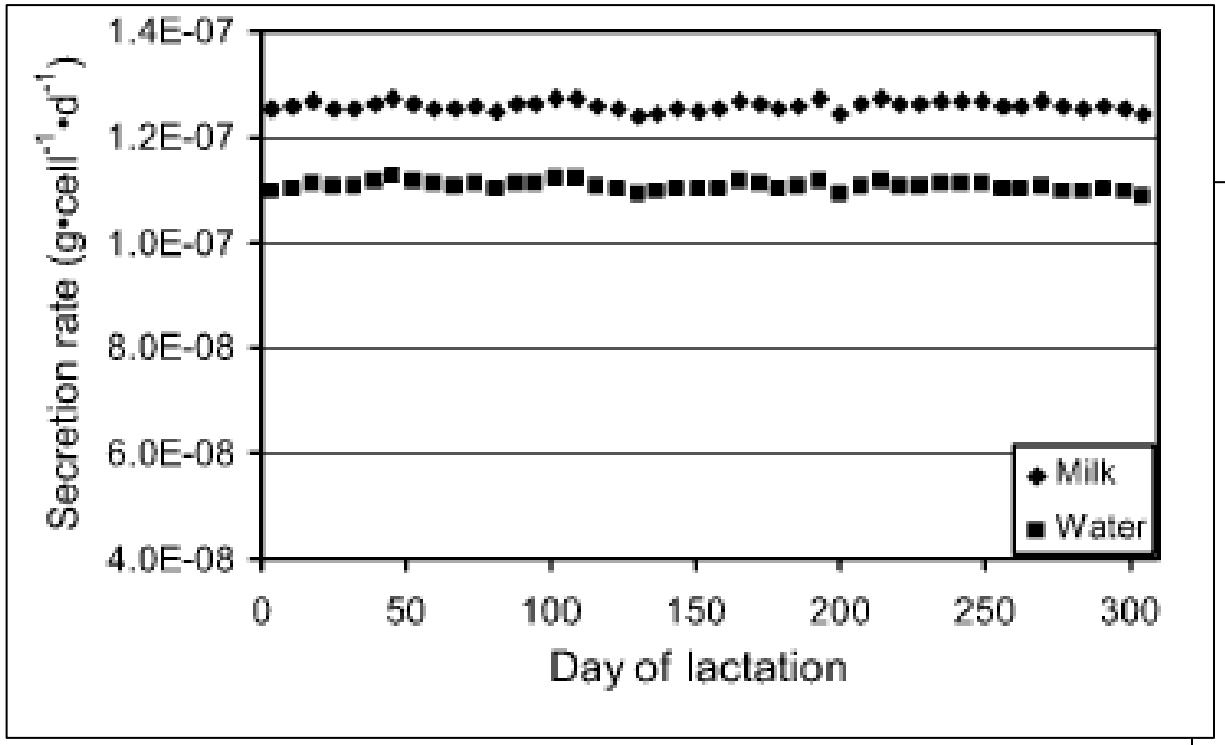
Proposed secretion rates throughout lactation (Pollott, 2004)



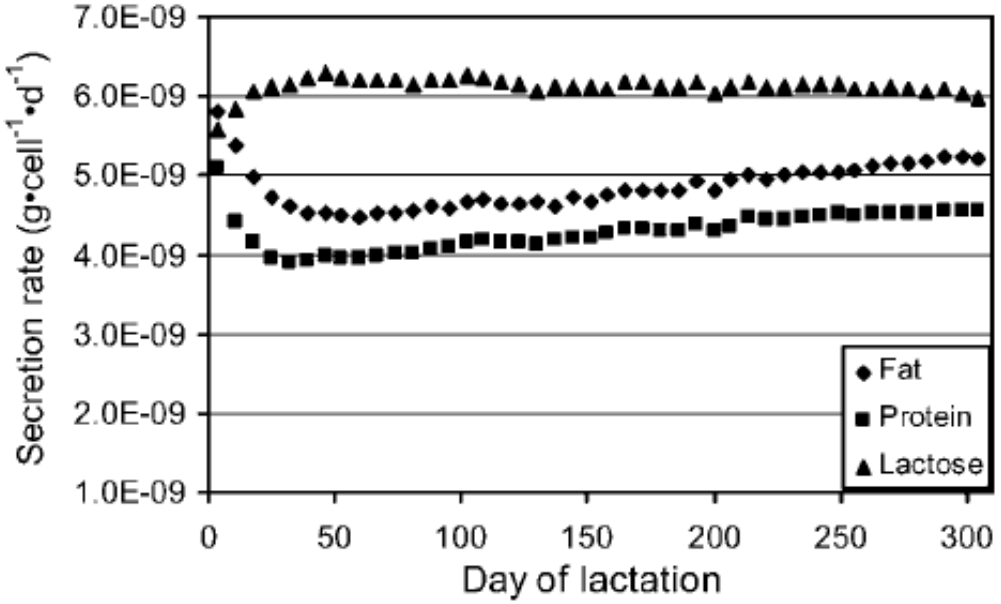


Figure 4. Secretion rate curves for the 5 components from overall least squares means, assuming a constant milk secretion rate throughout lactation and maximal number of secretory cells = 2.8×10^{10}.

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Gene expression study throughout lactation

New question: Can we use gene expression levels as an indicator of secretion rate throughout lactation?

Supplementary question: Can we do this with samples from a commercial herd?

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14 genes studied

- Lactose – *B4GALT1, LALBA, UGDH, UGP2*
- Prolactin – *JAK2*
- Protein – *CSN1S1, LALBA*
- Cell cycle etc. – *ARNTL2, CYSLTR2, FOXH1, UTRN*
- Fat – *ACACA, DGAT1, FASN, SCD*

Differences found in gene expression levels between cows for all genes except DGAT1

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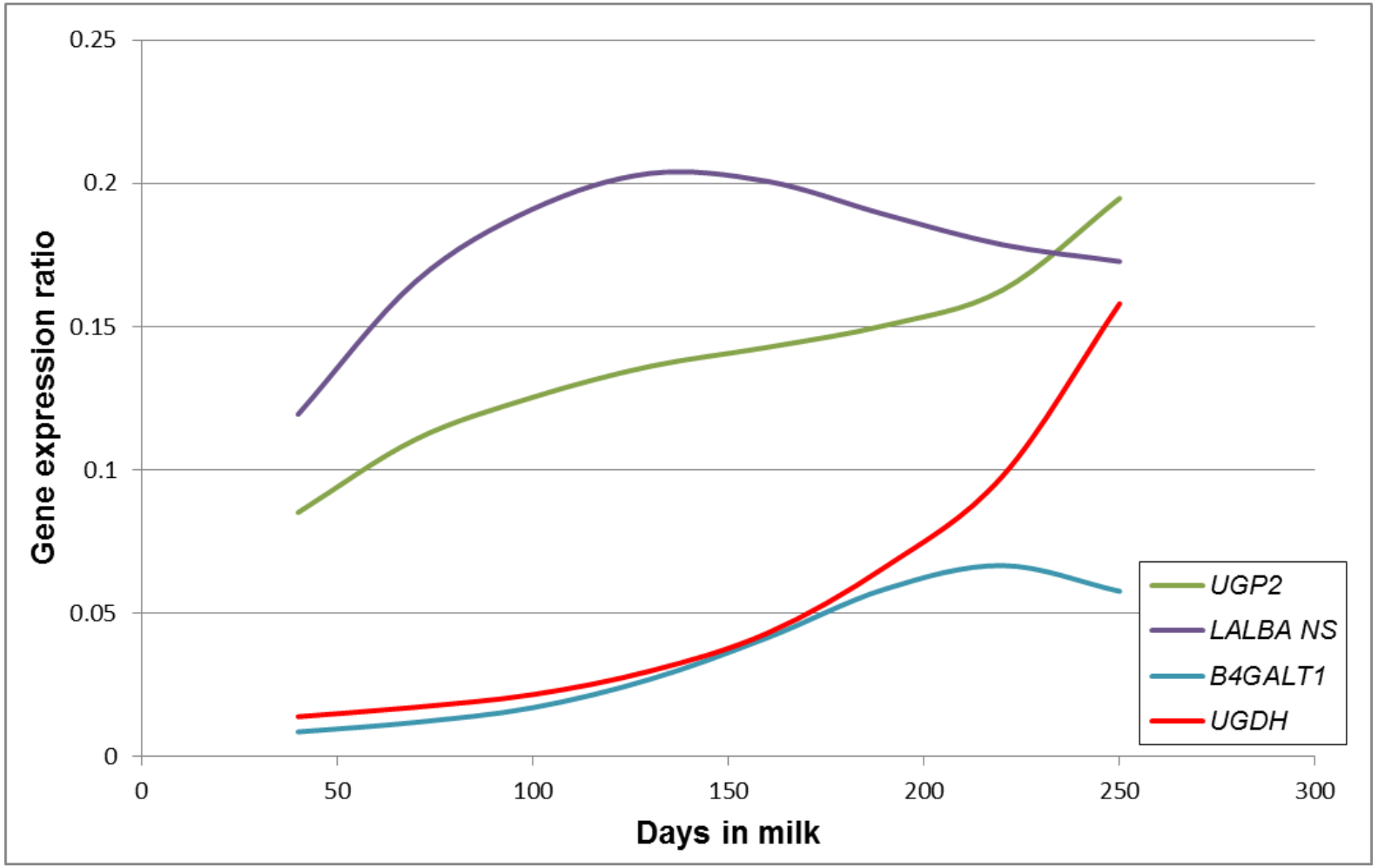
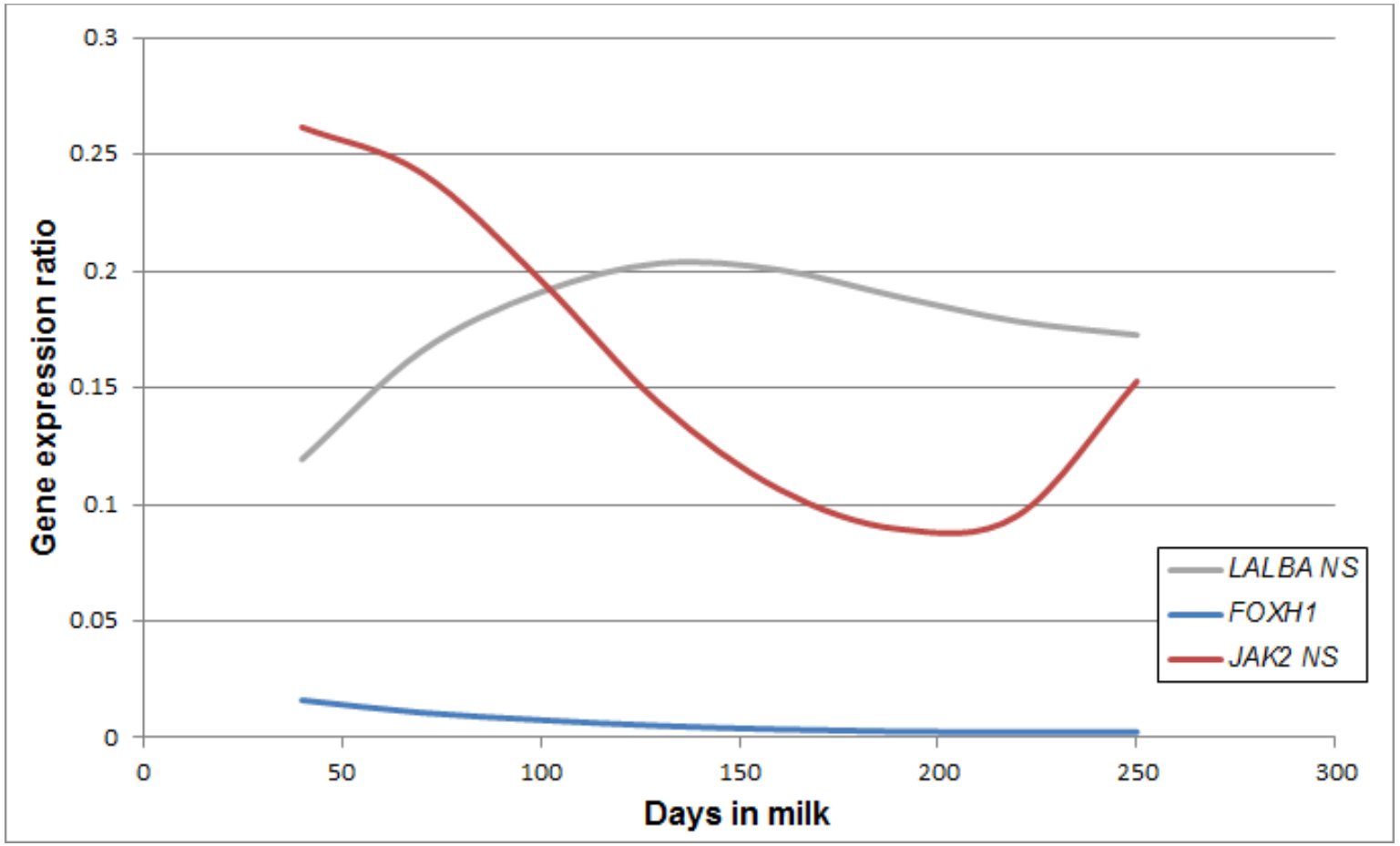
Lactose genes



Prolactin genes



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Correlations between gene expression and lactation curve parameters across cows

	Level of milk production (cow effect)	*Rate of increase in milk production in early lactation*	*Rate of decrease in milk production (apoptosis?)*
ACACA		**0.61**	
ARNTL2	**0.24**		
CSN1S1		**0.20**	**-0.21**
CYSLTR2		**-0.52**	
FASN			**-0.53**
FOXH1	**0.27**		**-0.48**
LALBA		**0.32**	
SCD		**0.49**	**-0.37**
UGDH	**0.27**	**-0.20**	
UTRN	**0.24**		**-0.35**

Implications

- RNA can be extracted from milk with biologically credible results
- Gene expression of several key genes varies across lactation
- Further analyses required to determine if GER can be used to estimate secretion rate in lactation
- GER in some genes related to lactation curve parameters

Daily milk yield- conclusions

Milk yield (M) on day t of lactation is:

Number of differentiated parenchyma cells – only estimable

minus

Number of differentiated cells dying – measureable with EV?

multiplied by

Cell secretion/offtake rate – constant but varies between animals

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Conclusions

- Encouraging start to investigating phenotypes in milk that may relate to lactation curve characteristics
- More work required on more cows in different environments to see how relationships vary
- Probably number of mammary cells produced has biggest effect on milk production

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