

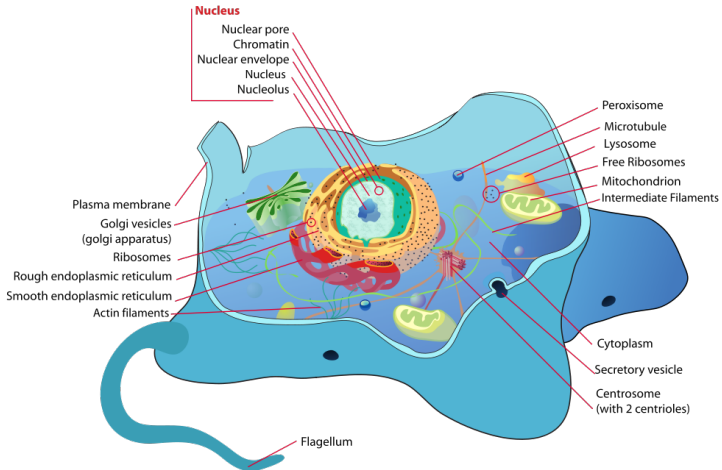
Computational Challenges in Mass Spectrometry-Based Spatial Proteomics

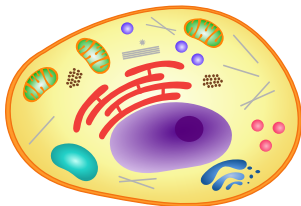
Laurent Gatto

University of Cambridge

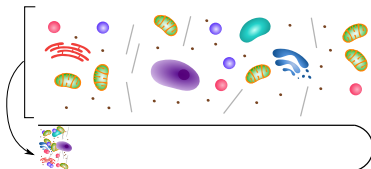
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8 October 2014



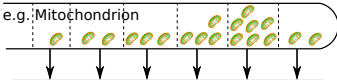


Cell lysis



Fractionation/centrifugation

e.g. Mitochondrion



Quantitation/identification

	Fraction ₁	Fraction ₂	...	Fraction _m
prot ₁	q _{1,1}	q _{1,2}	...	q _{1, m}
prot ₂	q _{2,1}	q _{2,2}	...	q _{2, m}
prot ₃	q _{3,1}	q _{3,2}	...	q _{3, m}
prot ₄	q _{4,1}	q _{4,2}	...	q _{4, m}
⋮	⋮	⋮	⋮	⋮
prot _i	q _{i,1}	q _{i,2}	...	q _{i, m}
⋮	⋮	⋮	⋮	⋮
prot _n	q _{n,1}	q _{n,2}	...	q _{n, m}

	markers	
...	<i>unknown</i>	...
	<i>organelle₁</i>	
	<i>unknown</i>	
	<i>organelle₂</i>	
⋮	⋮	⋮
	<i>organelle_k</i>	
⋮	⋮	⋮
...	<i>unknown</i>	

	Fraction ₁	Fraction ₂	...	Fraction _m

	⋮	⋮	⋮	⋮

Figure : Spatial proteomics data and meta-data.

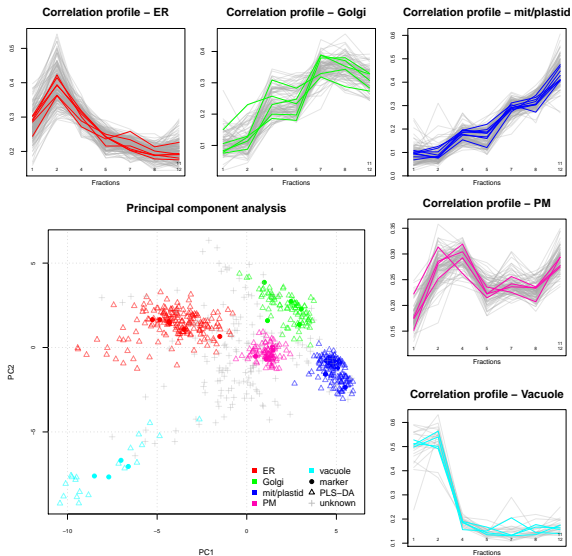


Figure : Visualisation, Gatto et al. (2010)

Challenges: resolution vs. missing data

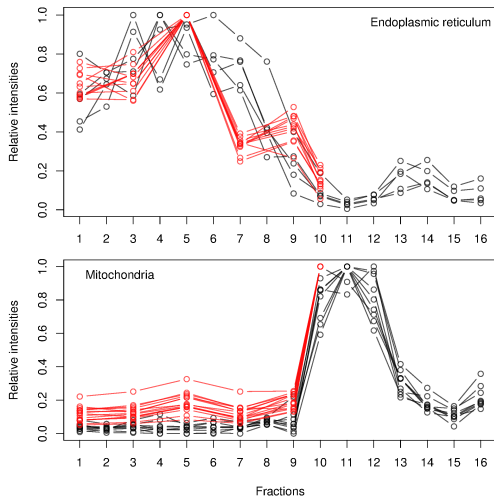


Figure : Gatto et al. (2014)

Challenges: resolution vs. missing data

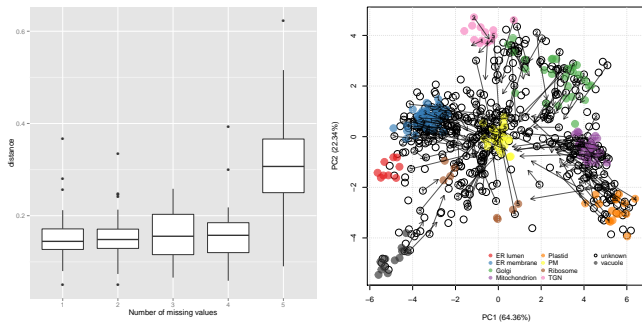


Figure : Gatto et al. (2014)

Spatial markers

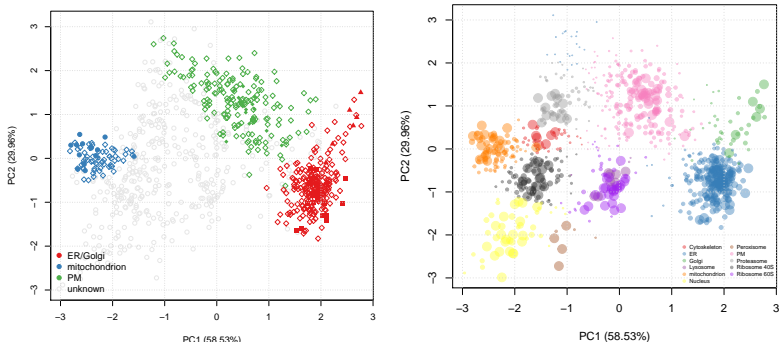


Figure : Sub-cellular diversity: Tan et al (2009) vs. Breckels et al. (2013)

Spatial markers

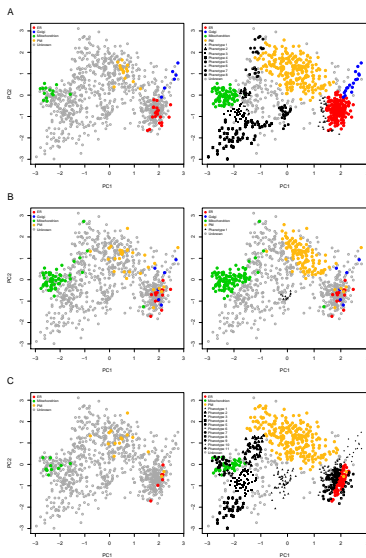


Figure : Quality of markers: Gatto et al. (2014)

Dual localisation

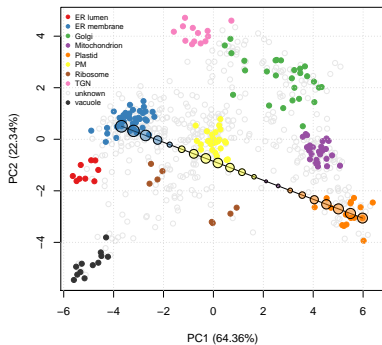
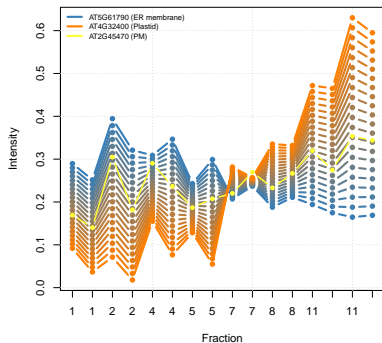


Figure : Gatto *et al.* (2014)

Dynamic changes

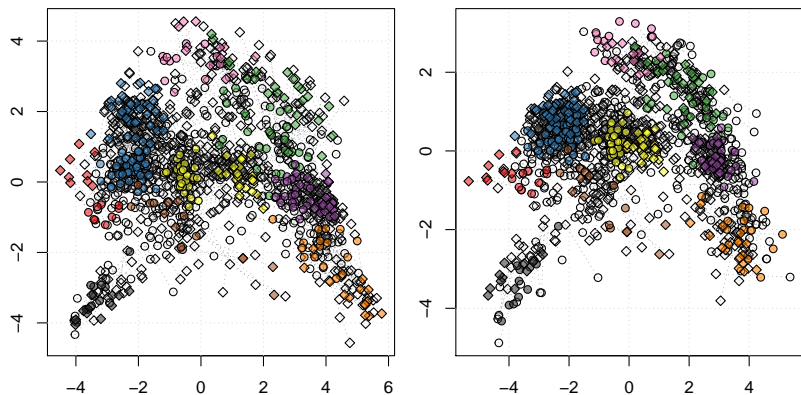


Figure : Normalisation, Gatto *et al.* (2014)

Dynamic changes

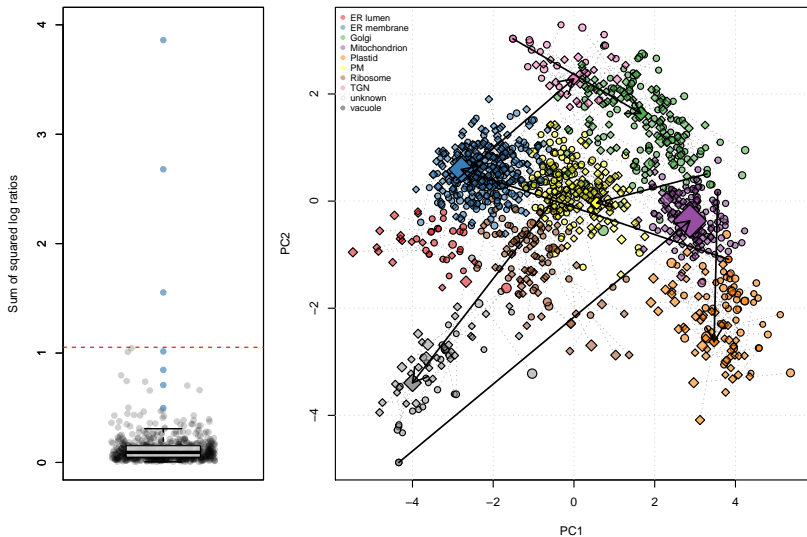
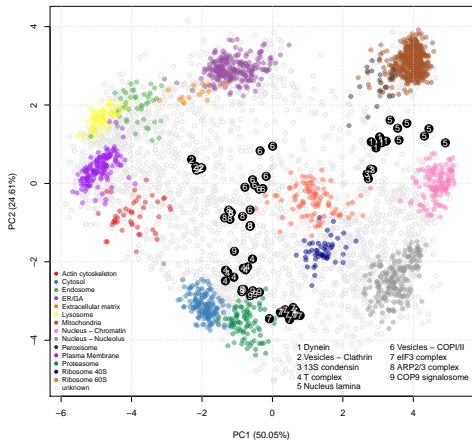
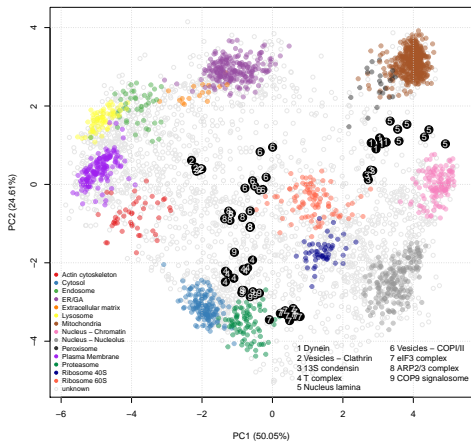


Figure : Statistics, Gatto *et al.* (2014)

Conclusions



Conclusions



- ▶ Mass spectrometry
- ▶ Experimental design
- ▶ Computational tools

- ▶ Funding: BBSRC and FP7 Prime-XS
- ▶ Kathryn Lilley
- ▶ Lisa Breckels



Gatto L. *et al.* *Organelle proteomics experimental designs and analysis*, Proteomics 2010, 10(22):3957-69 PMID: 21080489.



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<http://www.bioconductor.org/packages/release/bioc/html/pRoloc.html>