Raman spectroscopy for cancer diagnosis

Prof. Fiona Lyng
Centre for Radiation and Environmental Science
Dublin Institute of Technology

Outline

1 • Introduction to Raman spectroscopy

2 • Biomedical applications of Raman spectroscopy

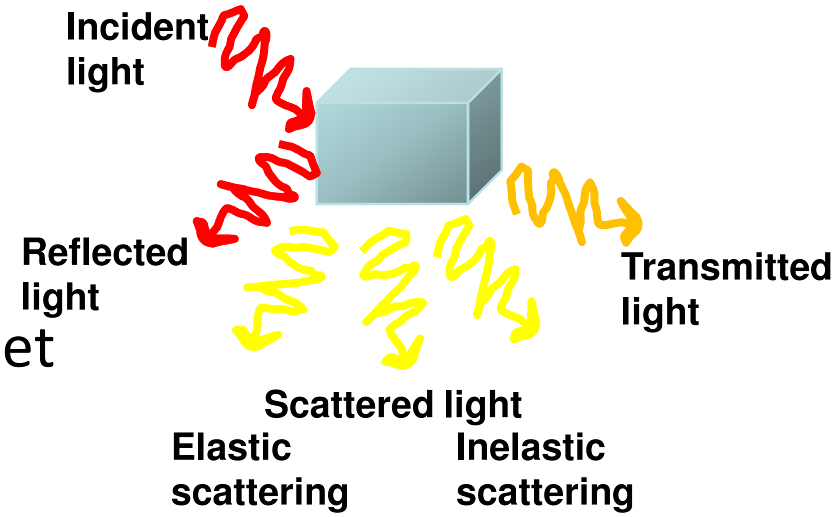
3 • Raman spectroscopy for cervical cancer

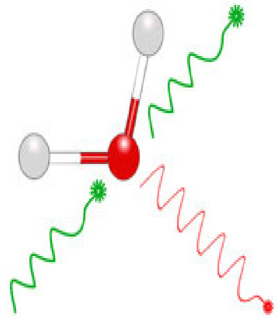
resc

focas institute/dit

What is Vibrational Spectroscopy?

- Spectroscopy involves the interaction of electromagnetic radiation with matter
- Vibrational Spectroscopy is a subset of spectroscopy which analyses vibrations within a molecule (or material)
- The spectrum of vibrational energies can be employed to characterise a molecular structure or changes to it



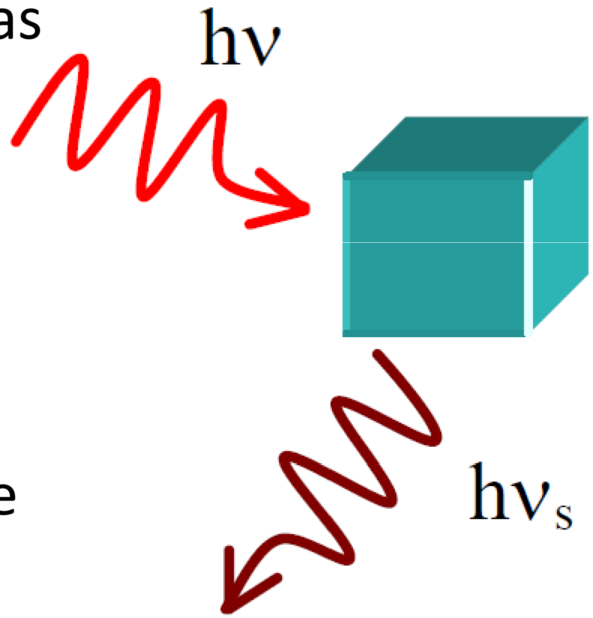


resc

focas institute/dit

Scattering

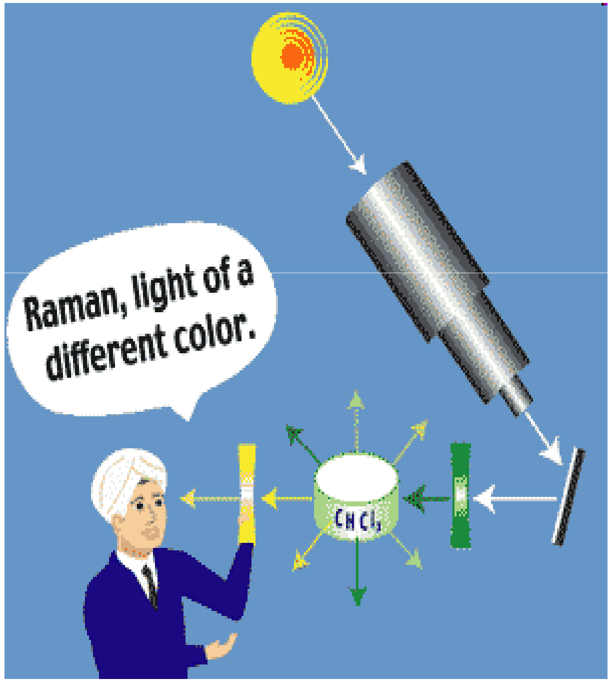
- Most of the light scattered by a sample will have the same energy (frequency) as the incident light – **Rayleigh Scattering (elastic scattering)**
- But a small portion of the light may be **inelastically scattered**
- Energy may be transferred between the light quanta and the molecules of the scattering medium **– Raman scattering**



Raman spectroscopy

- The difference in energy between the incident photon and the Raman scattered photon is equal to the energy of a vibration of the scattering molecule

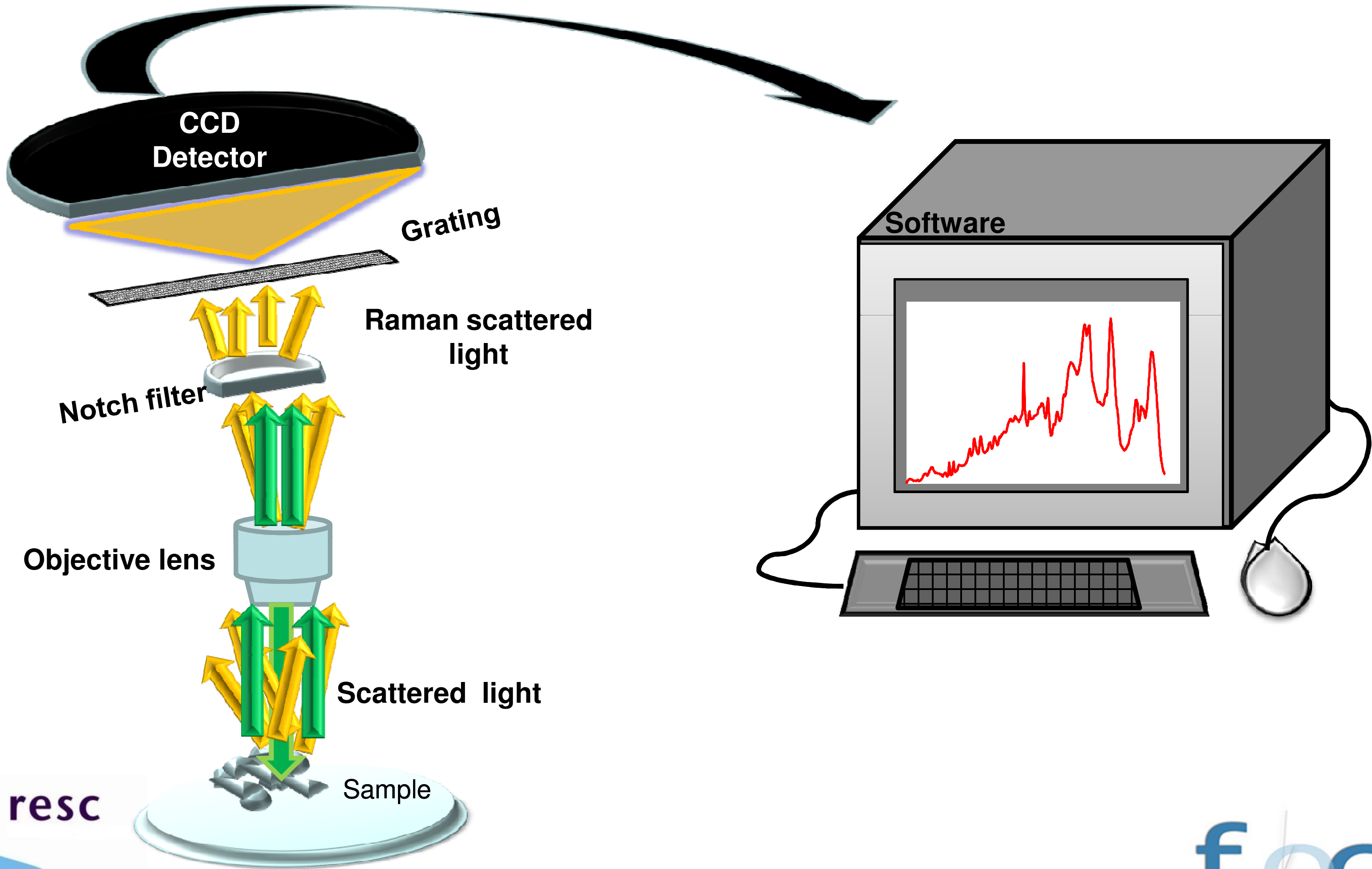
- A plot of intensity of scattered light versus energy difference is a Raman spectrum



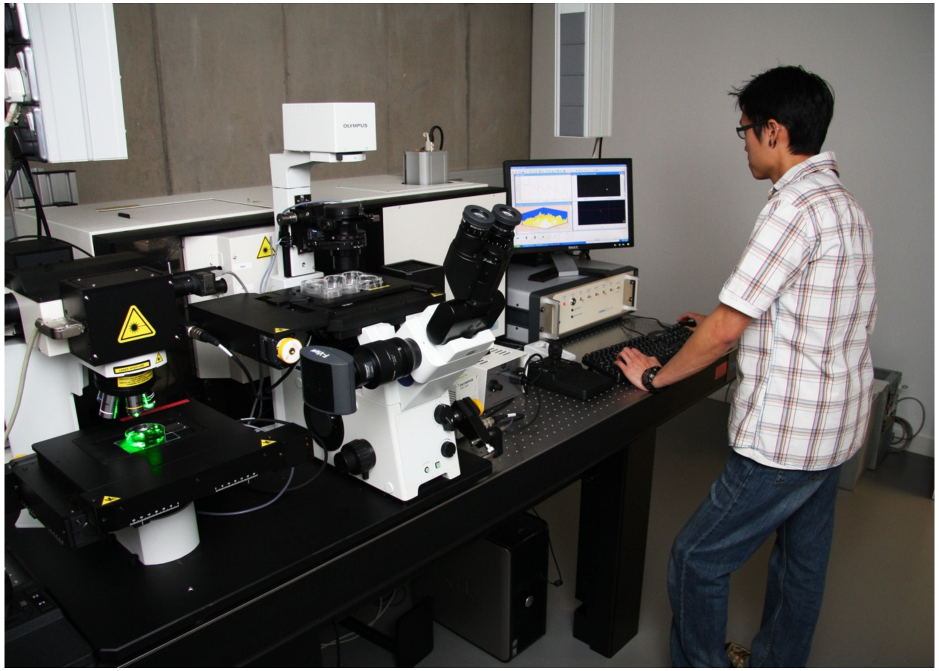
resc

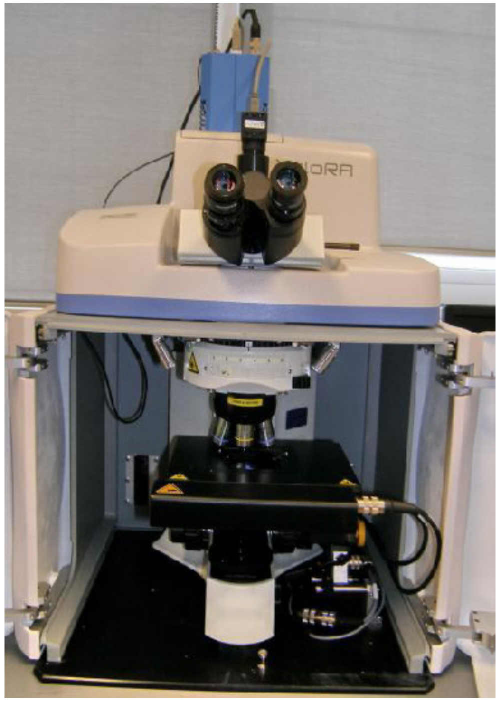
focas institute/dit

Raman instrumentation



Raman spectrometers



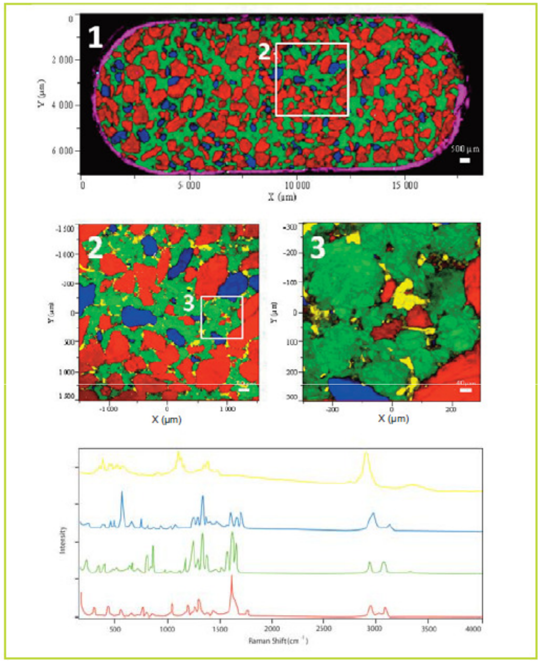


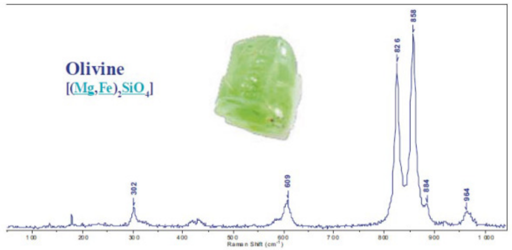
resc

focas institute/dit

Some applications of Raman spectroscopy

- Pharmaceuticals
- Art and Archaeology
- Forensics
- Materials
- Nanomaterials
- Geology
- Food Science

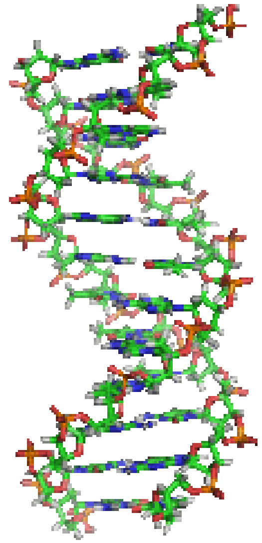




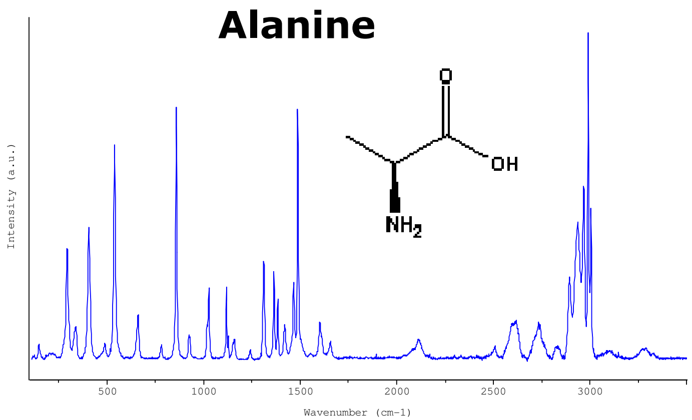
http://www.horiba.com/

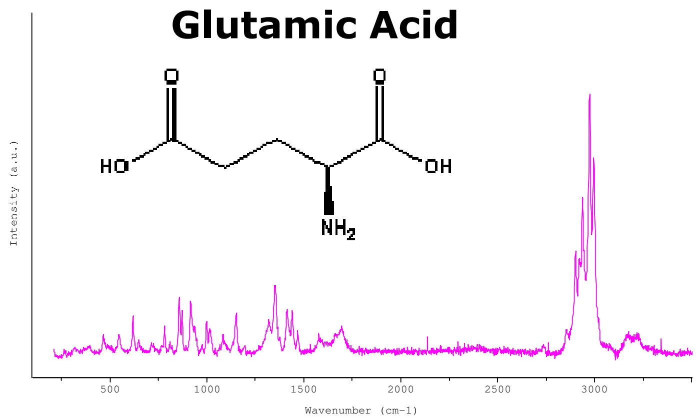
Biomedical applications of Raman spectroscopy

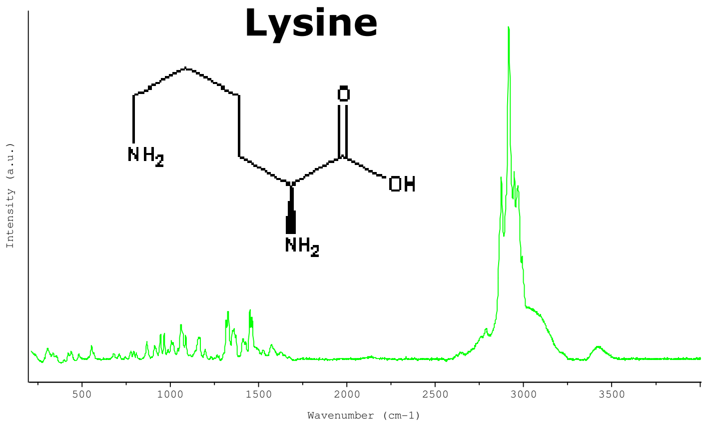
- Cells and tissue are composed primarily of water, proteins, nucleic acids, lipids and carbohydrates
- Tissue and cell types are characterised by a specific biochemical composition and molecular structure and pathological changes are accompanied by biochemical and molecular changes
- Proteins, nucleic acids, lipids and carbohydrates can all be probed and identified using vibrational spectroscopy and each molecule has a unique spectrum
- A Raman spectrum of a biological specimen can be thought of as a complete biochemical fingerprint

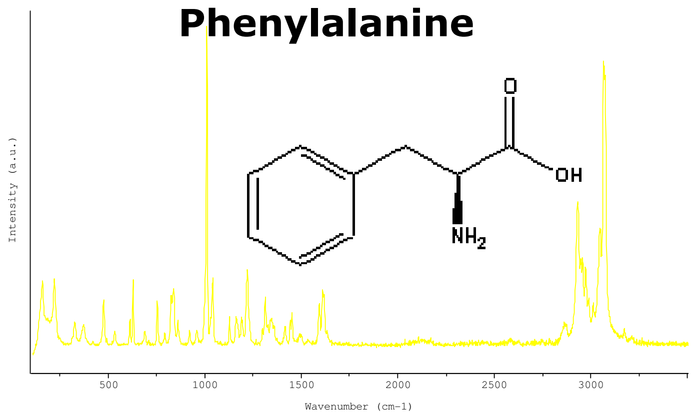


Raman spectra of amino acids

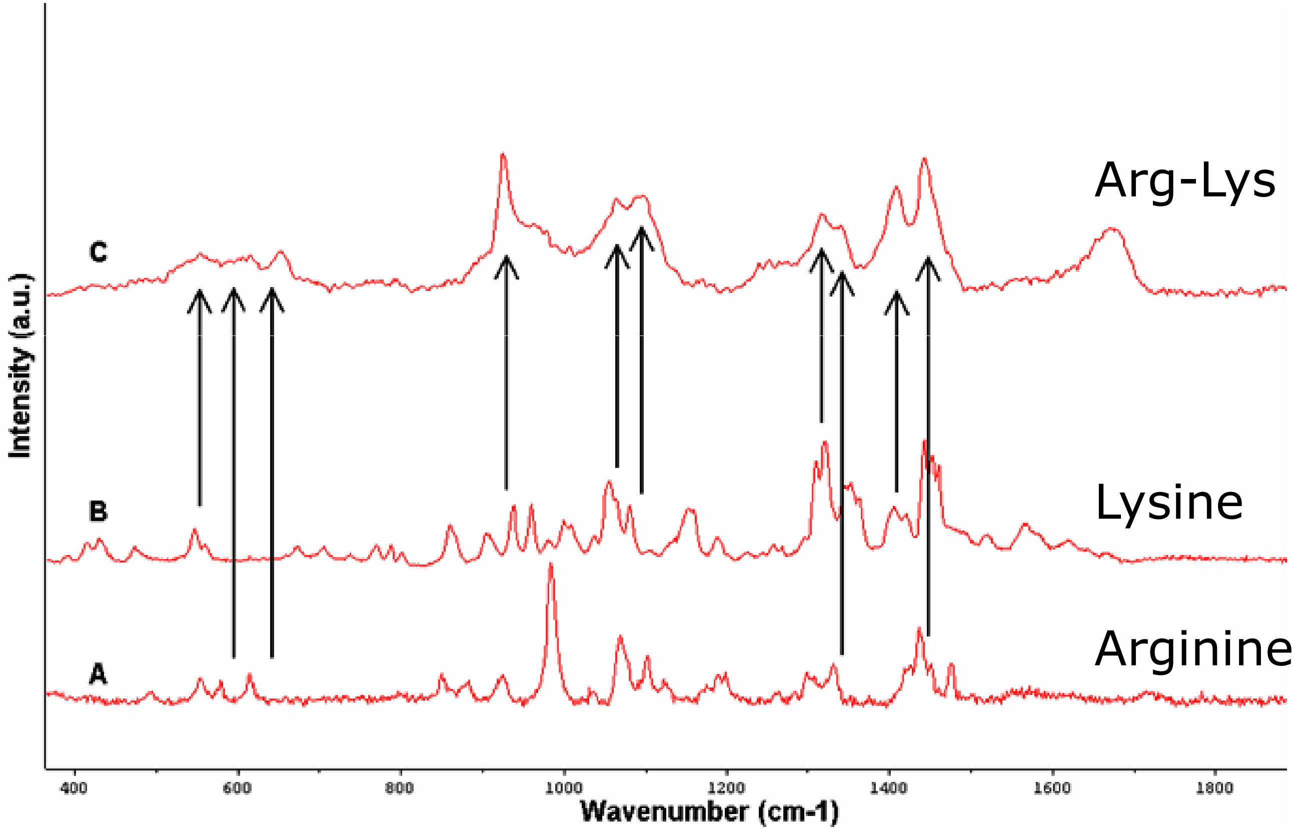


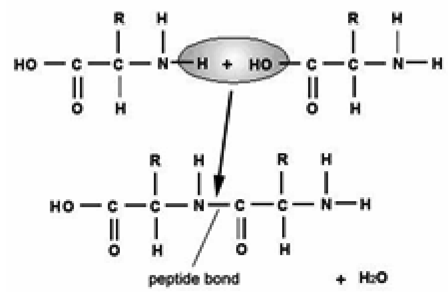




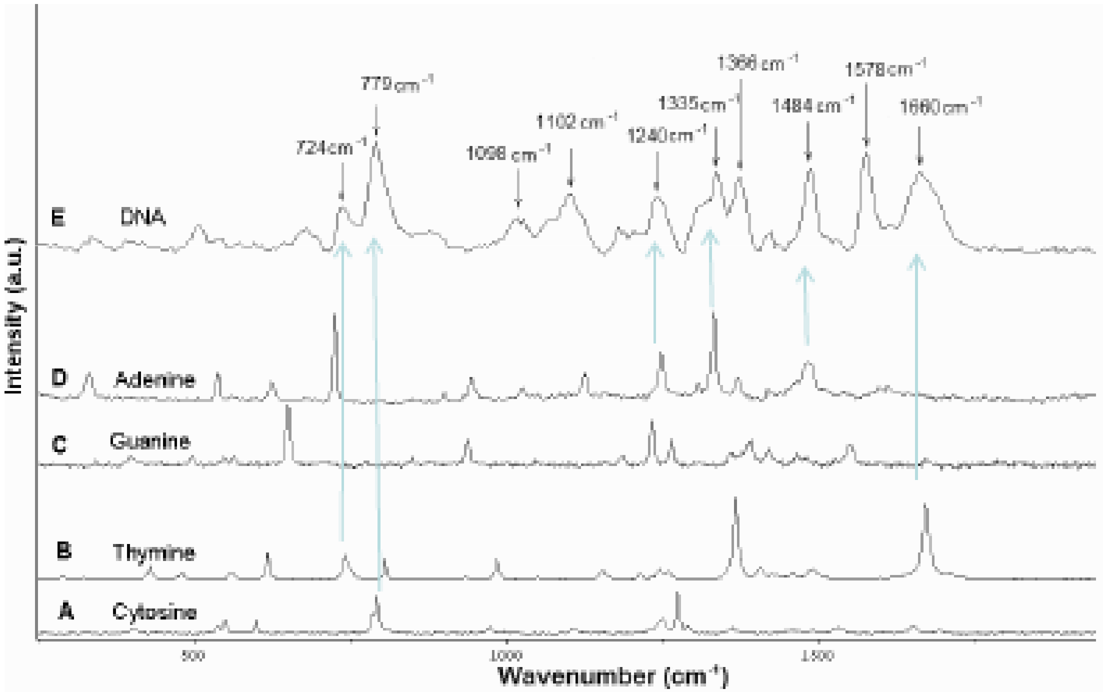


Raman spectrum of a peptide





Raman spectrum of DNA

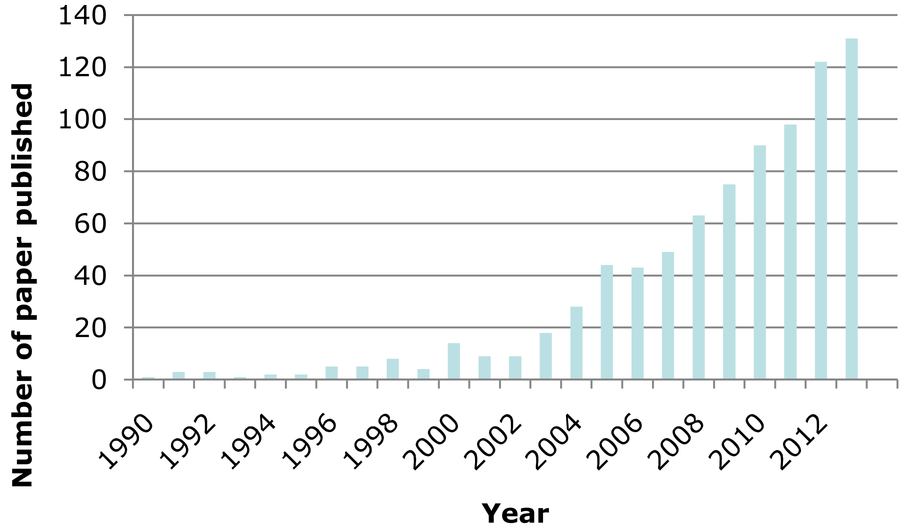


resc

focas institute/dit

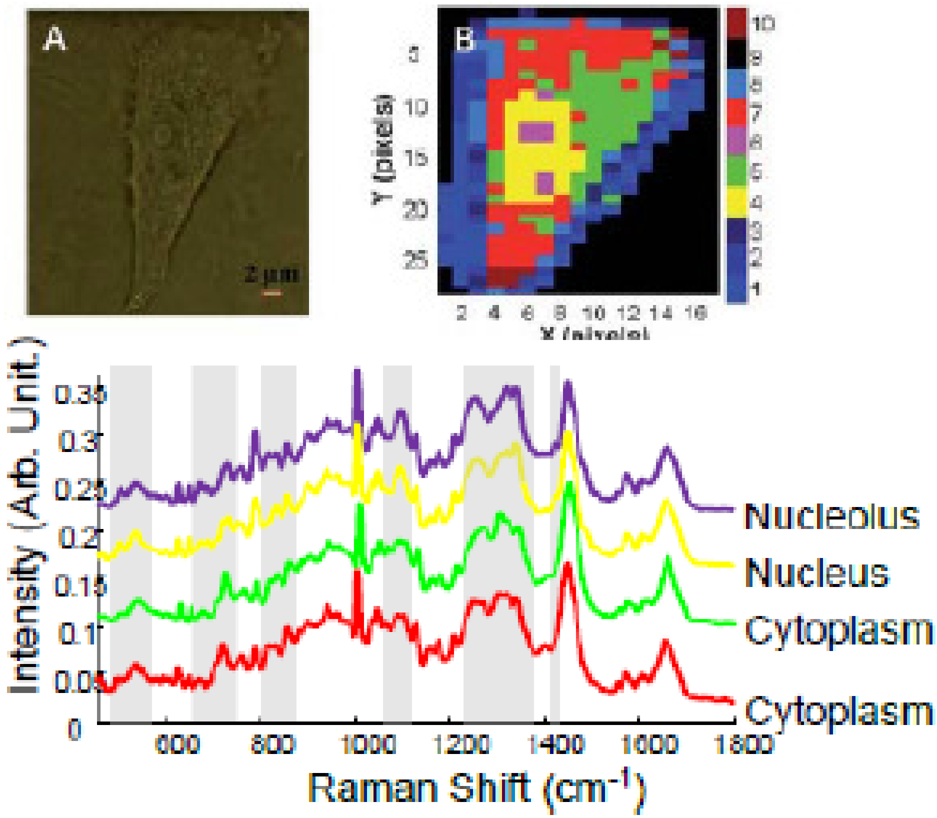
Biomedical applications of Raman spectroscopy

- Diagnostics - cancer, CVD, pathogen identification
- Therapeutics – chemotherapeutic agents
- Tissue
- Cells
- Biological fluids



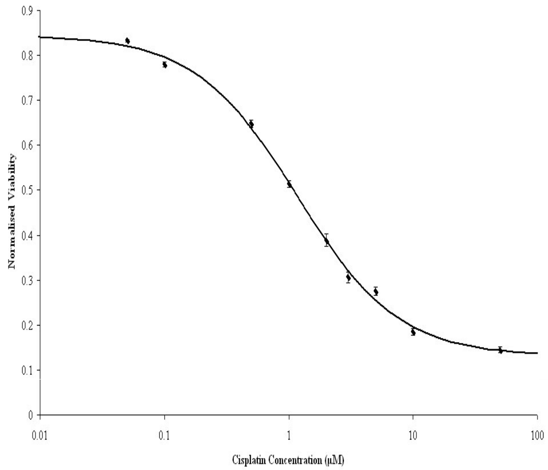
Ellis et al Analyst 2013; 138 (14) 3871-84
Kendall et al Analyst 2009; 134 (6) 1029-45

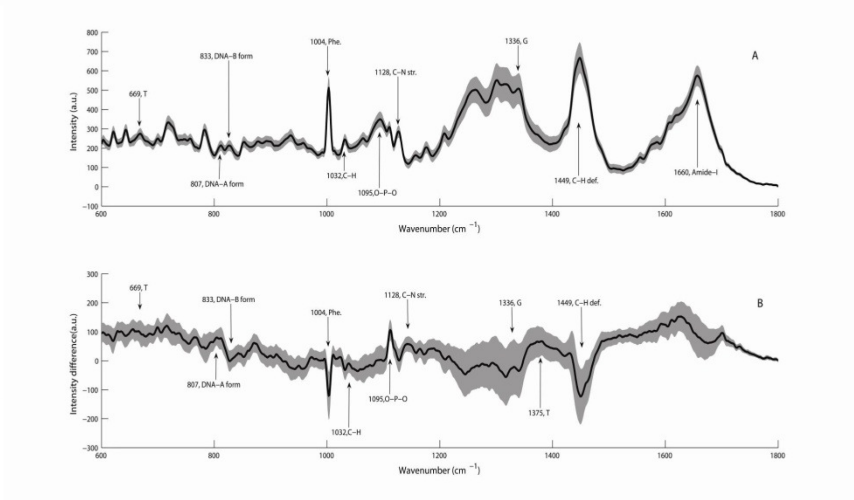
Subcellular analysis in live cells

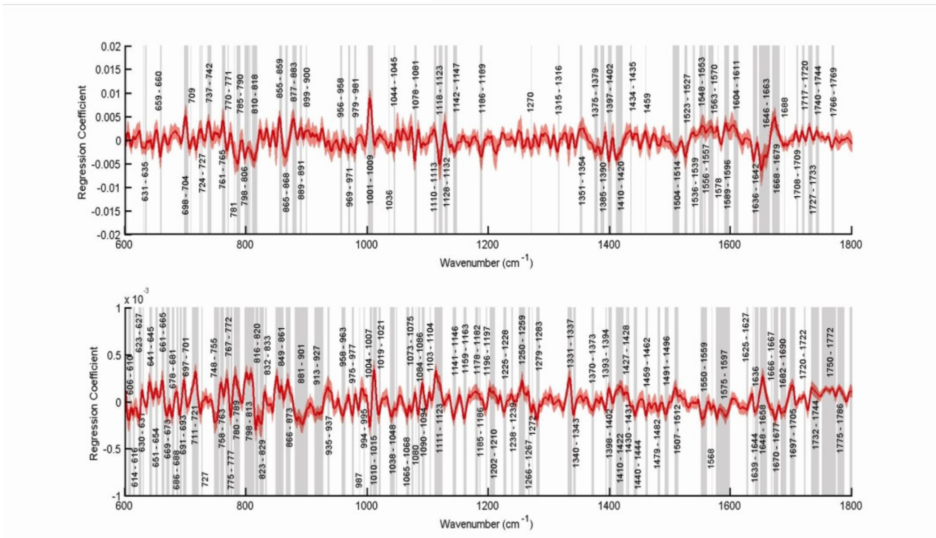


Bonnier et al, Analyst 2010

Chemotherapeutic response

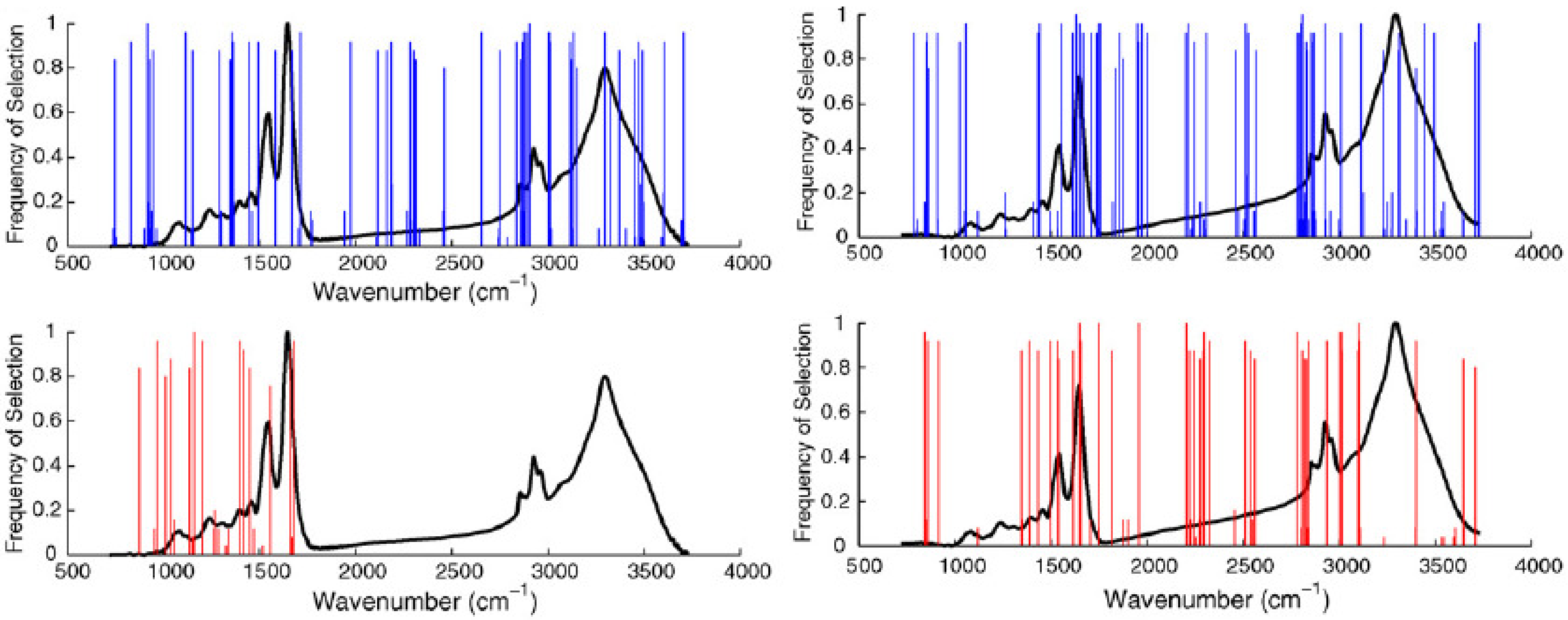






Nawaz et al, Analyst 2010, 2011

Radiation response



Meade et al, Radiation Research 2010
Meade et al, Mutation Research 2010

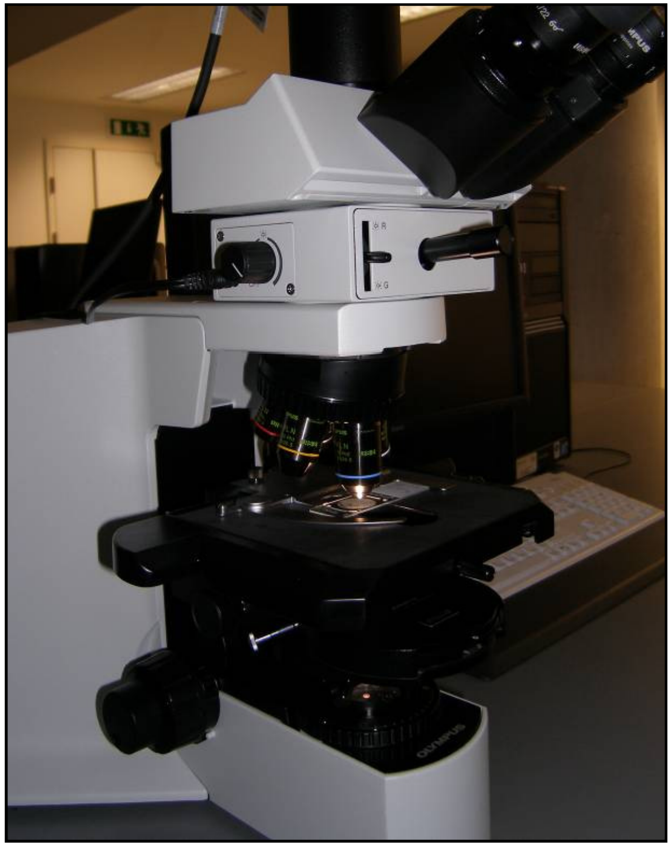
Cervical Cancer

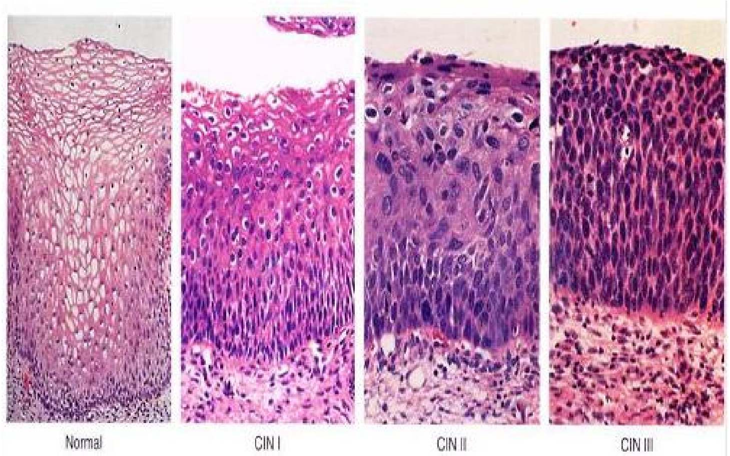
- Cervical cancer kills approx 300,000 women each year worldwide with 80% of the deaths occurring in developing countries
- 100% treatable if detected early
- Cervical cancer screening programmes commonplace in developed countries

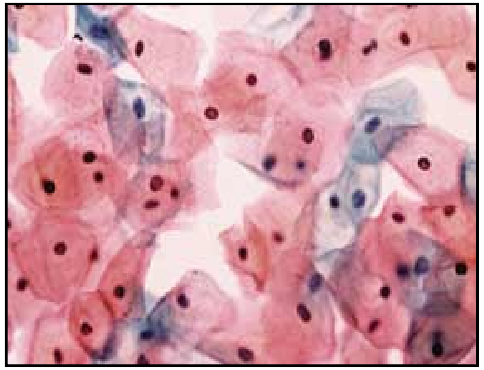
resc

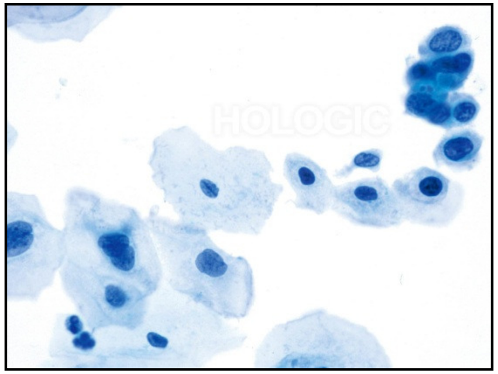
focas
institute/dit

Current methods for screening / diagnosis of cervical cancer





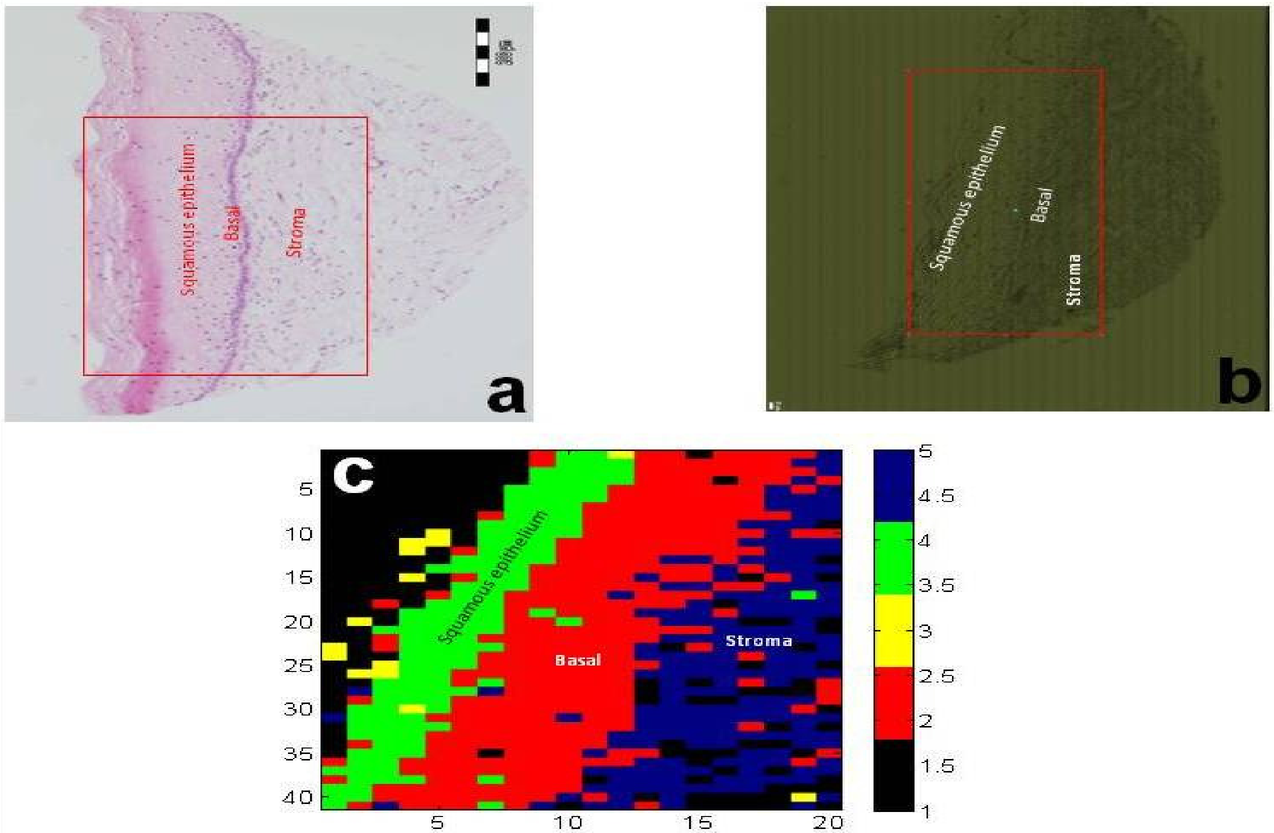




resc

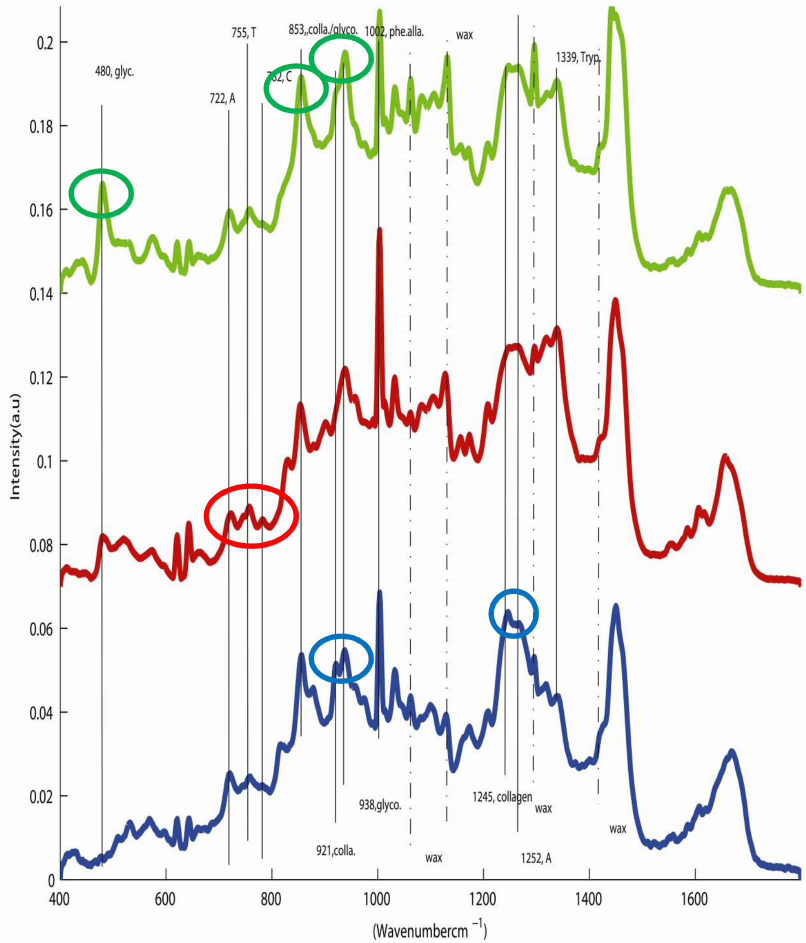
focas institute/dit

Raman imaging for histopathology – normal cervical tissue

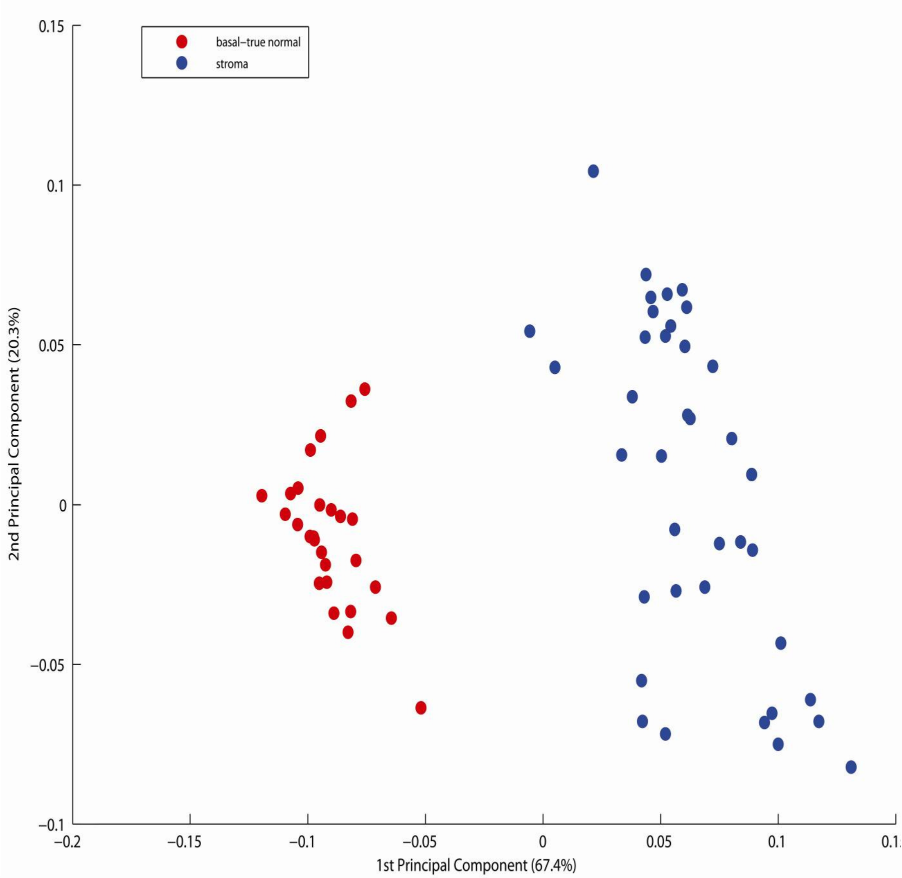


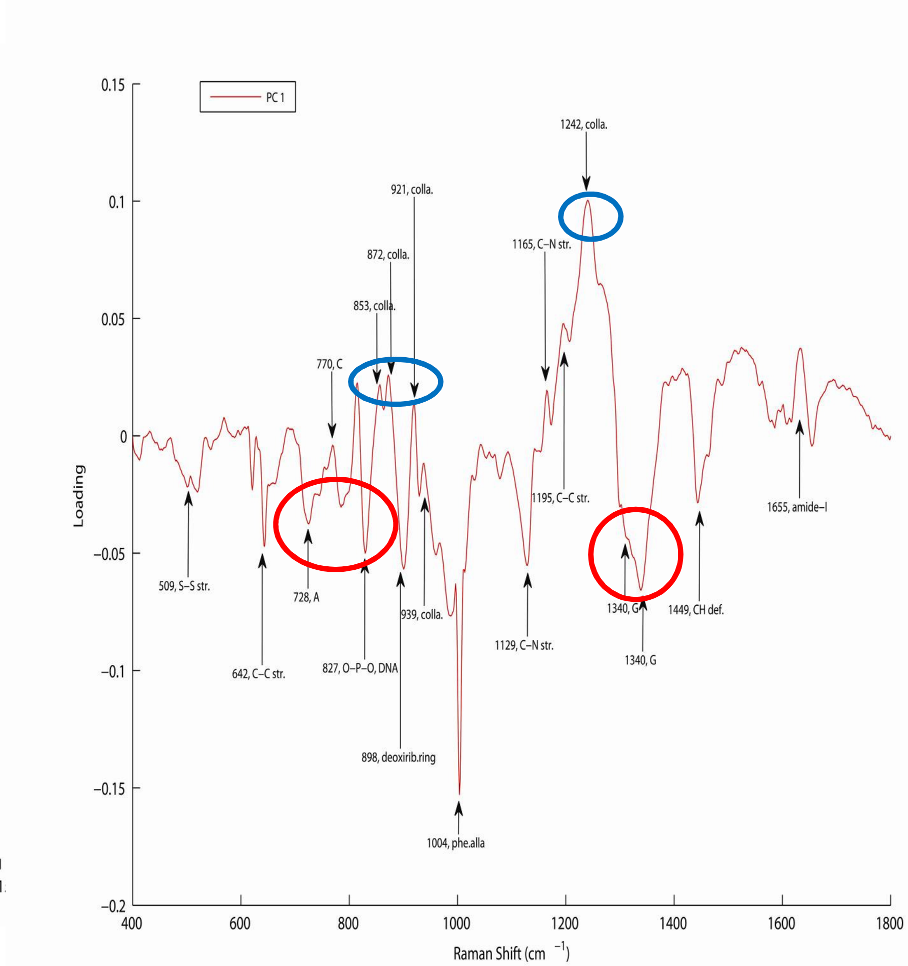
Rashid et al 2014

Raman imaging –
mean Raman spectra

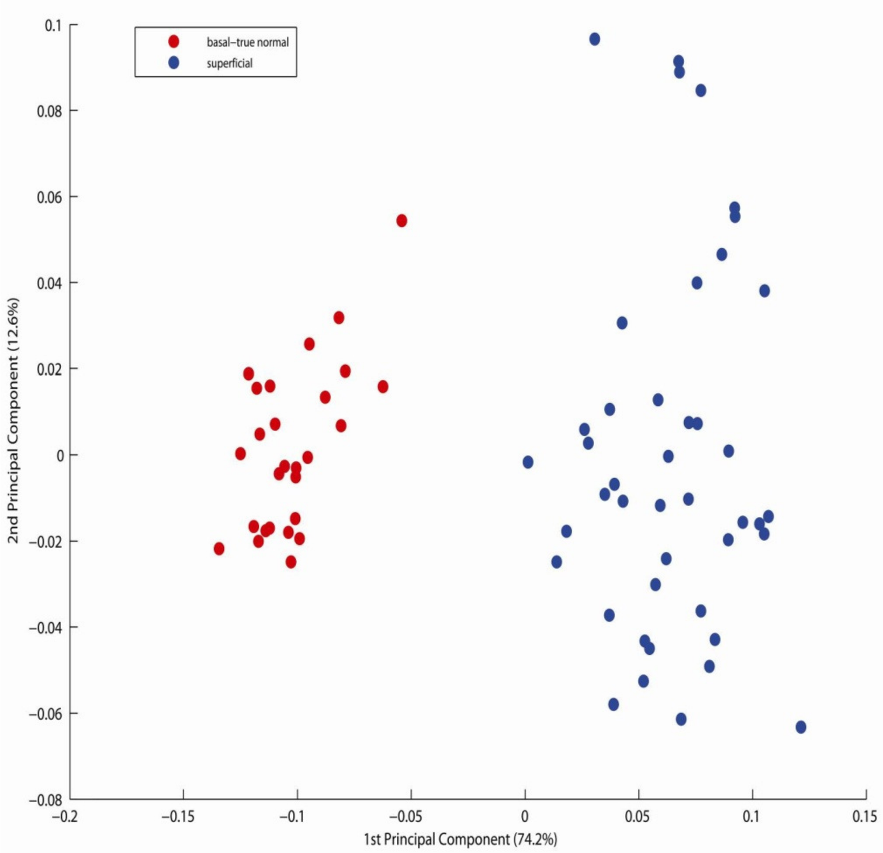


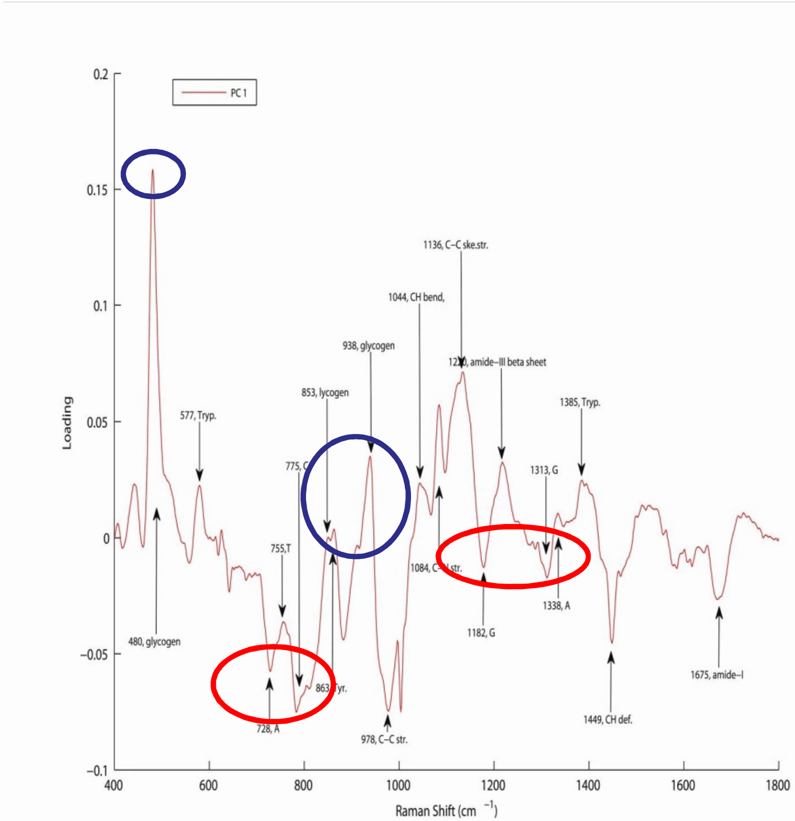
Multivariate analysis – basal layer vs. stromal layer





Multivariate analysis – basal layer vs. superficial layer

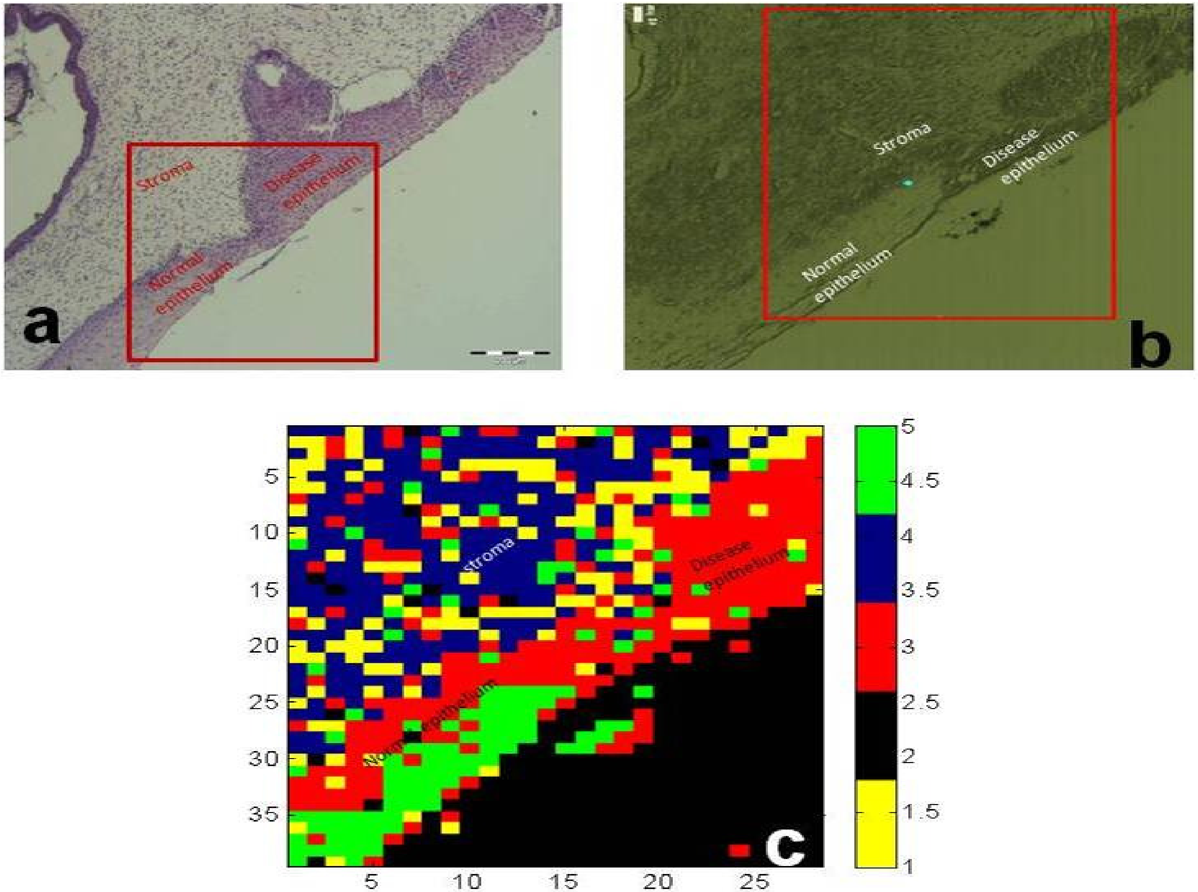




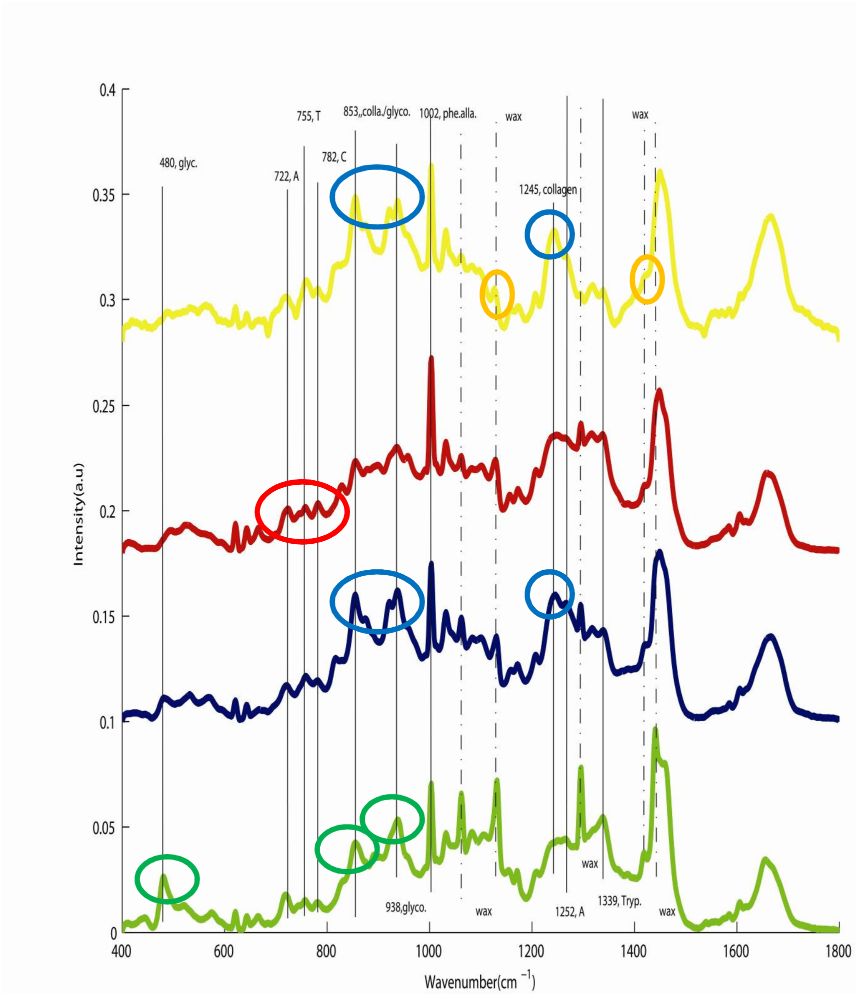
resc

focas
institute/dit

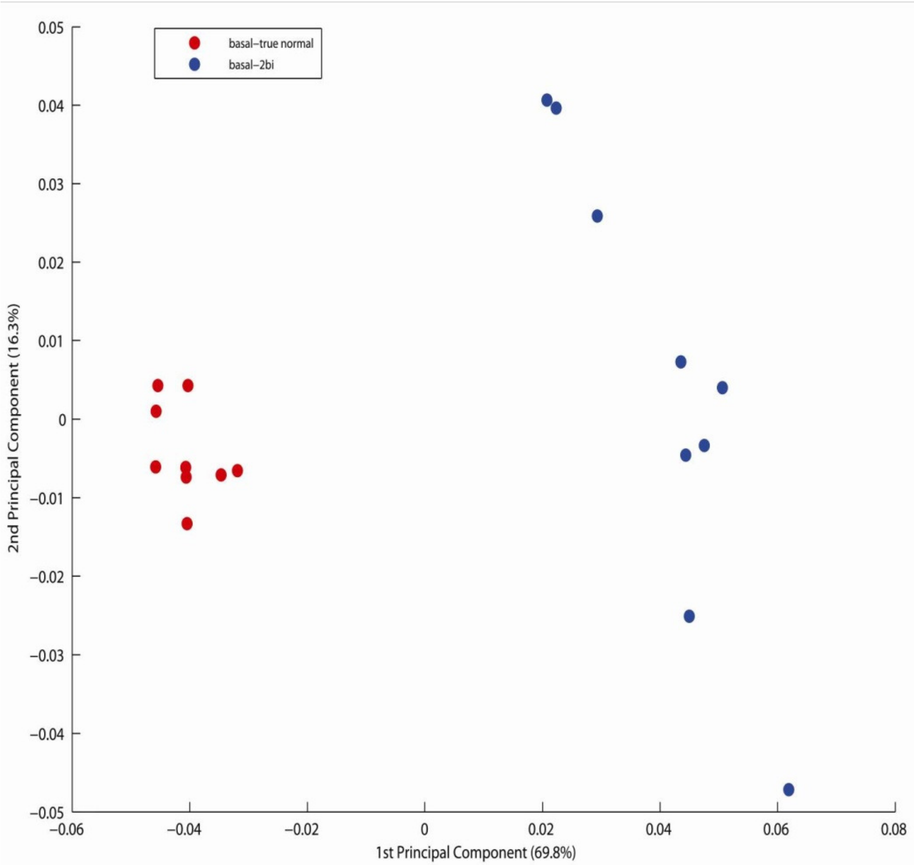
Raman imaging – abnormal cervical tissue

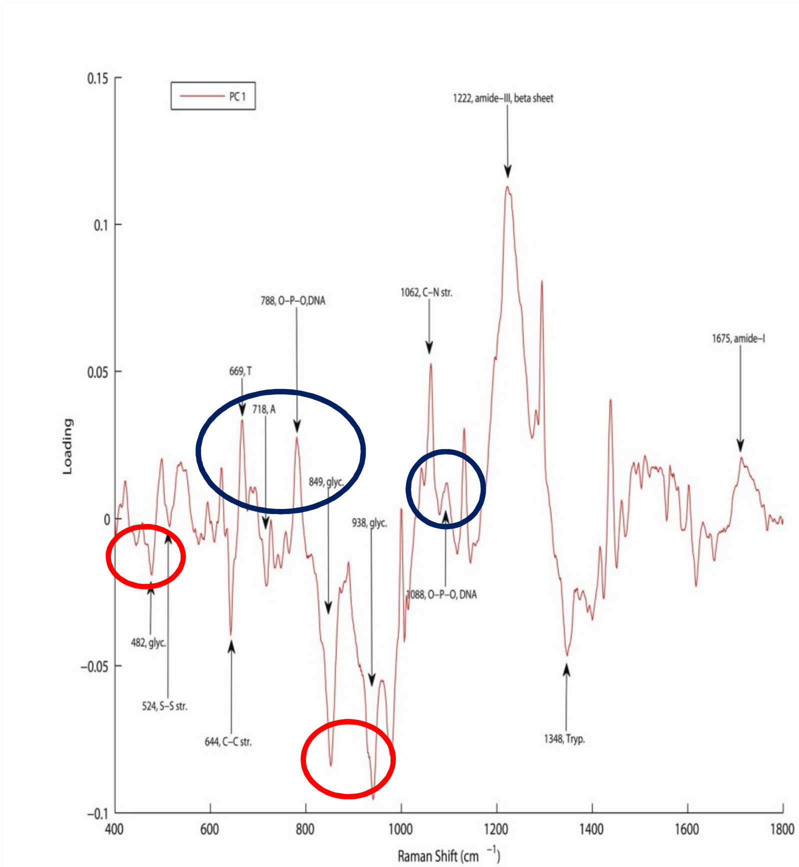


Raman imaging – mean Raman spectra

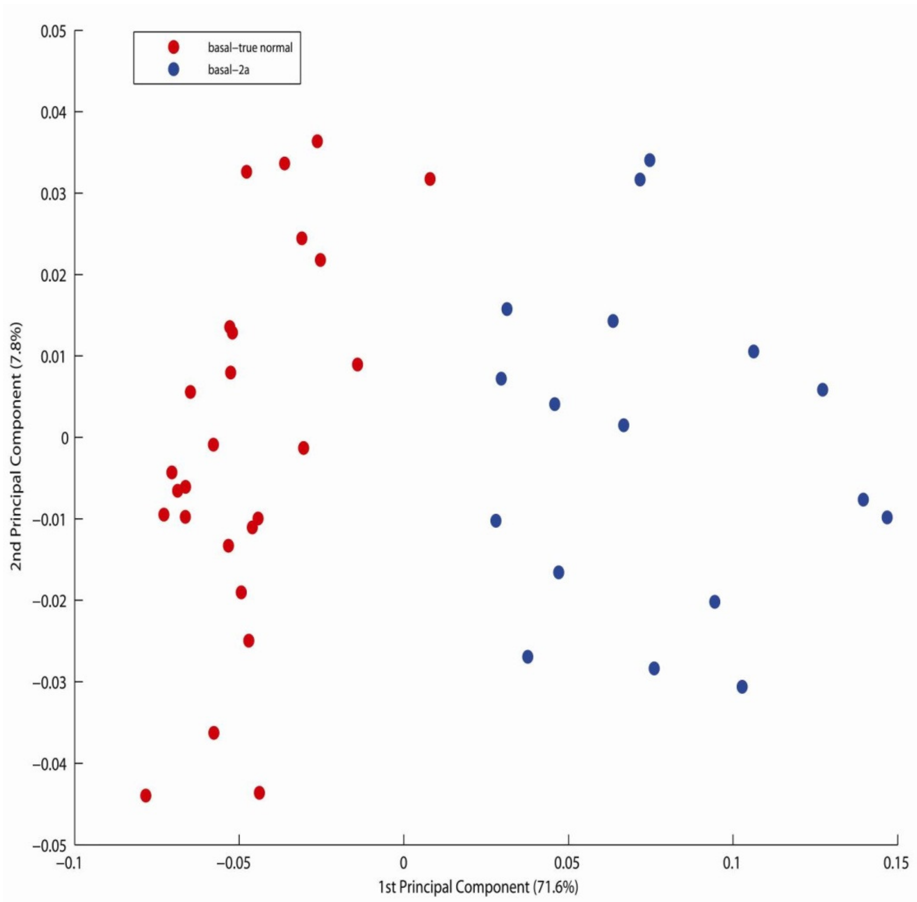


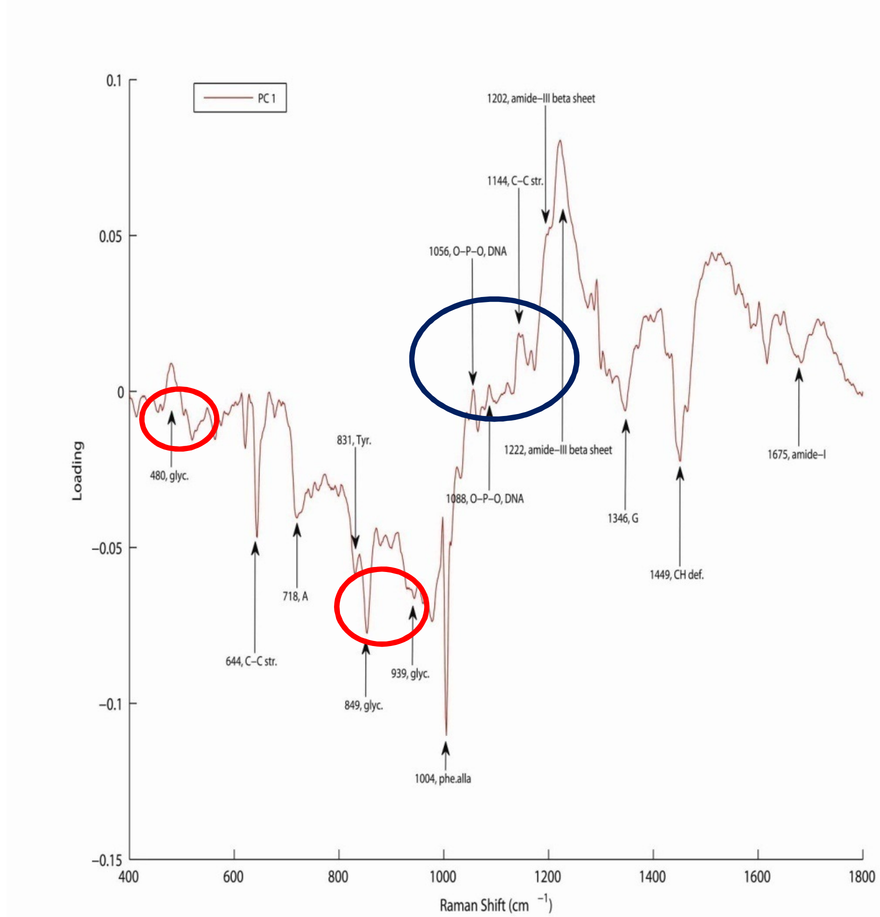
Multivariate analysis – normal basal layer vs. abnormal basal layer





Multivariate analysis – normal basal layer vs. ‘normal’ basal layer

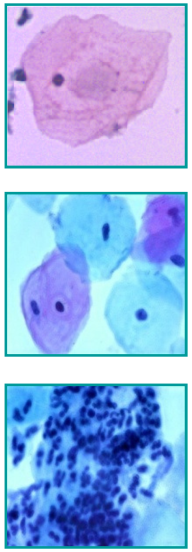


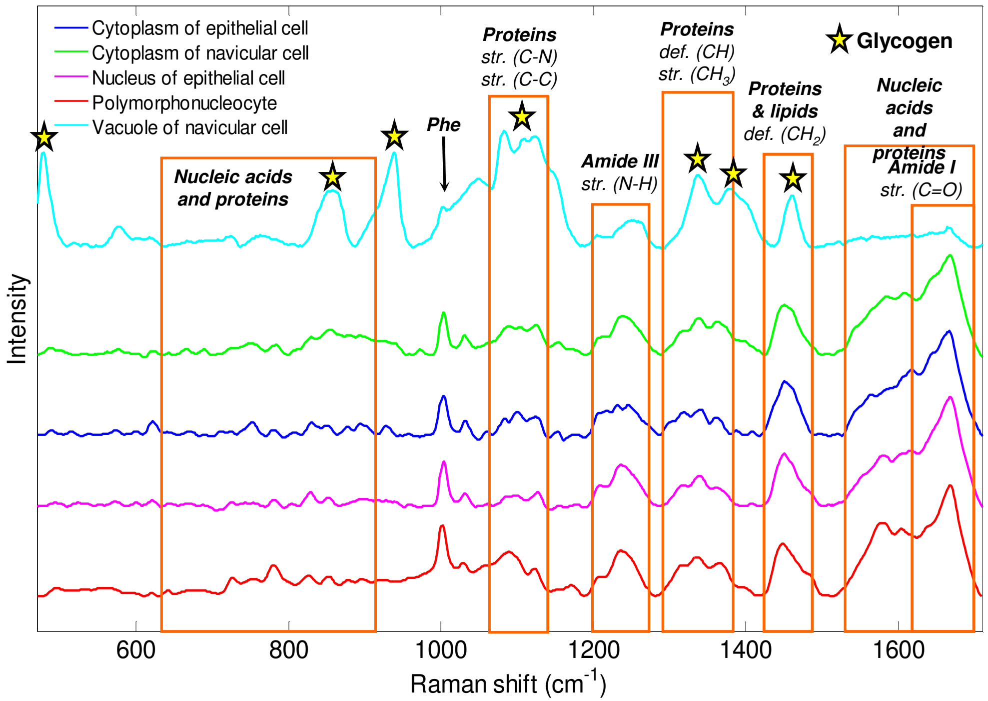


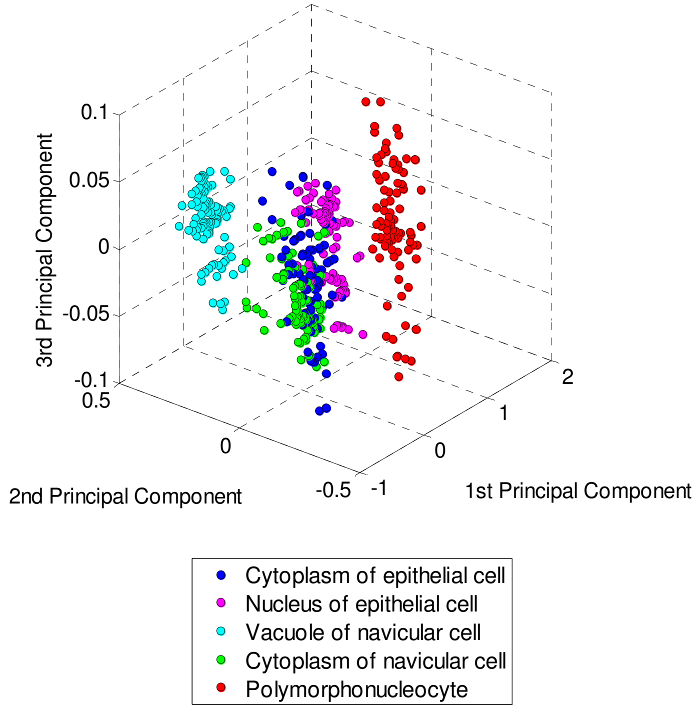
resc

focas
institute/dit

Raman spectroscopy for cervical cytology



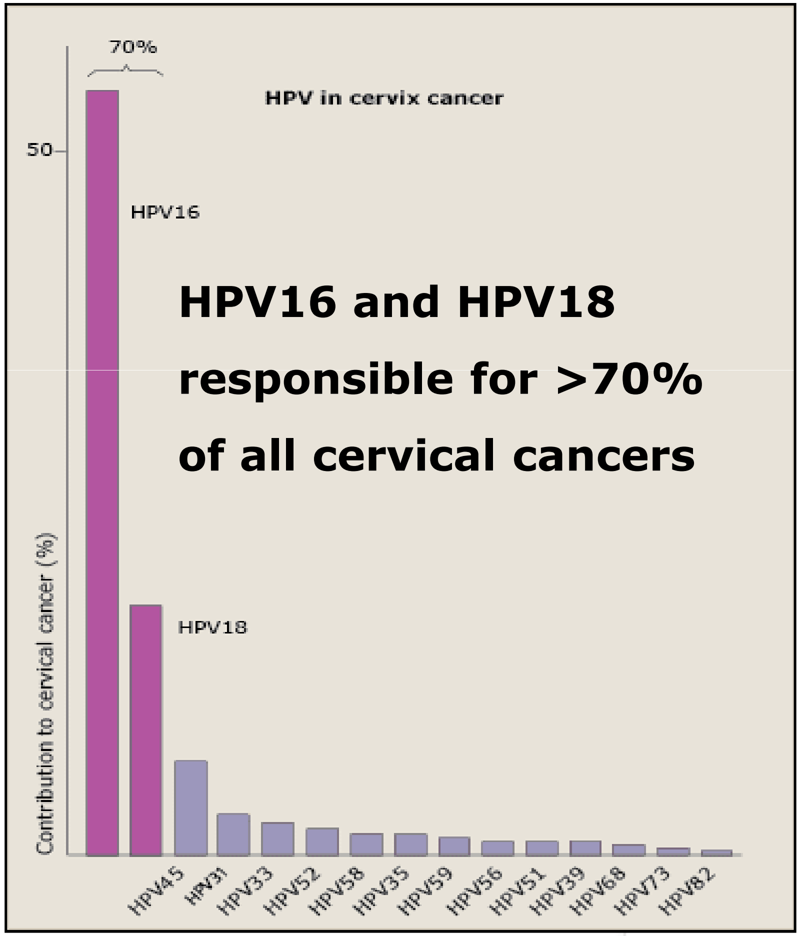




Ostrowska et al 2012

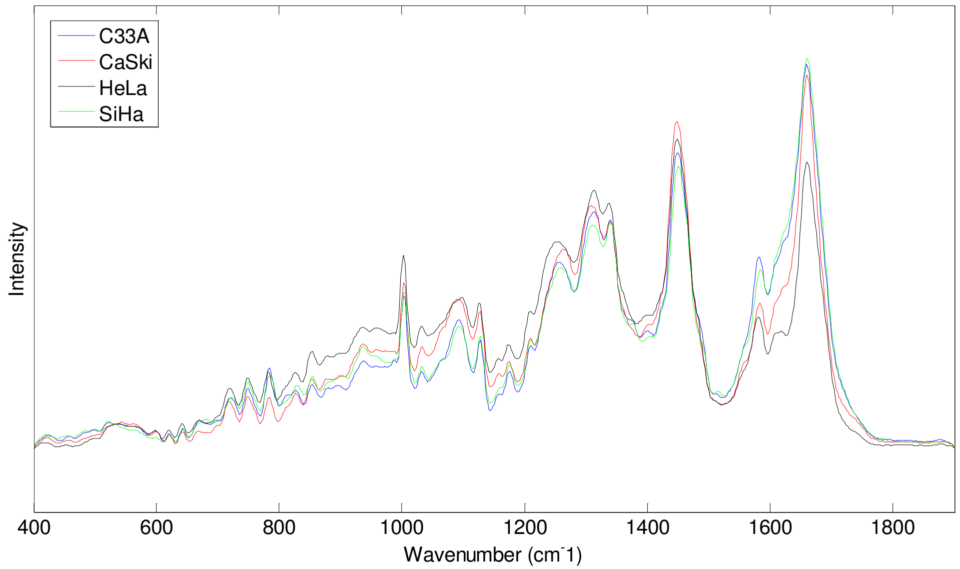
Can Raman spectroscopy detect HPV infection?

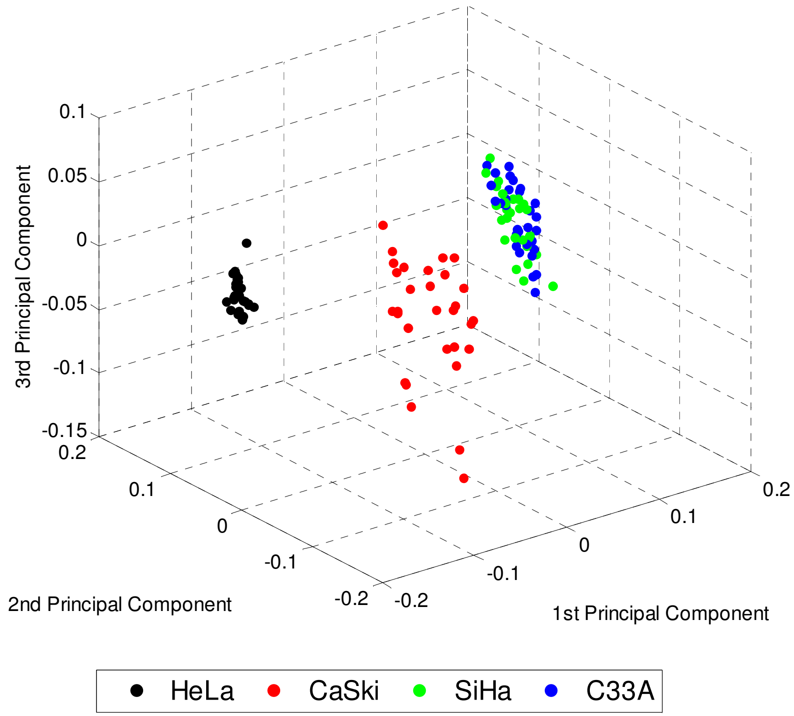
- Cervical cancer cell lines
  - C33A – HPV negative
  - SiHa – HPV16 positive (1-2 copies)
  - HeLa – HPV18 positive (20-50 copies)
  - CaSki – HPV16 positive (60-600 copies)



Ostrowska et al Analyst 2010

HPV negative vs. HPV positive cervical cancer cells





Ostrowska et al Analyst 2010

Take home message

Raman spectroscopy is a powerful molecular characterisation tool

- ✓ Raman spectroscopy can discriminate between normal and abnormal cells in cervical biopsy samples and cervical cytology samples
- ✓ Raman spectroscopy can discriminate between HPV positive and HPV negative cervical cancer cells
- ✓ Raman spectroscopy has great potential to improve cervical cancer screening and diagnosis

resc

focas institute/dit

Acknowledgements

- Coombe Women and Infants University Hospital, Dublin
  - *Prof John O'Leary, Dr Cara Martin, Dr Salih Bakhiet, Padraig Kearney*
- Altnagelvin Hospital, Derry
  - *Dr Michael McKenna, Dr Mary McMenamin*
- Dublin Institute of Technology
  - *Prof Hugh Byrne, Dr Aidan Meade, Dr Franck Bonnier, Kamila Ostrowska, Nosheen Rashid, Damien Traynor, Ines Ramos*

NBIPI THE NATIONAL BIOPHOTONICS & IMAGING PLATFORM IRELAND

Ireland's EU Structural Funds Programmes 2007 - 2013 Co-funded by the Irish Government and the European Union

HEA Higher Education Authority An tÚdarás um Ard-Oideachas

European Regional Development Fund

Enterprise Ireland

resc

focas institute/dit