Development of new Surface-Enhanced Raman Spectroscopy (SERS) fiber probes for *in vivo* and real-time identification of bile acid markers of the microbiota activity

Alexis Lebrun(1,2) , Hubert Fortin(2), Mathieu Lamarre(2), Nicolas Fontaine(2), Olivier Barbier(1) and Denis Boudreau(2)

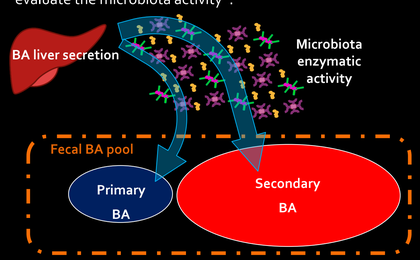
1 Laboratoire de Pharmacologie Moléculaire, Axe Endocrinologie-Néphrologie, Centre de recherche du CHU de Québec – Faculté de Pharmacie, Université Laval, Québec QC, Canada,
2 Département de Chimie and Centre d'optique, photonique et laser (COPL), Université Laval, Québec

Problematic

The increase in cardiometabolic diseases in Canada's northern population has recently drawn attention to the important shifts in diet, form a traditional to a western type diet. It is hypothesized that this shift in nutrition is causing important disturbances in the intestinal microbiome and could potentially drive pathogenic mechanisms of these diseases. Current analytical methods for gut microbiota metabolites are costly and time-consuming procedures, and furthermore, don't provide timely information of variation of CA with food intake. In this project, we aim to develop novel selective chemical sensors for *in vivo* study of gut microbiota activity.

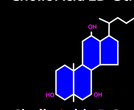
Bile Acids: potential markers of microbiome disturbance

Bile acids (BA) constitute the perfect example of host-microbiome co-metabolism. Indeed, primary bile acid, such as the cholic acid, are synthesized in the liver stored in the gallbladder and secreted in the intestine, where they are converted into secondary acids by gut microbiota. The in situ measurement of bile acid in the gut is therefore an efficient way to evaluate the microbiota activity[1].

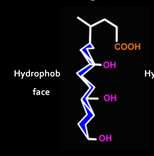


Physiopathological model of bile acids metabolism

Cholic Acid 2D Structure:

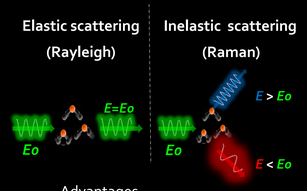


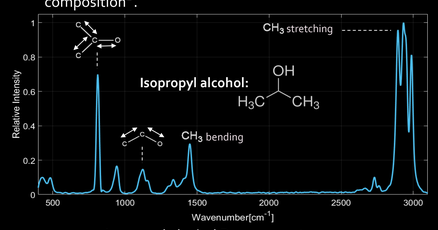
Cholic Acid 3D Structure:



Raman spectroscopy

Raman spectroscopy uses the inelastic scattering of light that comes from energy losses/gains occurring with molecular vibrations. This technique is non-destructive and produces a highly specific spectrum with various bands correlated to the sample's composition[2].





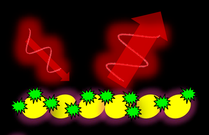
Isopropyl alcohol Raman spectrum

Advantages

- Label-free
- Water signal = low
- Highly specific

Disadvantages

- Easily affected by impurities and background fluorescence
- Raman effect is very weak

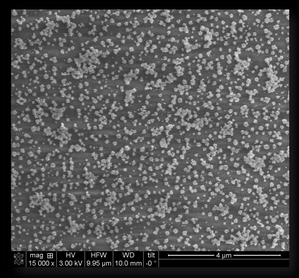


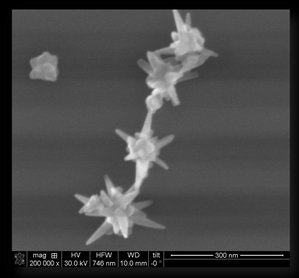
: Metallic SERS Substrate
: Sample

Surface Enhanced Raman Scattering (SERS)

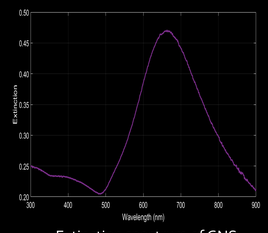
Raman scattering combined with the enhancement effect from the metal substrate allows considerable gain ($10^6 - 10^{12}$) on Raman intensity[3].

Results





- A wavelength of 633 nm is selected to avoid background fluorescence from cells.
- Gold nanostars (GNS) exhibit good absorptive and scattering plasmonic properties that overlap well with 633nm excitation wavelength.
- GNS are also characterized by intense field located at the ends of the spikes.



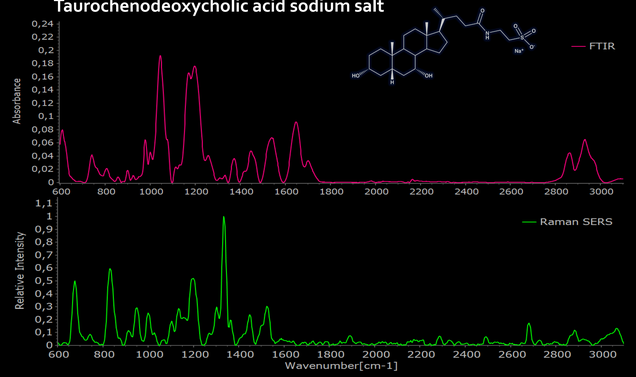
Extinction spectrum of GNS

SERS/FTIR Spectra

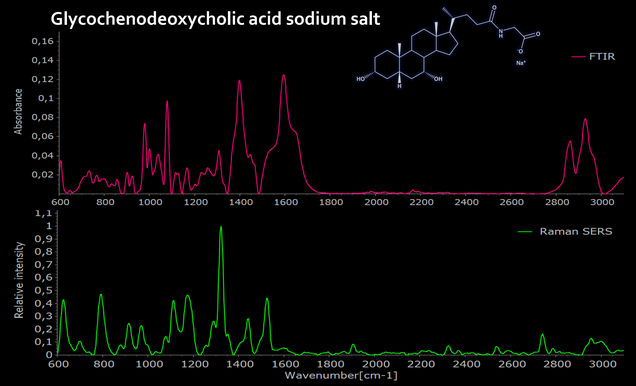
As a first proof of concept, spectral analyses were carried out on cholic acid salts which have distinct functional groups. Fourier Transform Infrared spectroscopy (FTIR) analyses were performed in parallel to optimize the identification of functional groups.

Raman spectra of BA with and without SERS

Taurochenodeoxycholic acid sodium salt

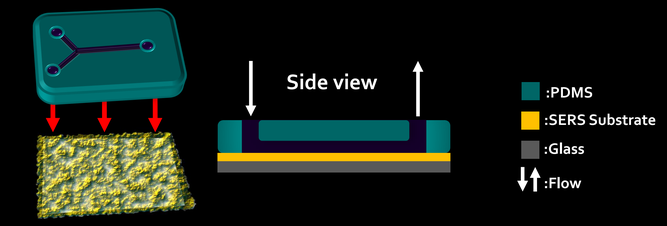


Glycochenodeoxycholic acid sodium salt



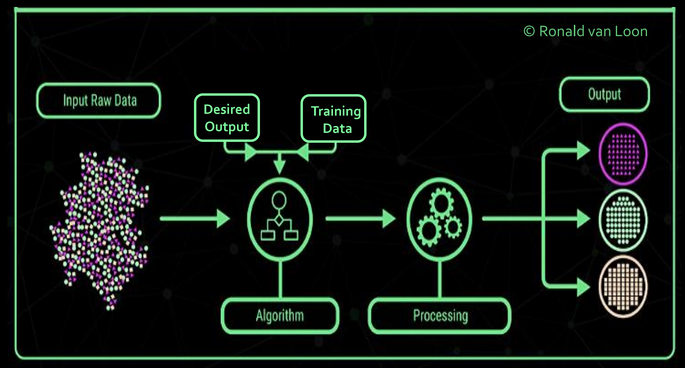
Future works

Microfluidic SERS device



Optical fiber with SERS substrate on tip

Machine learning algorithm



Conclusion

Studying cholic acids using SERS is a promising tool to improve the health of Canada's Northern population. Real-time and *in situ* monitoring of new key biomarkers can potentially be used for predictive diagnostic of cardiometabolic diseases, hence permitting us to gain a better understanding of the host-bacteria interactions in the gut microbiota.

References

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3. Le Ru, E., & Etchegoin, P. (2008). Principles of Surface-Enhanced Raman Spectroscopy: and related plasmonic effects. Elsevier.

Acknowledgements

CANADA FIRST RESEARCH EXCELLENCE FUND
Fonds de recherche Nature et technologies Québec
Sentinel North
CRSNG NSERC
INNOVATION.CA
CANADA FOUNDATION FOR INNOVATION | FONDATION CANADIENNE POUR L'INNOVATION

<alexis.lebrun.1@ulaval.ca>