Novel Enhancement Structures for Surface-Enhanced Raman Scattering from DNA: Towards Single Base Resolution for Long-Read Sequencing

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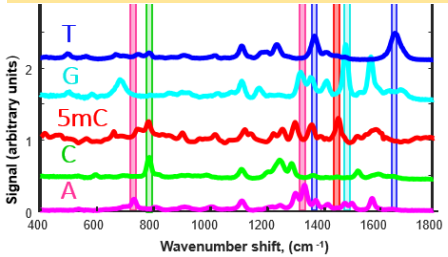
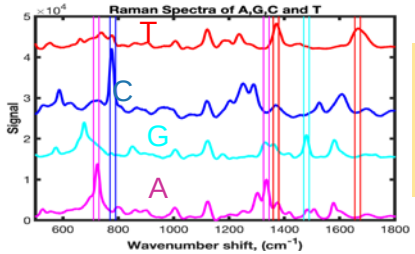
Raman scattering identifies the spectral fingerprint of a DNA base but its sensitivity is low. Novel SERS enhancement structures solve that problem providing: 1) spatial resolution of < 1nn^3; 2) simulated enhancement factors of ~ 1x10^9, and 3) lithographically defined separation of enhancement structure hot spots allowing highly parallel optical interrogation of single DNA molecules in multiple channels.

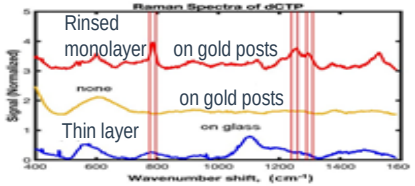
Signature Raman Spectra of DNA bases. Each base, has at least one unique Raman band that persists from solution (1) to SERS (2)



1. dNTPs in solution, 100mM. Characteristic peaks identified



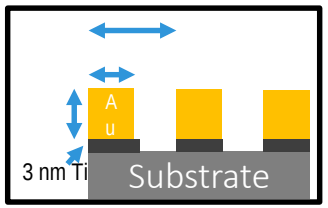
2. dNTPs as a dry monolayer on surface with gold posts . Same peaks persist

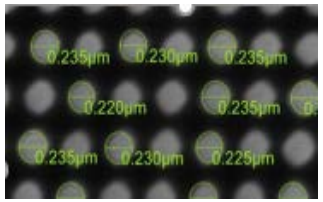


3. dCTP signal enhancement on gold posts.dCTP signature only on gold posts

Enhancement nanostructures for SERS:

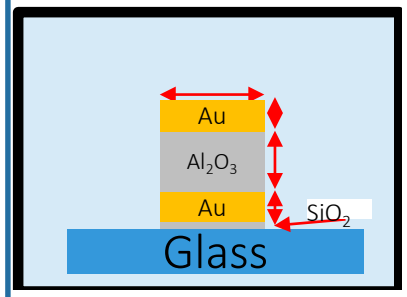
Gold posts (dimensions vary), schematic and ESM

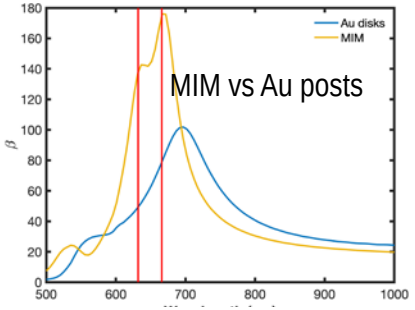


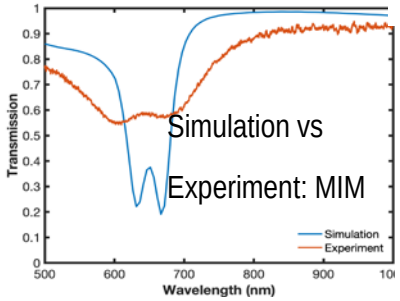


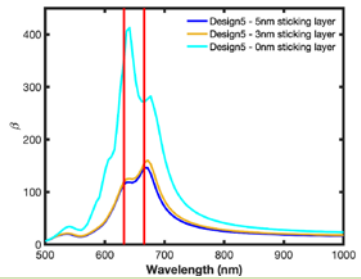
Estimated enhancement ~2x10^4

MIM (metal-insulator-metal) nanostructures; dimensions vary

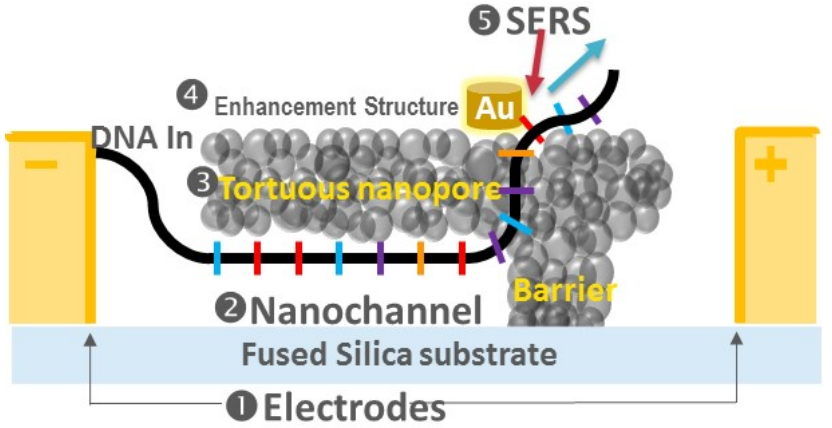






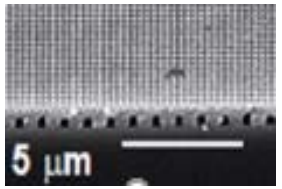


Simulated signal enhancement for optimized MIM ~ 2x10^9 , sufficient for single base sensitivity



Electrophoretic control (1) of nucleic acid translocation through **Nanochannels** (2) and through **Tortuous nanopores** (3) at the barrier to **Plasmonic enhancement structures** (MIM) (4) **and** optical readout by SERS .For chip details and DNA control in nanochannels a see a poster by Y. Kuznetsova

A



B

SEM of roof showing distribution of pores (A) and successful placing of MIM structures on the nanochip roof (B)

Pore density can be reduced by ALD/CVD processes to achieve one pore per MIM structure

Conclusions

- Raman Spectroscopy identifies spectral signatures of individual DNA bases as well as modified bases
- MIM sandwich structures are superior to simple gold posts in enhancing Raman signal
- Signal enhancement can reach levels sufficient for single base sensitivity

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