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SCAN ME

Novel lateral flow technology detecting infection earlier: Conjugated Polymer Nanoparticles

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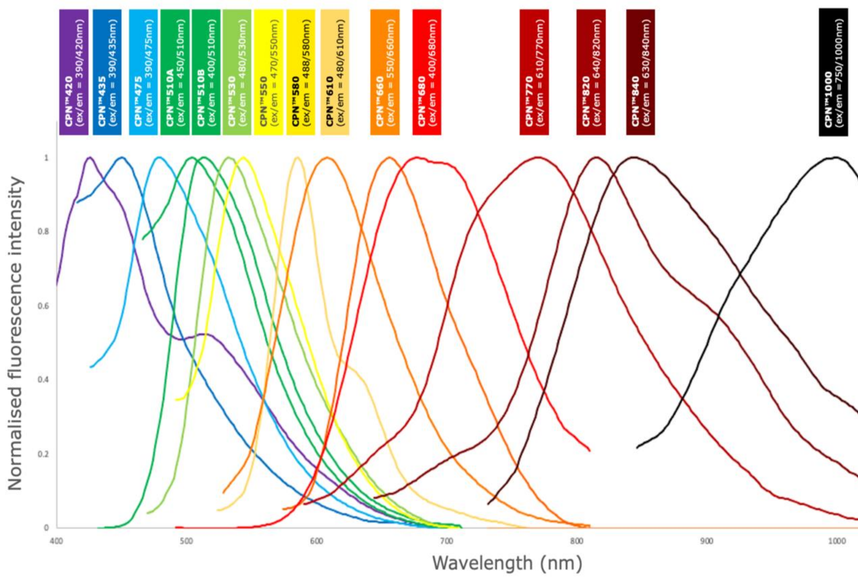
Lateral Flow 4.0 – High intensity fluorescence improving performance of LFTs

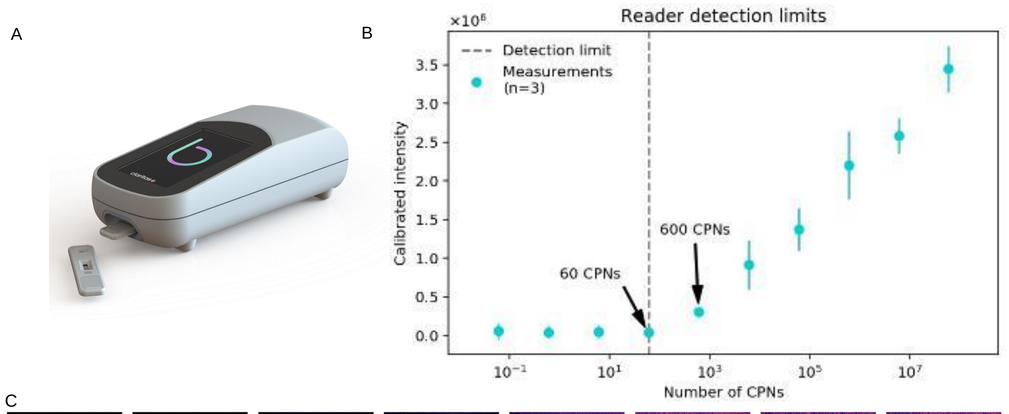
Lateral flow technologies play a vital role in the rapid diagnosis of numerous infections and diseases. CPNs are up to 1000x brighter than Quantum dots, their high fluorescent intensity enables very low levels of accurate target detection, potentially enabling earlier disease diagnosis. The wide CPN colour range extensively spans both the visible and IR spectrum, and can facilitate an ultra-sensitive, multiplexed, mass screening capability. This enables several targets to feature on one test strip for rapid and multiple disease diagnosis in the same test. CPNs have been tested in lateral flow devices across a wide range of disease targets including SARS-CoV-2 (COVID-19), influenza A and B, E. coli strains and cardiac arrest (troponin I and T).



CPN	ex/em	CPN	ex/em
CPN 420 (Violet)	390/420	CPN 610 (Orange)	480/610
CPN 435 (Indigo)	390/435	CPN 660 (Red)	540/660
CPN 475 (Blue)	390/475	CPN 680 (Red)	400/680
CPN 510A (Green)	455/510	CPN 770 (IR-I)	610/770
CPN 510B (Green)	400/510	CPN 820 (IR-I)	640/820
CPN 530 (Green)	455/530	CPN 830 (IR-I)	610/830
CPN 550 (Yellow)	470/550	CPN 840 (IR-I)	630/840
CPN 580 (Orange)	488/580	CPN 1000 (IR-II)	750/1000

The Claritas Reader – Fluorescence and infrared detection

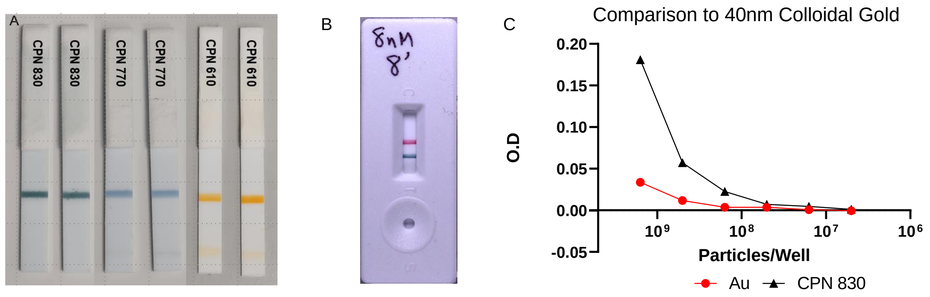
The Claritas platform is a highly sensitive and fully quantitative handheld fluorometer for the analysis of LFTs. The reader is capable of both fluorescent and infrared LFT analysis and can identify a positive signal from a few hundred CPNs.



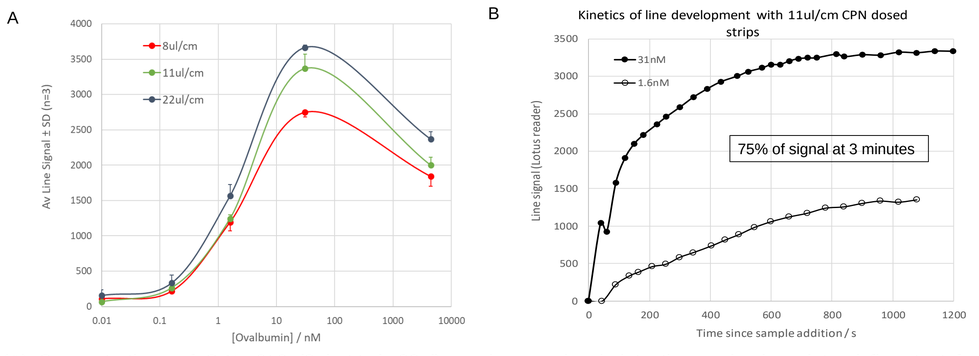
(A) The Claritas Reader. (B) The Claritas reader CPN detection limit. (C) CPN 610 dilution series with images taken using the Claritas reader.

Multi-coloured directly visible lateral flow test with higher sensitivity than gold

CPNs can also be used as highly sensitive visual detection agents (no reader) in lateral flow tests with a 40% greater absorbance than gold nanoparticles.



(A) Representative images of CPN 830, CPN770 and CPN 610 used as a visual detection agent in a lateral flow test. (B) CPN 830 binding to the test line and gold nanoparticles binding to the control line of a LFT. (C) Serial dilution of gold compared to CPN at matching particle concentrations. CPN830 has significantly more intense absorbance per particle.



(A) Concentrations of CPN 610 (8µl, 11µl, 22µl) used as a visual detection probe in a lateral flow test for ovalbumin (16700nM – 0.01 nM). (B) CPN Signal development kinetics in LFT. Time to result profile shows that the assay does not develop much more after 10 minutes. A 10 minute or less, quantitative 'production' test could be manufactured and validated.

High sensitivity fluorescent lateral flow tests

CPNs have been shown to be an ideal detection agent for infectious disease diagnostic platforms. The CPN based LFT platform and reader (Claritas, Brightline Dx) for SARS-Cov-2 enabled detection with sensitivity approaching PCR tests providing a sensitive, affordable, and rapid solution to disease and pandemic control. The already developed CPN based diagnostic platform and reader can be readily modified and utilised for other infectious diseases making it a powerful tool in future pandemic and disease outbreak control.

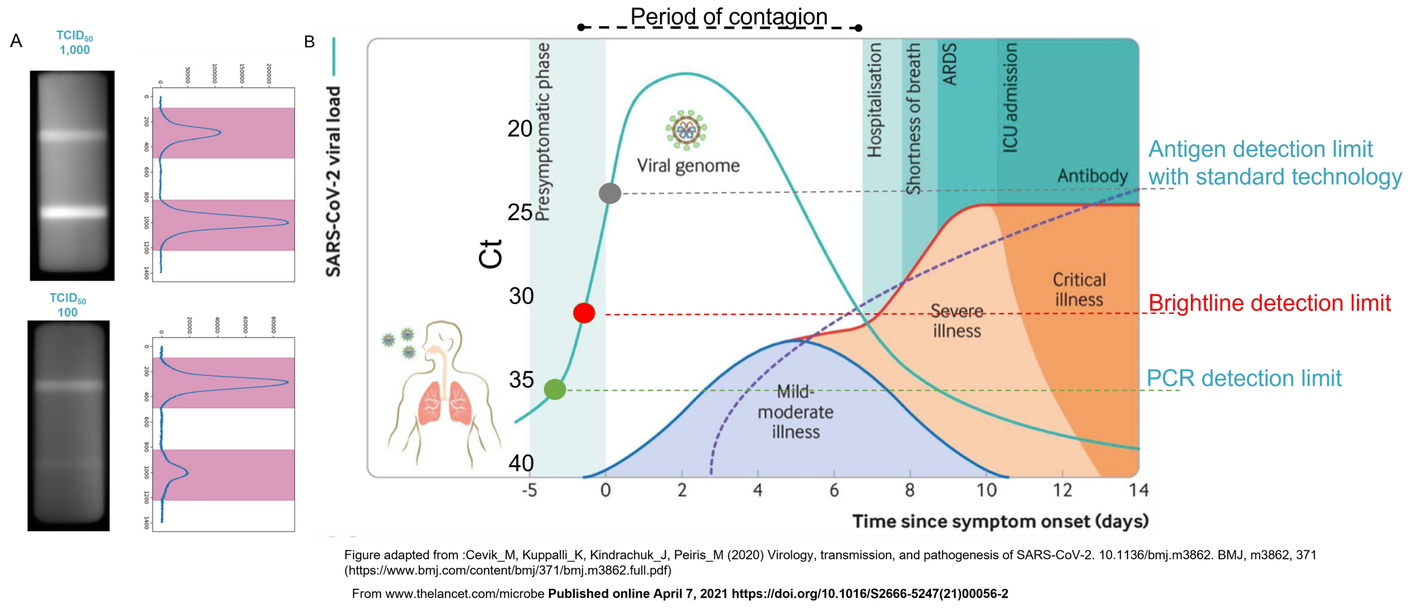
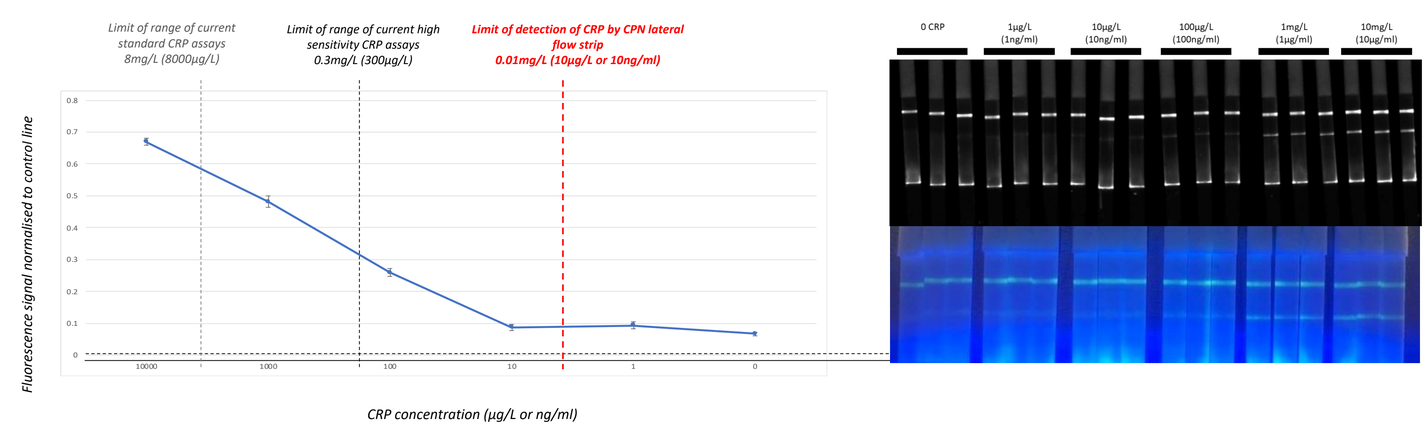


Figure adapted from :Cevik_M, Kuppalli_K, Kindrachuk_J, Peiris_M (2020) Virology, transmission, and pathogenesis of SARS-CoV-2. 10.1136/bmj.m3862. BMJ, m3862, 371 (https://www.bmj.com/content/bmj/371/bmj.m3862.full.pdf)

From www.thelancet.com/microbe **Published online April 7, 2021 https://doi.org/10.1016/S2666-5247(21)00056-2**

(A) The claritas Brightline platform results at TCID50 1000 and 100 for SARS-CoV-2. (B) A comparison of the claritas Brightline platform, conventional LFTs and PCR tests for the diagnosis of SARS-CoV-2 infection.

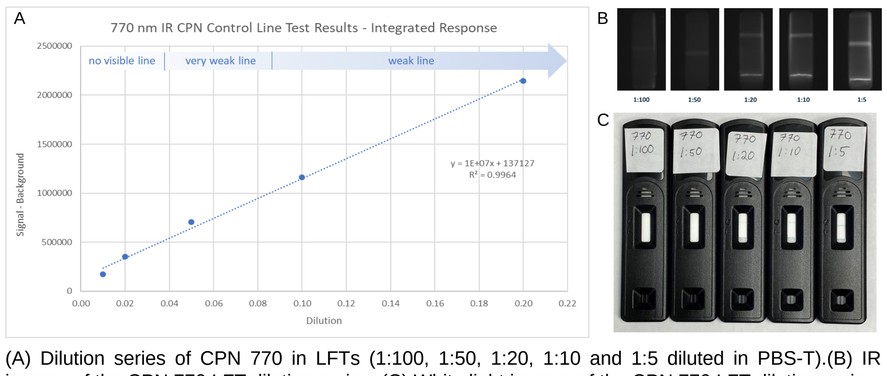
Limit of detection 800 times better than standard tests and 30 times better than the high sensitivity tests according to FDA regulatory information



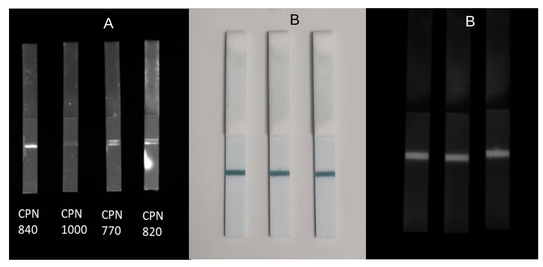
CPN based CRP detection lateral flow tests showing signal from 10mg/L (10ug/ml) to 10ug/L (10 ng/ml)) with clear and consistent controls lines visible.

Improve LFT performance with near infrared CPNs

There are a range of CPNs which fluoresce within the near infrared window (700nm-1000nm) which can penetrate surrounding materials and liquid media including biological fluids such as blood, effectively reducing background noise to zero resulting in an improved signal to noise ratio and extremely high sensitivity. These NIR CPNs offer a stable and high intensity infrared biosensor which can be incorporated into lateral flow tests and further diagnostics applications.



(A) Dilution series of CPN 770 in LFTs (1:100, 1:50, 1:20, 1:10 and 1:5 diluted in PBS-T).(B) IR images of the CPN 770 LFT dilution series. (C) White light images of the CPN 770 LFT dilution series.



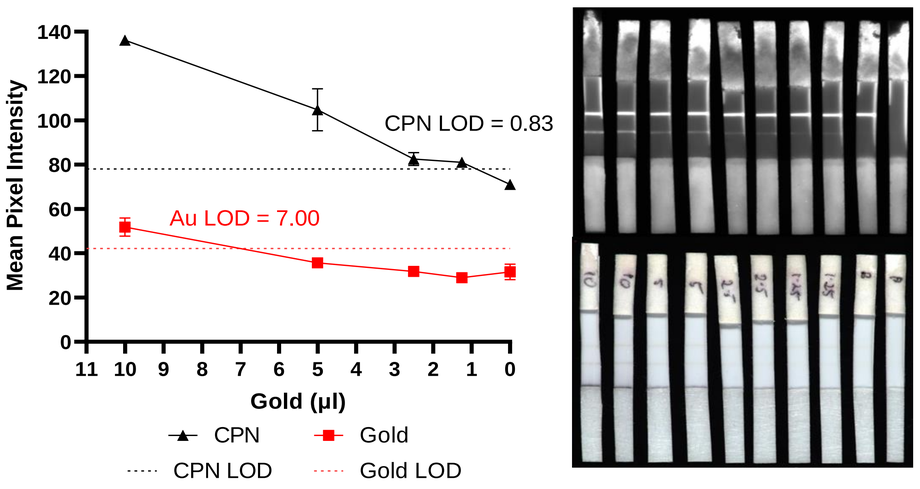
(A) IR CPNs+anti-mouse IgG imaged with infrared camera, LICOR detector Clear signals at the test lines. (B) CPN830: Control line, protein A/G binds the mouse primary antibody on the surface of the CPN (ex/em: 620/830nm). ImageQuant 800 used visible light for absorbance image and ex/em: 660/836.

Improving limit of detection of existing gold LFT with CPNs

CPNs can be used to improve the limit of detection of gold based lateral flow tests 8-fold.

CPNs can be modified to bind to the antibody on the surface of gold nanoparticles. This facilitates binding between the two nanoparticles at the test and control line of LFTs. The high intensity fluorescent signal is detectable at much lower concentrations than the visible signal from the gold, therefore enabling positive signal identification at much lower analyte concentrations.

CPNs can therefore improve the sensitivity of gold based LFTs and enhance the limit of detection.



CPNs targeted against gold in LFTs. The fluorescent CPN signal provides a greater signal than the visible gold signal resulting in an enhanced LOD.

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