**Supplementary Material**

S1: Principle component analysis scores vs sample plots for PC1 and PC1 for both blood and serum based analysis. Both the calibration and validation sets are shown. Samples are as follows: Day 0 (red), Day 1 (dark blue), Day 2 (purple), Day 3 (light blue), Day 4 (orange) and Day 7 (green). Mice A are shown as triangles, mice B as squares and mice C as circles. Corresponding loadings plots are as shown in Figures 4 and 5.

Blood samples
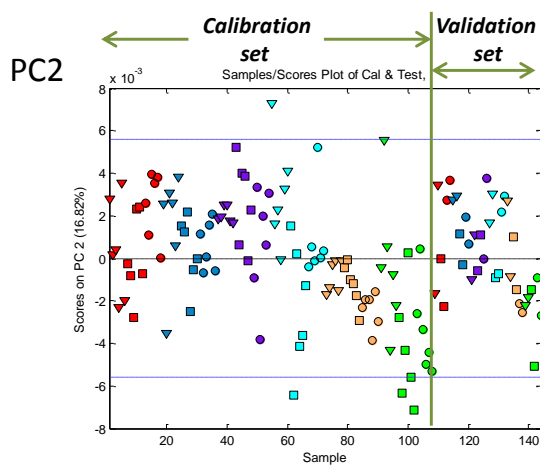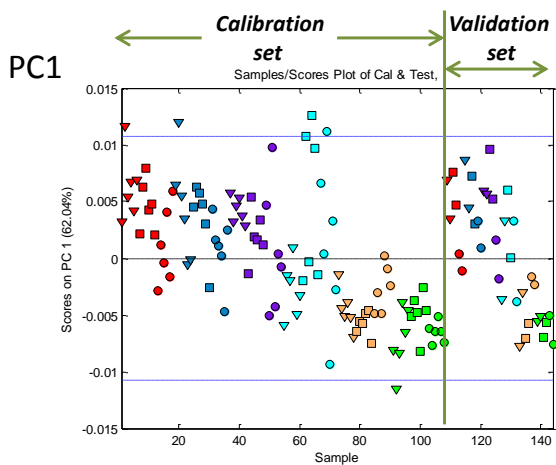
Plasma samples
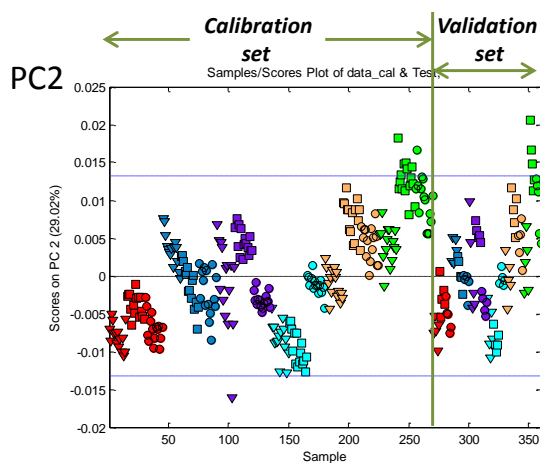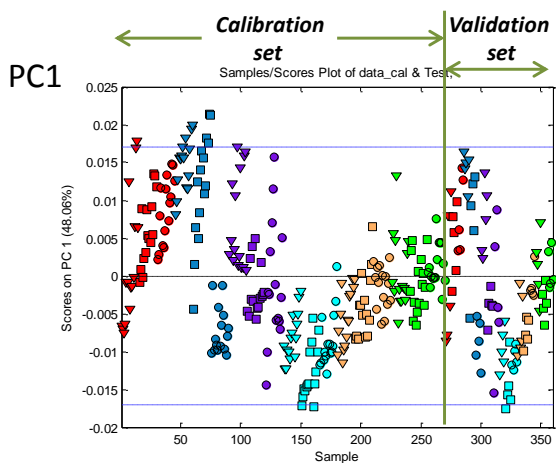
S2: PCA scores (left) and loadings (right) plots for the separation of hemoglobin (red), hemin (green) and hemozoin (black) reference spectra. Reference spectra were collected as described in the experimental section. Five replicates of each sample were used for the PCA analysis. The spectra were preprocessed using a 5pt smoothing function, a 6th order polynomial weighted least squares baseline correction, normalised and mean centred prior to PCA which was cross validated using random subsets with 5 data splits and 5 iterations. PC1 shows the spectral features that separate hemoglobin from hemin and PC2 shows those that separate hemoglobin and hemin from hemozoin. The loadings plots have been used as an aid for the interpretation of the PCA results from the blood and plasma samples.
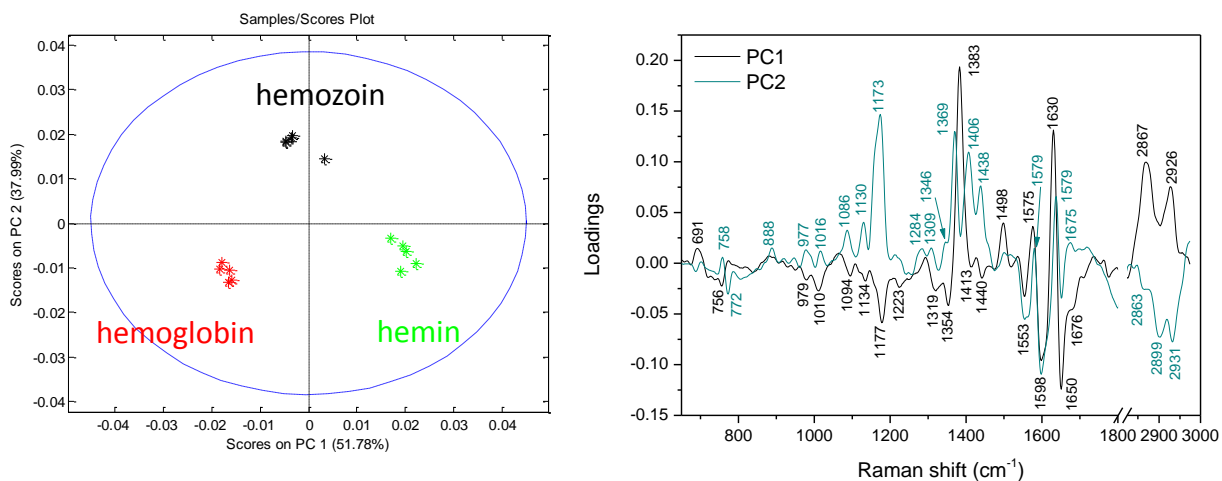
S3: PCA of hemozoin-spiked plasma samples. (a) sample vs score on PC1, (b) sample vs score on PC2, (c) PC1 vs PC2 scores plot and (d) loadings plots for PC1 and PC2. Naieve plasma samples were spiked with known concentrations of hemozoin (concentrations are shown in the figure key) and Raman spectra were recorded in the same manner as the other plasma samples. The spectra were preprocessed using a 5pt smoothing function, a 6th order polynomial weighted least squares baseline correction, normalised and mean centred prior to PCA which was cross validated using random subsets with 5 data splits and 5 iterations. This figure shows that changes on both PC1 and PC2 contain some bands from hemozoin, but while the scores plots from PC1 indicate some spectral changes at low concentrations of hemozoin, PC2 does not reflect any changes in scores for samples with hemozoin concentrations below 0.195 mg/ml. Taking this as a conservative estimate, this approach using Raman spectroscopy in conjunction with PCA analysis is capable of detecting 0.195 mg/ml hemozoin in plasma. This equates to a hemozoin concentration of approximately 40 micromolar.