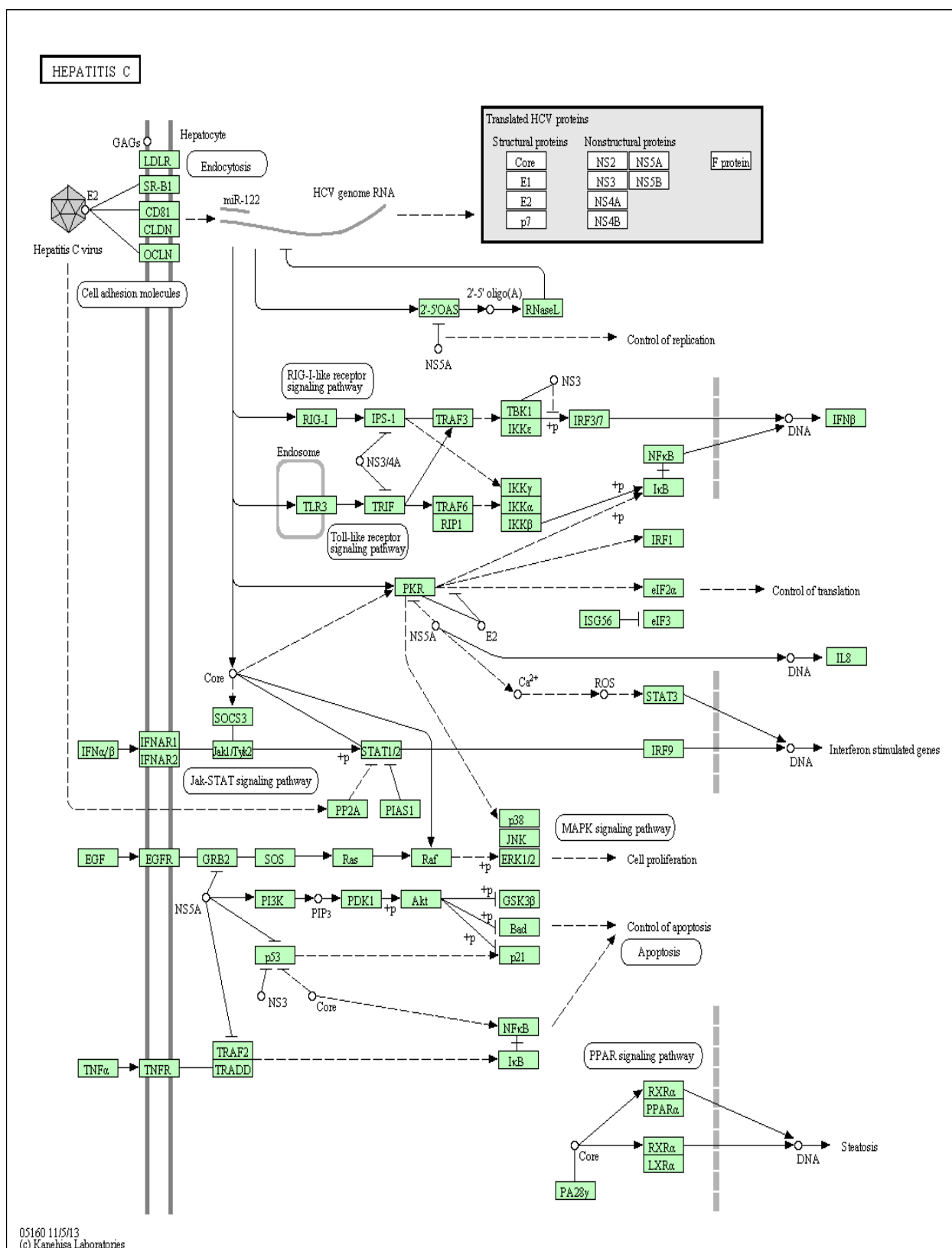
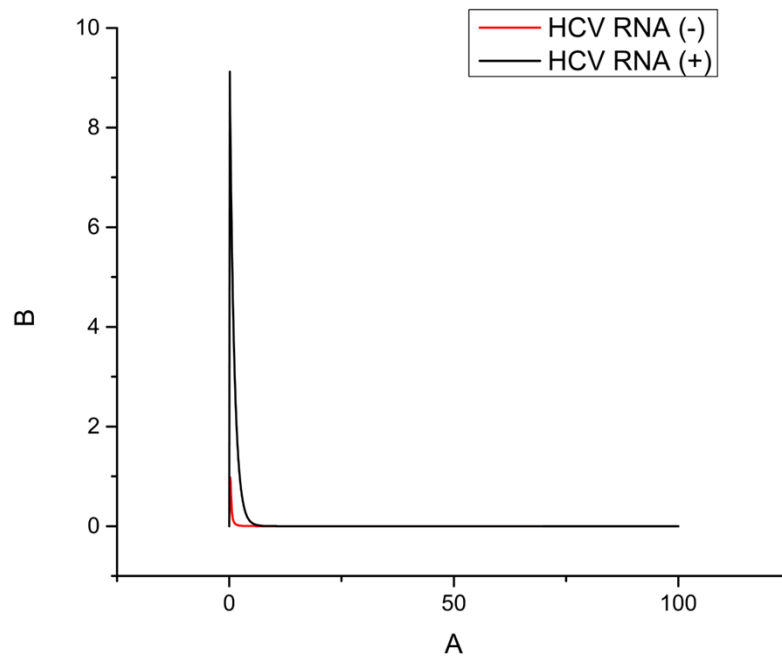


Supplementary file 1:

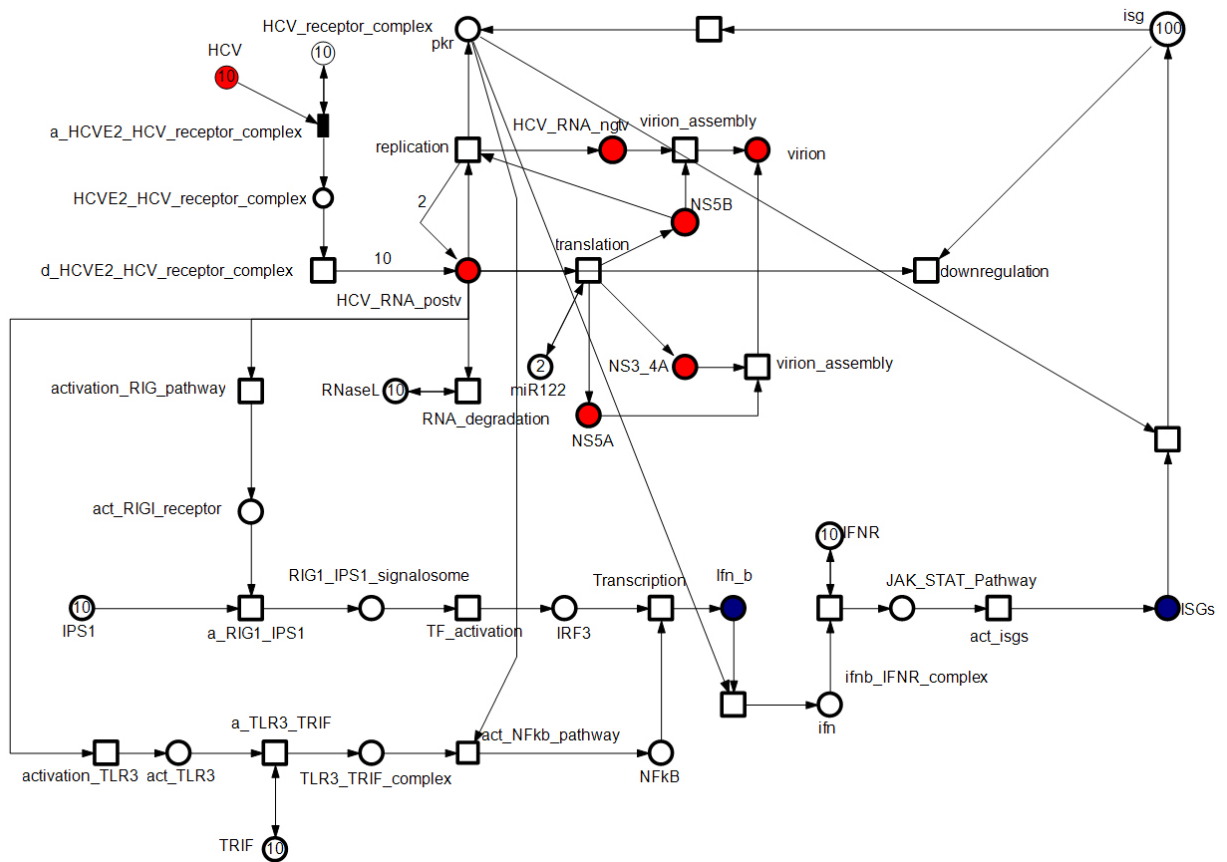


Supplementary File 2:



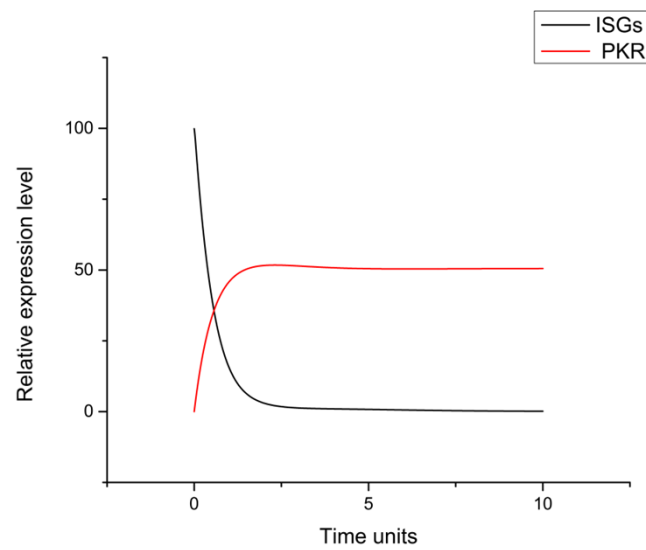
Supplementary File 2: Simulation result for 100 time units: Relative concentration of HCV RNA (+) and HCV RNA (-) represented on y-axis with time units on x-axis. The entities achieve a steady state after initial oscillations. As observed, the behavior does not change and remains stable for 100 time units.

Supplementary File 3:



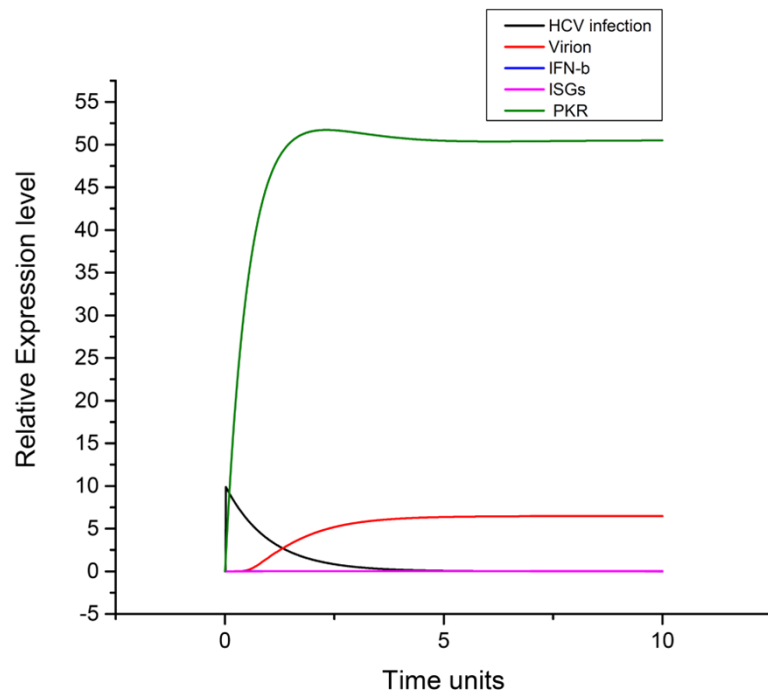
Supplementary File 3: Illustration of the HPN model elucidating the role of Protein Kinase R (PKR) in HCV infection pathway. Token concentration of ISGs was increased in order to show their high basal level resulting in PKR activation prior to HCV infection in the hepatocytes. PKR activation results in the overall translational suppression in the cell, assisting HCV proliferation. A standard place is illustrated as a circle \bigcirc representing HCV proteins, cellular enzymes, and receptor complexes. Red places represent important HCV proteins selected for this study, while blue places represent important end products of host immune responses selected for this study in particular. A continuous transition is depicted as \square representing all cellular processes including endocytosis, exocytosis, transcription, translation and activation. A \longrightarrow directed arc connects a place with a transition and vice versa.

Supplementary File 4:



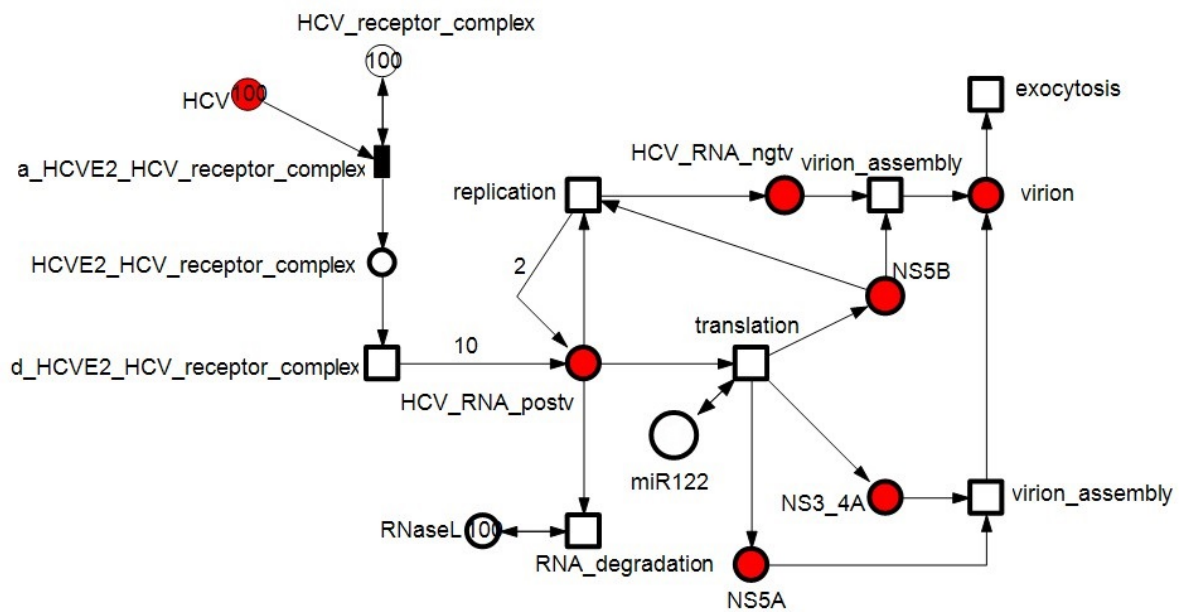
Supplementary File 4: Relative expression and activation of PKR in the cell prior to HCV infection: X-axis shows time units, while y-axis represents relative expression levels of ISGs and PKR. In certain non-responder patients, ISGs are already activated due to some other infection in body, which might result in activation of PKR ⁸². Black line represents ISGs while red line represents activation of PKR. As the signal is transferred from ISGs to PKR thus black line shows a gradual decrease while red line shows a relative gradual increase in concentration, representing activation of PKR to maintain a basal activation level of PKR prior to acute HCV infection.

Supplementary file 5:

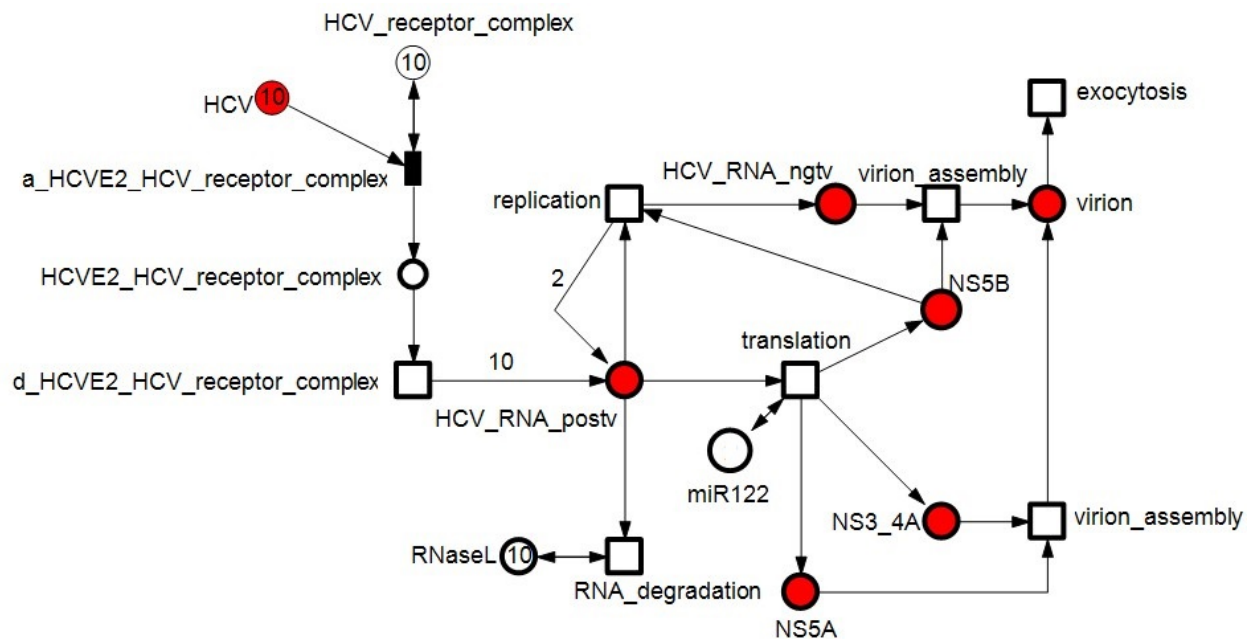


Supplementary file 5: Relative expression levels of PKR, IFN- β , ISGs and virion during acute HCV infection: X-axis shows time units while y-axis represents relative expression levels. The black line represents HCV infectious particles, the red line represents virion production, the green line represents PKR activation, the pink line and the blue line represents ISGs and IFN- β respectively. As soon as acute infection of HCV occurs, IFN- β and ISGs induction does not occur in substantial amount (pink line) to induce effective immune response. As shown in the graph, virion level (red) increases steadily while IFN- β and ISGs (pink) are not expressed due to translational control exhibited by PKR (green).

Supplementary file 6 A:



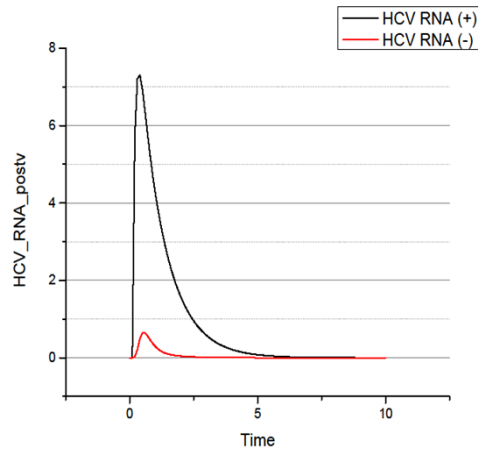
6B:



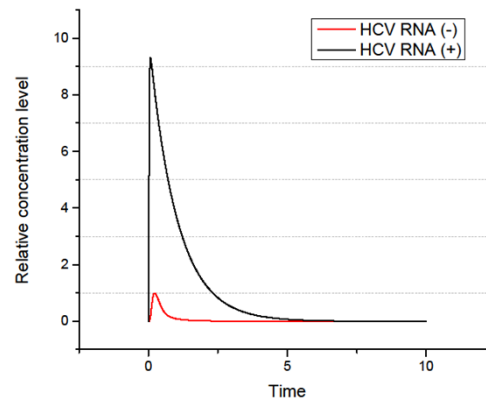
Supplementary File 6 A & B: Illustration of HCV entry and replication with 10 and 100 tokens. Figure 6A & 6B represent illustration of the simplified PN model showing HCV entry and replication of its genome. In order to clarify our point, we have shown below (Figure 6C & 6D), simulation graphs for both 6A and 6B, with 10 tokens and 100 tokens respectively. A standard place is illustrated as a circle \bigcirc representing HCV proteins, cellular enzymes, and receptor complexes. Red places represent important HCV proteins selected for this study, while blue places represent important end products of host immune responses selected for this study in particular.. A continuous transition is depicted as \square representing all cellular processes including endocytosis,

exocytosis, transcription, translation and activation. A \longrightarrow directed arc connects a place with a transition and vice versa.

6C :



6D:



Supplementary file 6 C & 6D: Simulation graphs for relative concentration of HCV RNA (+) and HCV RNA (-) in the cell having 10 and 100 tokens. X-axis represents time units while y-axis shows relative concentration level. Figure 6C and 6D shows that varying the tokens does not change the relative ratio (~10:1) of the entities.

Supplementary File 7, Source files (zip-archive)