Introduction
Several MRI and DTI methods already delivered a whole brain structural connectome [1], however none of them are able to directly probe the causal functional (effective) brain connectivity using native electrical signaling. The study of cortico-cortical evoked potentials using high-density stereoelectroencephalographic (SEEG) recordings represents perhaps the most direct way of exploring brain connectivity. However, SEEG investigations are limited to the patients with drug-resistant epilepsy, which may present disrupted connectivity patterns [2,3]. In order to dissociate pathological from physiological connectivity, we propose a method that combines individual patient’s connectivity with saliency maps and epheligenotopy of the cortical areas calculated retrospectively on a larger patient dataset.

Methods
24 patients with refractory epilepsy (Table 1) were implanted with depth electrodes for presurgical evaluation. Single pulse electrical stimulation, using biphasic pulses with 3ms pulse duration and current intensity in the 0.25-5mA range was applied to each pair of adjacent contacts and responses evoked by stimulation were recorded from other contacts located in remote brain areas. We calculated the RMS value over the 10-150 ms interval after each stimulation pulse. We considered that a contact is activated by stimulation if the responses are correlated with the stimulation current (Spearman’s ρ>0.5, p<0.05) and the mean RMS value across all stimulation pulses in a trial is higher than the 9th quartile value (Q3) of all the responses recorded within a patient [4]. Responses from the activated contacts were weighted by the epheligenotopy of each area and averaged for each patient. Further weighting was performed by calculating the saliency of each non-pathological connection in the patient database. We use the terms “inbound” and “outbound” to illustrate the connections ending on and starting from each brain structure, respectively.

Results
Over the 24 patient set, we have inserted a total of 13 ± 2.5 depth electrodes, probed 609 sites using electrical stimulation and recorded 36980 events in 1481 locations. A number of 9448 (25.3%) recorded responses met our amplitude and correlation with stimulus criteria and were used for calculating the physiological effective connectome (Figure 1). The physiological effective connectome contains 70 brain structures from both hemispheres and has a mean directional factor (DF) ± SD of 0.63 ± 0.40.

Conclusions
Using direct electrical stimulation, we obtained a physiological effective connectome covering a 70 brain structures from both hemispheres. There was a significant directionality in the functional connections between structures. This data can be used as reference tool for planning the SEEG implantations and for differential analysis of altered versus normal brain connectivity in epileptic patients.

Acknowledgments
Supported by Romanian government UEFISCID research grant PN-III-PCE-2011-3-0240.

References