

Closed-Loop Epileptic Seizure Control Device

Karen Moxon ¹, Michael Sperling ², Ashwini Sharan ²

Animal model: Pilocarpine Induced Spontaneous Seizure

- Pilocarpine: an excitotoxic agent widely used in epilepsy studies
- A small amount is infused into the hippocampus of rats
- Rats exhibit seizure activity immediately after infusion
- After a few days, rats display sudden spontaneous seizures
- Seizure model is very similar to human temporal lobe epilepsy, the most common form of human epilepsy

Animal Proof of Concept:

- **Neural synchrony is increased in the minutes before seizure onset**

1. between neurons
2. between neurons and the on-going oscillations in the brain

- **100% of seizures predicted with 30% false positive rate**

1. in real-time
2. using a single neural-synchrony variable

Human Study (Offline Data Analysis)

Patient Summary

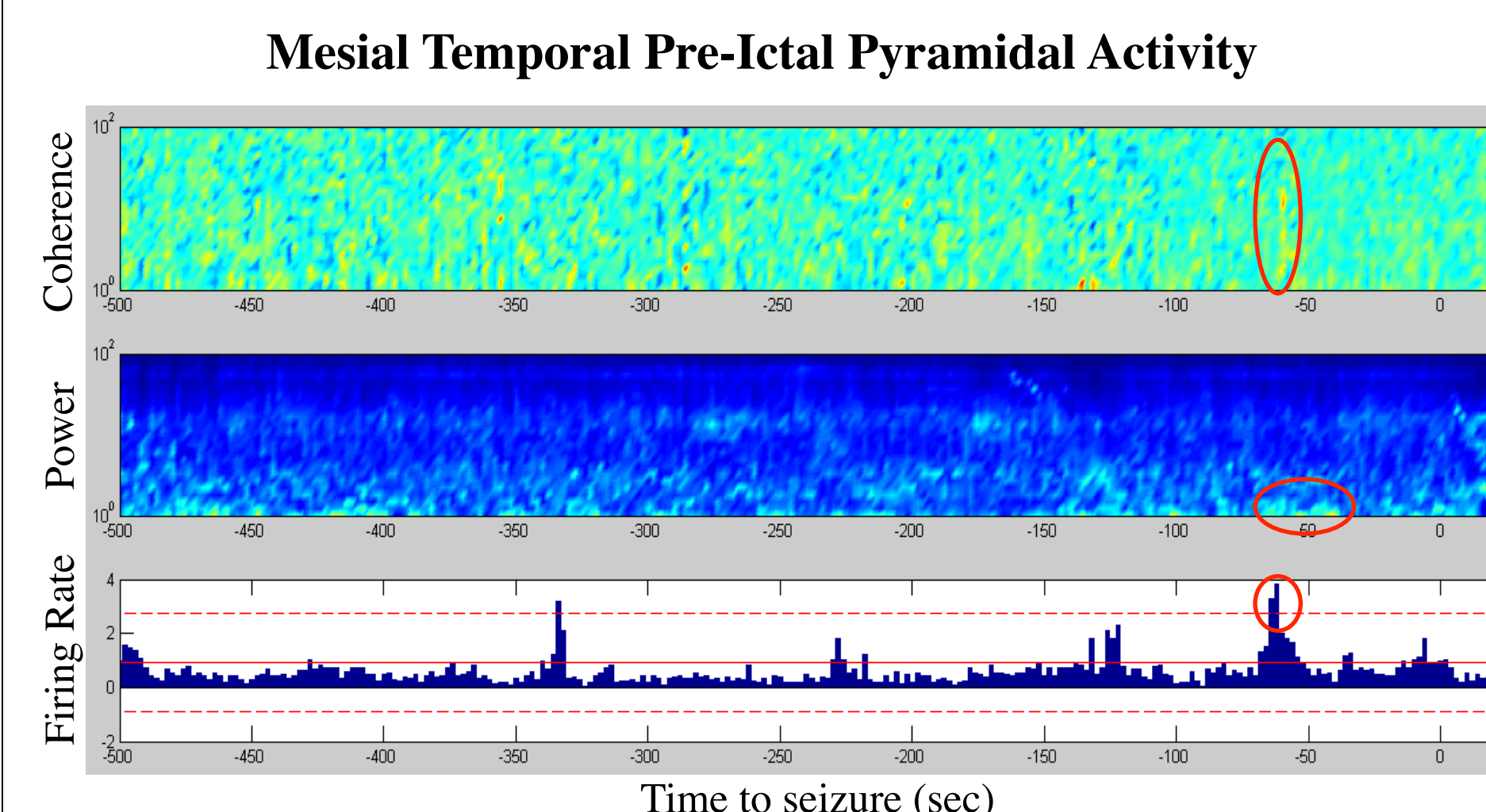
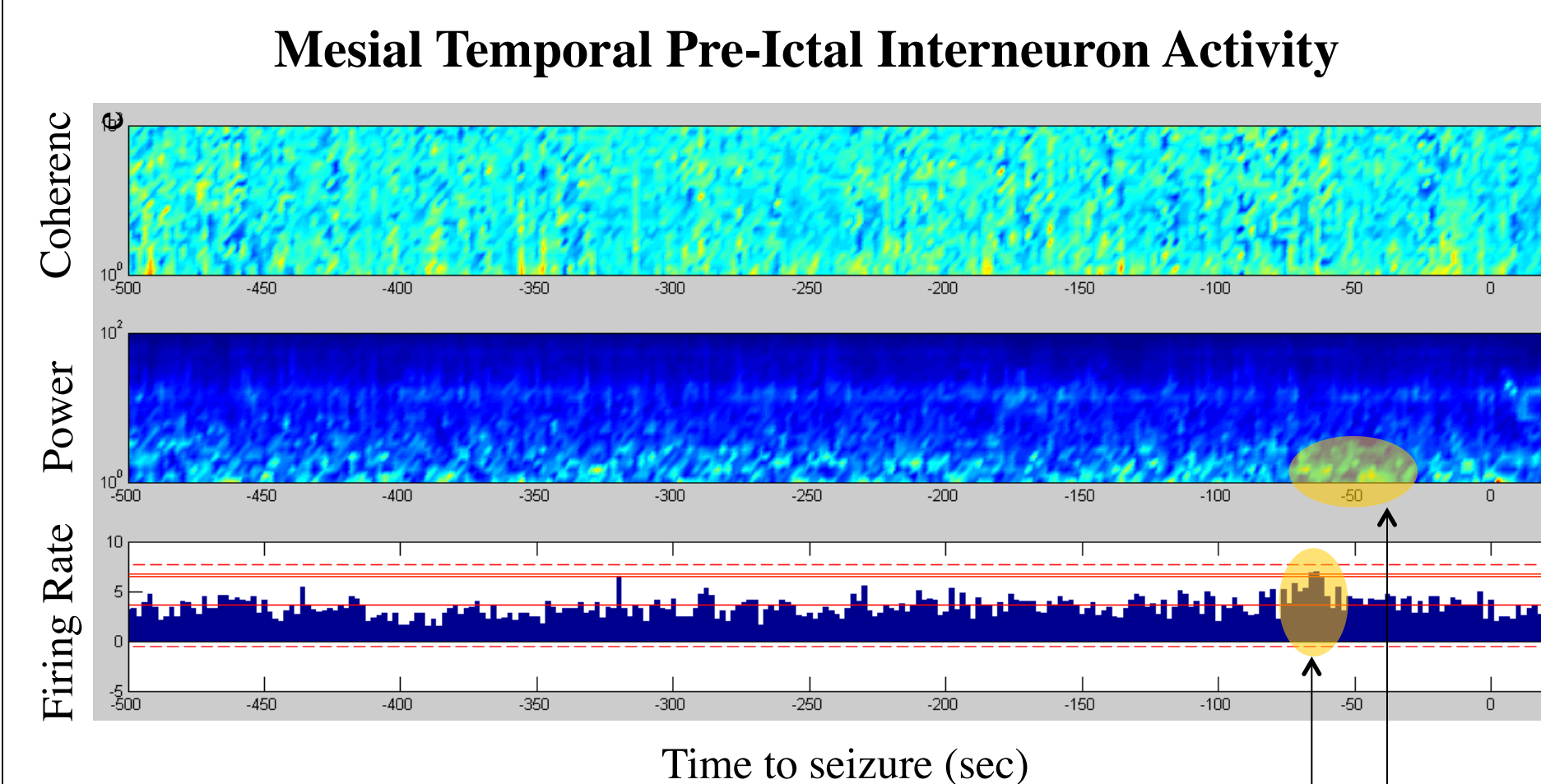
| Patient ID | # of Seizures | # Recorded | # Containing single neurons | # Int | # Pyr |
|------------|---------------|------------|-----------------------------|-------|-------|
| TJ038 | 7 | 4 | 3 | 2 | 6 |
| TJ039 | 0 | 0 | 0 | 0 | 0 |
| TJ041 | 2 | 2 | 1 | 9 | 9 |
| TJ042 | 1 | 1 | 1 | 2 | 4 |
| TJ045 | 4 | 4 | 2 | 5 | 4 |
| TJ048 | | | | | |
| TJ049 | | | | | |

Analysis in Progress
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- Human data was obtained from patients with intractable epilepsy in Thomas Jefferson Hospital
- Consent from each patient was required
- All data was de-identified before use.

Measures Used:

1. **Coherence:** how synchronized was the neuron to the local field potential (LFP), decomposed in time (about 10mins before the ictal spiking, 2s binsize) and frequency (1-100Hz, 1Hz binsize).
2. **Power:** the time-frequency decomposition of the neural signal recording. Same binsizes as in coherence.
3. **Firing Rate:** the intensity of neuronal firing within a certain time window.



Testing The Algorithm on Human Data (offline):

Tested on 3 generalizing seizures to mesial temporal lobe

Sensitivity: 100%
False Positive Rate: 5/hr

Epilepsy - a disabling neurological disorder Result of hyperactive electrical discharge in the brain

Impact on US alone:

- 3 million Americans
- 200,000 new diagnoses annually
- Direct Annual Healthcare cost of \$17.6 billion
- Indirect Cost
 - loss of lifetime earnings
 - high incidence of depression & psychosis among epilepsy patients

Unmet Medical Needs

Anti-Epileptic Drugs (AED)

- First-line treatment
- Approximately 70% respond to AED

Alternative Treatments

- Epilepsy Surgery
 - Only 8% are eligible
 - Effective 50-60%
- Vagus Nerve Stimulation: 30% of those eligible have ≥ 50% reduction
- Neuropace RNS: > 50% reduction in seizures for ~ 50% of patients tested

Approximately 20% of all epileptic patients do not respond to any available treatments

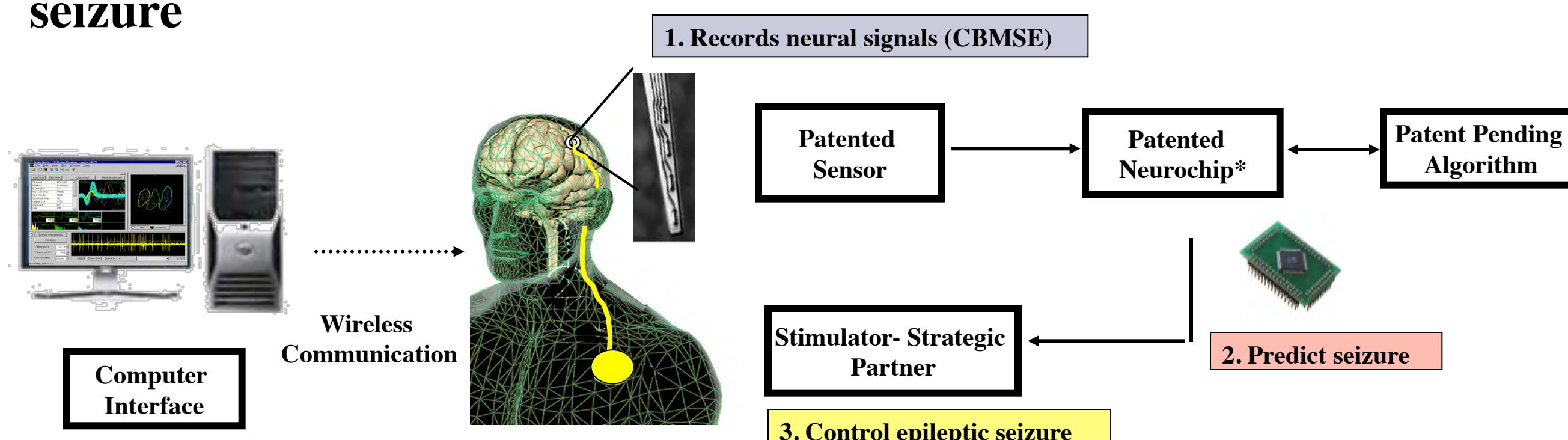
Innovative Approach: Closed-Loop Neuromodulation System that incorporates Patented Technologies

1. Record single neuron activity with our patented technology



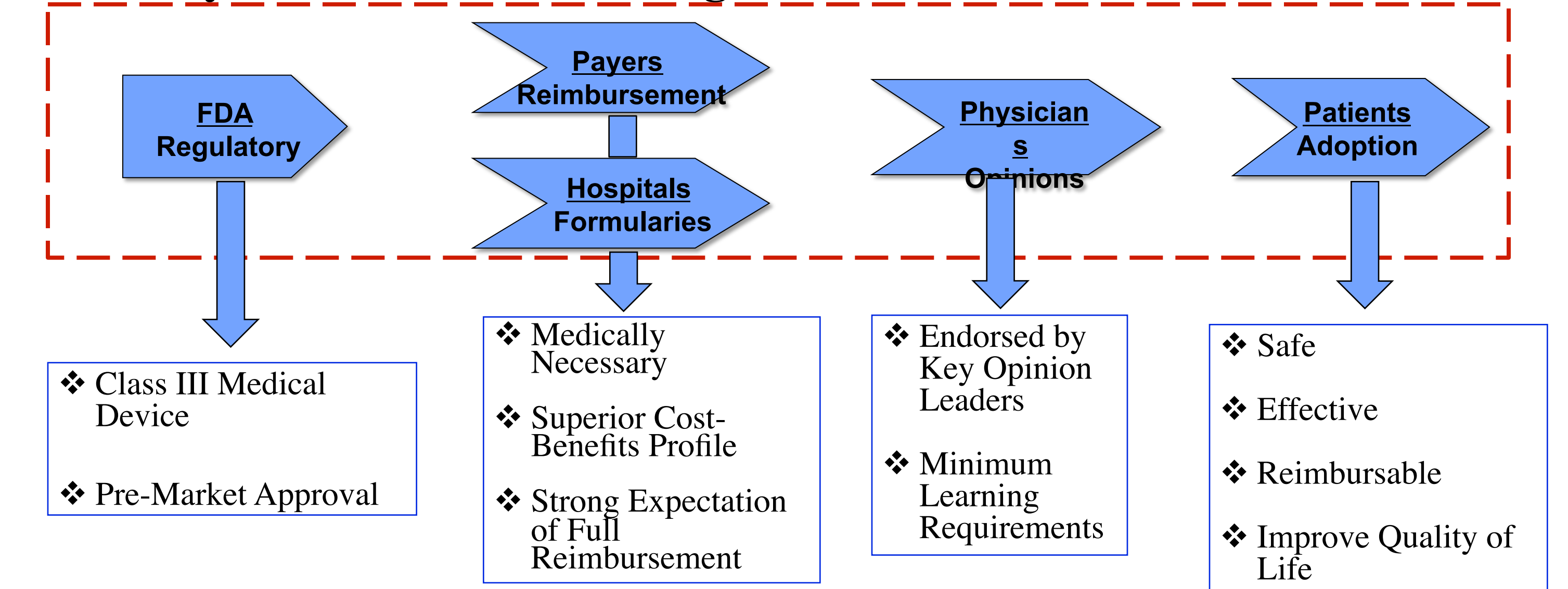
Using our patented Ceramic Based Multi-Site Electrode (CBMSE), we can directly record the electrical activity of multiple single neurons. This method is a direct approach to recording from the epileptic focus and provides for efficient data interpretation.

2. Creating a closed-looped technology to predict and prevent a seizure



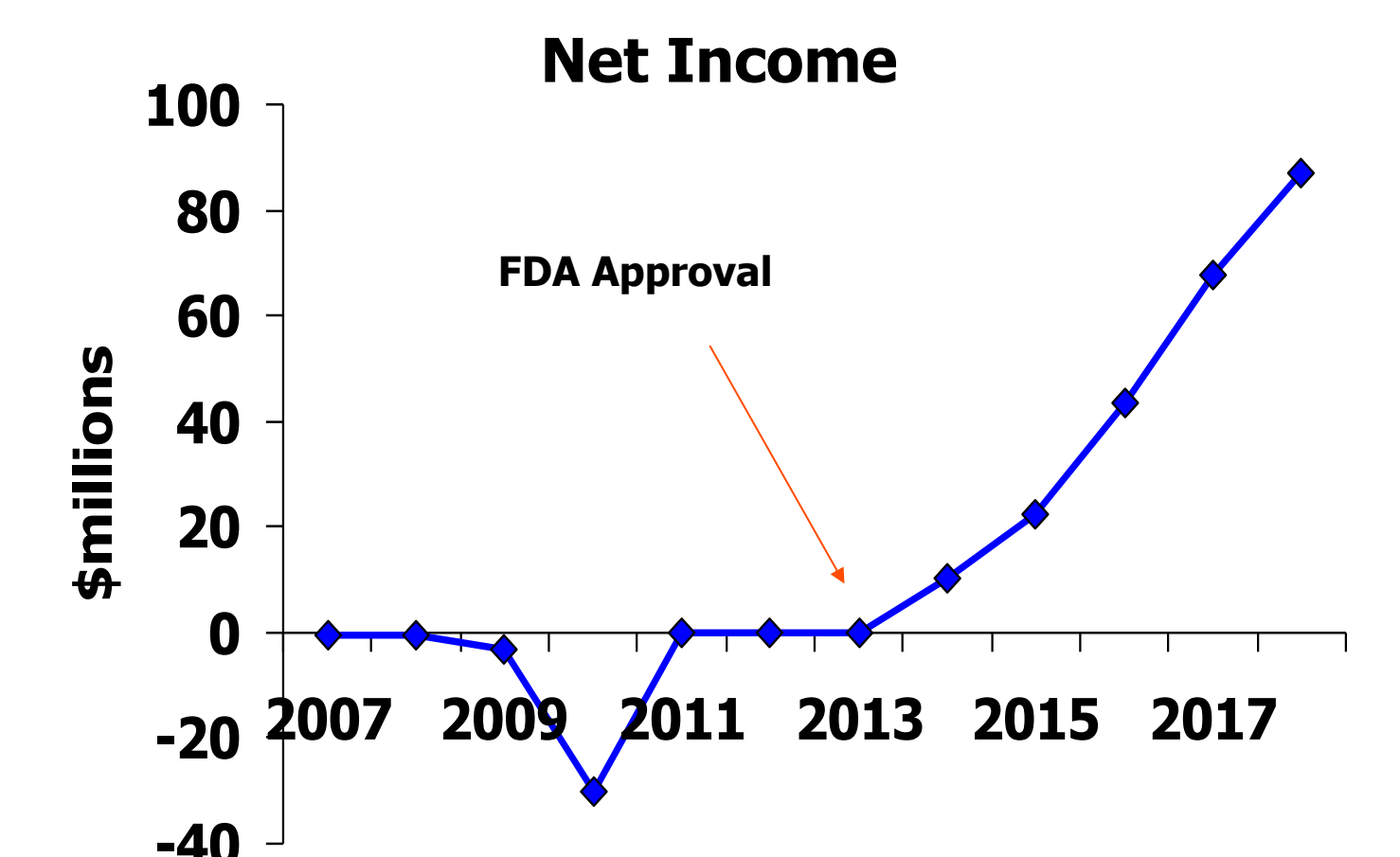
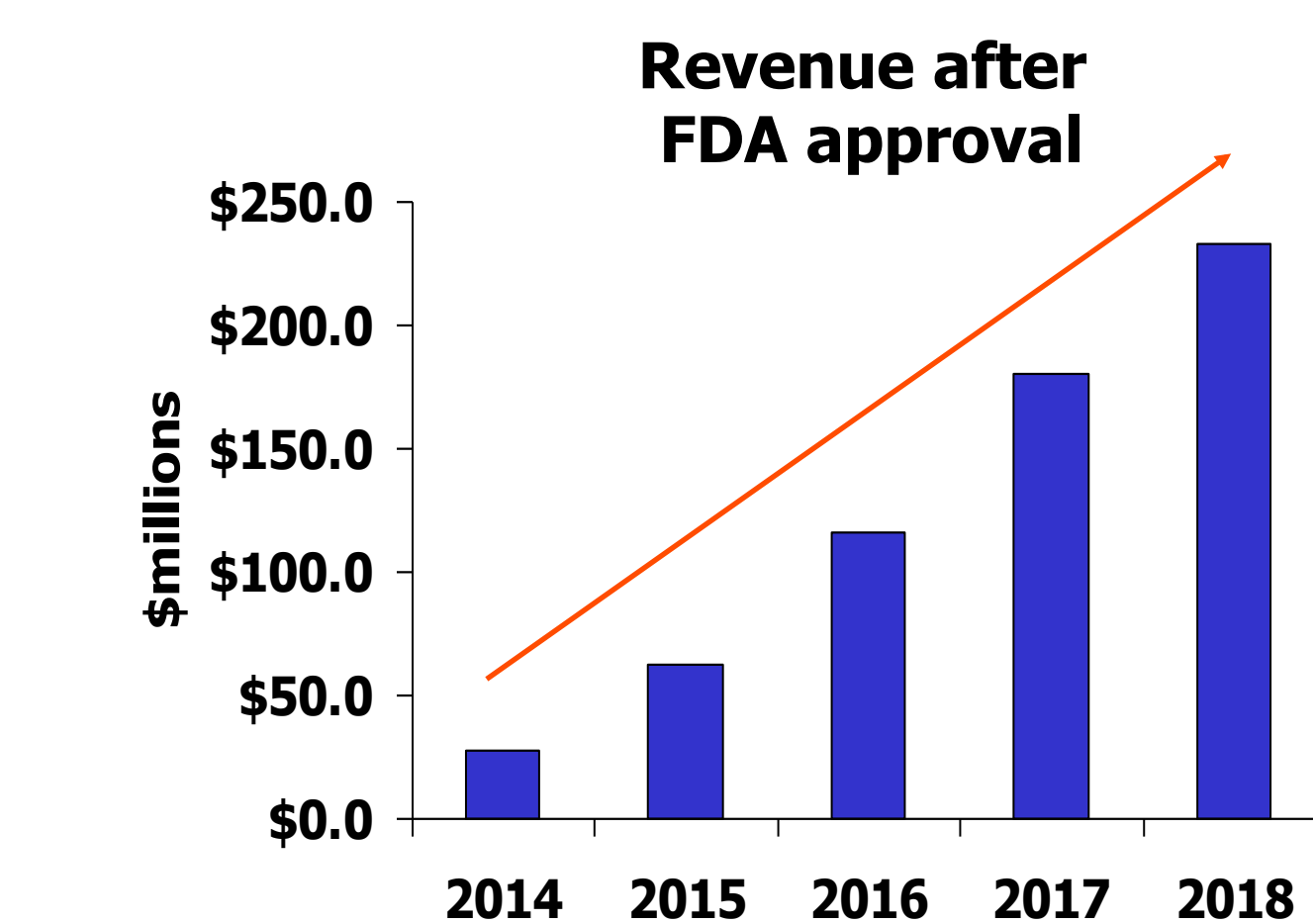
Translational Potential

Pathway to Market & Advantages:



Financial Projections:

| Year | 2014 | 2015 | 2016 | 2017 | 2018 |
|-------------------|---------|---------|---------|---------|---------|
| Treatment Centers | 20 | 25 | 35 | 45 | 50 |
| Target Market | 140,000 | 164,440 | 213,684 | 262,436 | 285,801 |
| Adoption rate | 2% | 4% | 6% | 8% | 10% |
| Units sold | 2,800 | 6,578 | 12,821 | 20,995 | 28,580 |



Conclusion

- Preliminary results show similar trending in interneuron behavior as seen in animal studies at about 60 seconds prior to clinical seizure onset. Limited numbers of neurons limit our ability to run automated detection algorithms, but optimization in recording technique have already improved yield. Novel findings of synchronous pyramidal cell firing coincides with the behavior of interneurons one minute prior to seizure and will be incorporated to make prediction algorithms more robust.
- Proven technology with high growth potential
- Clear commercialization strategy with validated models
- Strong industry know-how
- Favorable exit opportunities with active M&A activities in industry
- Patent protected technology with future patents on complimenting technologies

Future Directions

- Begin construction and bench testing of the stimulation system to prevent seizures
- Obtain IDE to make the device fully implantable in humans

Acknowledgements

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