OpenRiskNet

RISK ASSESSMENT E-INFRASTRUCTURE

Integrating multiple predictions

ModelRX Case Study

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OpenRiskNet: Open e-Infrastructure to Support Data Sharing, Knowledge Integration and *in silico* Analysis and Modelling in Risk Assessment
Project Number 731075

Problem

Given multiple evidences make a **consensus** prediction about a blood-brain barrier penetration and estimate its **uncertainty**

Approach

Dempster-Shafer theory (DST) provides framework for such integrated risk assessment

The idea behind DST - single evidence

Will it rain tomorrow?

- A friend predicts 70 % chance of rain (30 % chance of no-rain)
- We estimate his reliability to 60 %

What shall we expect?

- Probability of **rain**: $0.7 \times 0.6 = \mathbf{0.42}$
- Probability of **no-rain**: $0.3 \times 0.6 = \mathbf{0.18}$
- **Uncertainty**: $1 - 0.6 = \mathbf{0.4}$

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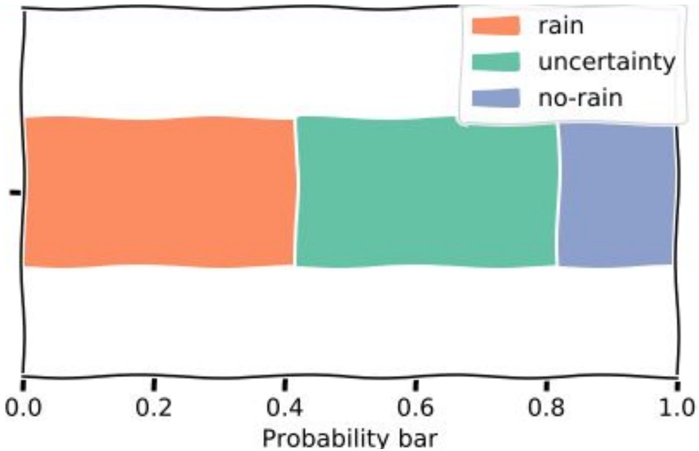
DST prediction: **equivocal**



The idea behind DST - multiple evidences

Will it rain tomorrow?

- A friend predicts 70 % chance of rain (60 % reliability)
- Newspaper predicts 60 % chance of rain (80 % reliability)
- Individual predictions are equivocal

What shall we expect?

- DST provides framework to combine such evidences into a consensus prediction

The idea behind DST - multiple evidences

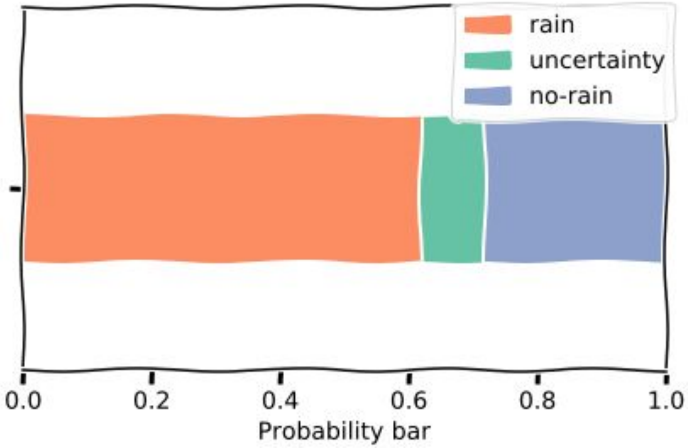
Will it rain tomorrow?

- A friend predicts 70 % chance of rain (60 % reliability)
- Newspaper predicts 60 % chance of rain (80 % reliability)
- Individual predictions are equivocal

What shall we expect?

- Probability of **rain**: **0.62**
- Probability of **no-rain**: **0.28**
- **Uncertainty**: **0.10**

DST prediction: **rain**



ModelRX case study

- **Predictive models** for blood-brain barrier penetration:

  Lazar, Jaqpot, WEKA JGU, Venn-ABERS

- **Reliability** of each model (cross-validation):

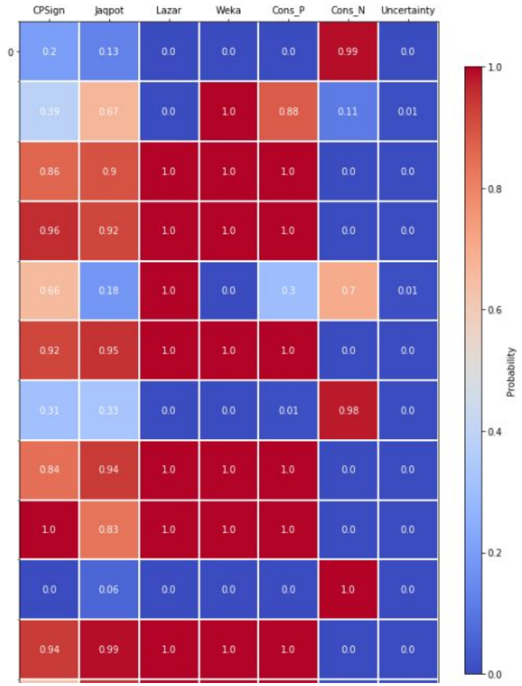
  Positive predictive value (% true positive of all predicted positive)

  Negative predictive value (% true negative of all predicted negative)

- **Test set** of ~ 400 compounds

ModelRX case study

- GitHub: [OpenRiskNet/workshop/ModelRX/Blood-brain barrier - Consensus]()
- Jupyter notebook: [consensus-batch-offline.ipynb]()
- Consensus predictions for 11 compounds of test set



Hands-on exercise

- Consensus prediction using 2 predictive models (Lazar, CPSign)
- GitHub: OpenRiskNet/workshop/ModelRX/Blood-brain barrier - Consensus
- Jupyter notebook: consensus-single-web-CL.ipynb

Main steps:

1. Provide compound structure (SMILES)
2. Access web services through REST API (Lazar, CPSign)
3. Make a consensus prediction using Python library dst.py

Hands-on exercise

1. Provide compound structure (SMILES)

```
smiles = 'COCCC'
```

2. Access the Lazar API

```
r = requests.post(
    url = 'https://lazar.prod.openrisknet.org/model/5ae2dd885f1c2d01323270ee',
    data = {'identifier': smiles},
    headers = {'accept': 'text/csv'}
)

result = json.loads(r.text)

print('Prediction:', result['prediction']['value'])
```

```
Prediction: penetrating
```

Hands-on exercise

3. Access the CPSign API

```
r = requests.get(
    url = "http://blood-brain-barrier-penetration-cvap-cpsign.prod.openrisknet.org/v1/predict",
    params = {'molecule': smiles},
    headers = {'accept': 'application/json'}
)

result = json.loads(r.text)

result['prediction']
```

```
[{'probability': 0.006, 'label': 'non-penetrating'},
 {'probability': 0.994, 'label': 'penetrating'}]
```

Hands-on exercise

4. Make a consensus prediction

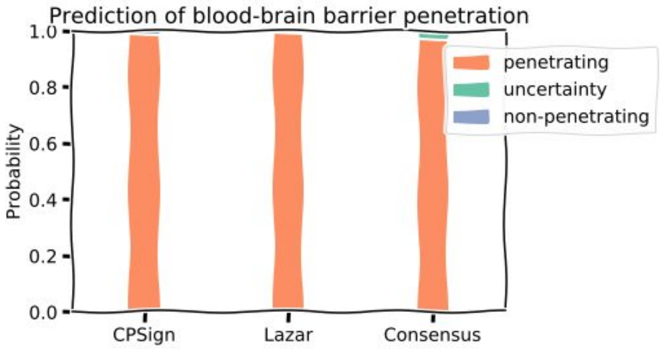
```
print('Prediction:\t', models_pred)
print('Probability:\t', models_prob)
print('PPV:\t\t', models_ppv)
print('NPV:\t\t', models_npv)
```

```
Prediction:     {'Lazar': 'P', 'CPSign': 'P'}
Probability:    {'Lazar': 1.0, 'CPSign': 0.994}
PPV:            {'CPSign': 0.809, 'Lazar': 0.886}
NPV:            {'CPSign': 0.701, 'Lazar': 0.489}
```

```
beliefs, plausibilities, result = dst.predict_Dempster(models_pred, models_prob, models_ppv, models_npv)

print('Beliefs:\t', beliefs)
print('Plausibilities:\t', plausibilities)
print('Result:\t\t', result)
```

```
Beliefs:        {'P': 0.9775762072502536, 'N': 0.0005557460659842, 'PN': 1.0}
Plausibilities: {'P': 0.9994442539340158, 'N': 0.022423792749746436, 'PN': 1.0}
Result:         P
```



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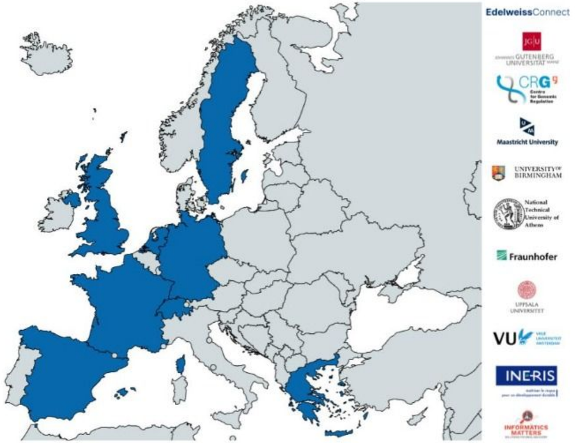
Project partners:



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