A Causal Perspective on Challenges for AI in Precision Medicine

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TL;DR
• We provide a classification of tasks in precision medicine.
• Many of them require answering causal questions.
• Many popular AI methods are not designed to consider causality.
• We provide causal interpretation rules.

Classification of Tasks

<table>
<thead>
<tr>
<th>Non-Causal</th>
<th>Causal</th>
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</thead>
<tbody>
<tr>
<td>- diagnosis</td>
<td>- risk factor identification</td>
</tr>
<tr>
<td>- genotyping/phenotyping</td>
<td>- treatment recommendation</td>
</tr>
<tr>
<td>- disease outbreak/progression prediction</td>
<td>- genotype to phenotype mapping</td>
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<td></td>
<td>- treatment development</td>
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<td></td>
<td>- treatment effect prediction</td>
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<td></td>
<td>- understanding of disease mechanism</td>
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Prediction with AI

Supervised Machine Learning: Learn function \( \hat{f} : X \rightarrow Y \) such that empirical risk \( E[\mathcal{L}(\hat{f}(X), Y)] \) is minimal.

Minimal Bayes optimal set of features: Minimal set of features \( R \) such that all other variables \( X_i \in \Omega \setminus R \) become independent of \( Y \) \( (Y \perp X_i | R) \). This so-called Markov Blanket may not only include variables that cause \( Y \). A change of \( Y \) (model) as a result of a change in \( X \) may therefore not correspond to a change in \( Y \) (real world).

Left: Underlying causal graph. Right: Dependencies as perceived by the AI model.

Given a target \( Y \) (black) not only causes (yellow), but also effects (blue) and context variables (grey) are in \( R \) (here thick black outline).

Causal Interpretation Rules

<table>
<thead>
<tr>
<th>assumptions</th>
<th>types in R</th>
<th>types not in R</th>
</tr>
</thead>
<tbody>
<tr>
<td>causal sufficiency (CS) no observed</td>
<td>⊗</td>
<td>⊗</td>
</tr>
<tr>
<td>no observed</td>
<td>⊗</td>
<td>⊗</td>
</tr>
<tr>
<td>CS and no observed</td>
<td>⊗</td>
<td>⊗</td>
</tr>
<tr>
<td>CS and no observed</td>
<td>⊗</td>
<td>⊗</td>
</tr>
</tbody>
</table>

Type Legend:
- \( \bullet \) causes = direct causes
- \( \circ \) effects = direct effects
- \( \circ \circ \) no cause or effect = direct cause of and indirect effects

Based on [5]. Causal sufficiency: No variable that causes more than one observed variable is unobserved.

Examples

Collider/Differential diagnosis: When assessing the presence of hypertensive retinopathy, knowledge about whether the patient has diabetes helps distinguish the condition from diabetic retinopathy. Inspired by [1].

Hidden Confounding/Associated Signs: UV radiation causes both the ageing of skin (wrinkles) and genetic mutation that leads to skin cancer. Wrinkles may therefore be included in a skin cancer diagnosis model.

Target dependence: A medical doctor may place a ruler in photographs of tumors to indicate their size. Depending on whether our label reflects the doctors belief (target 1) or the actual condition (target 2) a model may rely on the presence of a ruler for its diagnosis. Inspired by [2, 3]. Photograph taken from [4].

References