Inducing natural invariance in deep segmentation pipelines for generalizable detection of colorectal polyps

Any short subtitle

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Abstract

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Preface

Chapter 1

Introduction

Colorectal cancer is one of the leading causes of cancer related deaths, causing approximately 900 thousand deaths worldwide per year (cite). Early detection thereof is as a consequence of significant importance. Polyps are often an early warning-sign of developing tumor, and early detection thereof can as a result significantly reduce fatality rates. Polyps are, however, often missed during colonoscopies, owing to the significant variability in the shapes an sizes of polyps, as well a the high degrees of similarity to surrounding tissue. Hence, automatic segment polyps via deep learning has the potential to significantly increase the likelihood of early detection and effective treatment.

However, clinical applications of deep learning are known to fail in deployment, despite exhibiting excellent performance during development. This is known as generalization failure, and is ubiquitous in the domain. While there has been a growing body of research dedicated to identifying and analyzing its root causes, there is still limited research into approaches to mitigating generalizability failure.

This thesis presents a novel approach to increasing generalizability, whereby the model is trained to not only minimize segmentation-loss, but also minimize the effects of the data being perturbed by an ensemble of transformations, including color-transformations, geometric transformations, additive noise, and adding extra polyps to the image using a GAN-inpainter. This endows the pipeline with the ability to more readily infer causally viable inductive biases by explicitly forcing the model to be robust to any combination of the aforementioned transformations.

Generalizability is then measured by evaluating several vanilla-pipelines consisting of several models on a number of separate datasets, which itsthen compared toroot causes, the results of the modified piresults show that (...)

Chapter 2

Background

2.1 Colorectal Polyps, Medical Imaging, and Deep Learning

Polyps are small growths found in and around the inner lining of the large intestine. These polyps, also referred to as adenomas, can in time develop into cancerous tumours, or carcinomas, in a process known as the adenoma-carcinoma sequence [10]. Though the majority of polyps do not undergo this process, identifying polyps nonetheless constitutes an important step towards preventing colorectal cancer. Indeed, resection of these polyps has been shown to reduce the incidence of colorectal cancer by a significant margin [14].

Though colorectal cancer remains as one of the leading causes of cancer-related death worldwide (source), mortality rates have nonetheless declined in large part to increased use of screening colonoscopy, which in turn allows for the opportunity for preemptive treatment. Polyps are, however, by nature somewhat difficukt to detect and are routinely missed by clinicians, with miss rates ranging upwards of 27% for diminutive polyps [8, 11].

Naturally, reducing this miss rate has the potential to further reduce incidence rates. There has been a significant body of work dedicated to for instance workflow optimization using both optical and mechanical approaches, for instance chromoendoscopy, wherein stains or dyes are applied at the time of endoscopy, or the use of alternative lighting such as narrow-band imaging, which increases the textural details that help distinguish polyps from their surrounding tissue.

These systems do, however, require more equipment, training and expertise to effectively employ. Thus, automatic polyp segmentation using deep learning and convolutional neural networks (CNNs) has been identified as another diminutive detection method. This requires minimal training time on the part of the clinician, no additional equipment, and has been show to significantly increase detection rates when deployed in a clinical setting [1].

Naturally, these results are not unique to the detection of polyps. Indeed, medical imaging has in recent years proven to be one of the most

promising applications of artificial intelligence and deep learning, having the capacity to significantly improve both the accuracy and efficiency of detection, diagnosis, and treatment of a wide variety of diseases [13].

There are, however, still several hurdles to overcome; recent research has shown that even state of the art deep-learning pipelines are prone to generalisation failure when deployed in practical settings, particularly when exposed to distributional shifts such as changes in demographics, imaging equipment, noise, and more despite exhibiting high performance on hold-out sets [2, 4, 7, 15]. There is no reason to expect that polyps are exempt from this problem, given how pervasive such shortcomings are in similar tasks.

Naturally, such systems are rendered practically useless should they fail to perform sufficiently outside of the very carefully controlled conditions upon which they are trained. Thus, for AI-assisted detection to be on any considerable merit, it has to infer causally reasonable patterns in the data that generalize well to other hospitals, demographics, imaging equipment, resolutions, and so on. Though a human would not find this type of generalisation very difficult, deep-learning (and for that matter, other data-driven approaches) regularly seem to fail in this regard.

2.2 Generalisation failure in the Wild

The medical domain is characterized by a number of key features that separate it from other areas where deep-learning typically excels. Training data is often scarce, the pathologies that constitute the classification targets are unevenly distributed and often exhibit high degrees of inter-class variability, and there can be a significant number of confounding variables.

For instance, a deep-learning based classifier which successfully detected pneumonia in X-ray scans across a number of hospitals with striking accuracy was determined to be basing its predictions not on any lesions or otherwise pathologically relevant features in the images, but rather on a hospital-specific metal token that was on every image, which it used in conjunction with learning the prevalence rate of pneumonia for the hospitals from which the data was collected. As a result, when deployed on data from hospitals that it had not seen during training, the system failed to generalize [15].

In another study, it was shown that a classifier intended to detect diabetic retinopathy exhibited significant variability in performance depending on the type of camera used. The same study also showed that the same type of performance variability could be found when detecting skin-conditions across demographics with differing skin tones. [4].

Though there has been limited literature detailing the generalisability of pipelines trained to segment polyps, there is no reason to believe that it is somehow exempt from the same problems that impact the aforementioned tasks. To illustrate this, a brief meta analysis can be performed. Table There has been astonishingly little research into determining the generalisability of models designed for polyp-detection.

Model	IID	Mean OOD
DeepLabV3	...	...
U-Net	...	...
FPN	...	...
DDA-net	...	...
Divergent-net	...	...

As a result, a meta-analysis of a selection of such models is required. Several models, consisting of DDANet, DivergentNet, (...), were trained according to the hyperparameters provided in their respective papers and repositories. Table (...) shows their results when evaluated on separate datasets. Methodological details can be found in chapter (...).

Naturally, non-medical domains are in no way immune to generalisation failure. In fact, one could easily argue that the vast majority of deep-learning pipelines fail to generalize altogether, and instead merely infer some set of inductive biases that, although perhaps causally incorrect, perform sufficiently well for general use. It has for instance been shown that CNNs trained on imagenet, one of the largest and most diverse datasets in the domain of computer vision, are heavily biased towards textural features[6]. Naturally, this is not necessarily causally accurate; a cat is not a cat because it has cat-like fur; nor is an elephant an elephant only because it has the skin of an elephant. By manually increasing shape bias, it has been shown that the performance of such CNNs improves both in robustness to perturbations and iid accuracy.

Another characteristic of deep learning that supports this argument is the effectiveness of adversarial attacks [9], which specifically target weaknesses in the inductive biases within DNNs through any number of means in an attempt to induce high rates of incorrect, yet highly confident predictions. Gradient-based adversarial attacks, for instance, use the gradients of the model to break even the most sophisticated and well-trained pipelines merely by adding some carefully crafted, yet visually imperceptible noise to the inputs [3]. Even without access to the gradients, there exists a multitude of so-called black-box attacks that only use output samples to generate similarly effective attacks (cite). Finally, it has been shown that adding minor visual distractions to objects, for example adding bits of tape or graffiti to stop signs, dramatically increases misclassification rates [5].

Even benign, but nonetheless confounding perturbations also have the potential to induce failure. It has for instance been shown that sophisticated natural language processing models can and readily do fail if one adds peripheral information to the input. (Example, citation)

2.3 Generalisability Theory

Exactly why and how DNNs seem to so persistently fail to generalize is a topic of ongoing research, and the available literature seems to suggest

that the problem is multifaceted. This section is an attempt to summarize and distill the findings and analysis performed in the field. It will cover the theoretical basis of generalisation and why one might expect DNNs to generalize, discuss the key characteristics of generalisation failure and their origins, and finally introduce a probabilistic perspective of generalisation.

2.3.1 Generalisation through Empirical Risk Minimization

Naturally, deep learning would not have experienced as much of a revolution in the last decade or so if there was not some semblance of an expectation that their striking performance was generalisable and performant also outside the idealized settings typically involved in research. The theoretical basis that informs this belief in (most) modern deep learning pipelines is the idea of so-called empirical risk minimization, wherein it is assumed that the dataset upon which the model is trained is a representative sample of the distribution of all possible samples in the relevant domain. In other words, it assumes that the dataset is independently and identically distributed (iid) to the domain distribution. To better understand this assumption, it is beneficial to consider the it from first principles:

At the most fundamental level, the goal of machine learning is to learn a mapping between two spaces of objects X and Y. This mapping, namely the function $f : X \to Y$, maps some input object $x \in X$, an image for example, to a corresponding and application-relevant output object $y \in Y$, for instance a segmentation mask or a class probabilities. It is worth noting, however, that f is not as much a function in the mathematical sense as much as it is an abstraction of whatever ground-truth relationship that the deep learning system is intended to capture, and consequently cannot typically be modelled explicitly. Instead, machine learning systems aim to find a representation of this mapping automatically by leveraging a training set $\{x_i, y_i\}_{0\ldots n}$ to find a sufficiently performant approximation of f. This is referred to as supervised learning, and the resulting approximation found using the training set is denoted by $h : X \to \hat{Y}$, and typically referred to as a hypothesis.

To find such an approximation, we assume that there exists a joint probability distribution over X and Y, namely $P(x, y)$, and that the training data $\{x_i, y_i\}_{0\ldots n}$ is drawn from this probability distribution such that the resulting sample distribution is independent and identically distributed to $P(x, y)$. This is the so-called iid assumption. By modelling the mapping as a joint probability distribution, one can model uncertainty in the predictions by expressing the output as a conditional probability $P(y|x)$. In conjunction with a loss-function $L(h(x), y)$ which measures the discrepancy between the hypothesis and the ground truth, these assumptions allows us to quantify the expected performance of a given hypothesis:

$$R(h) = \boldsymbol{E}[L(h(x), y)] = \int L(h(x), y) dP(x, y) \tag{2.1}$$

Using this framework, one can then find an iid-optimal hypothesis, often called a predictor, by finding the predictor h^* among a fixed class of

functions (defined by network architecture) $\mathcal{H}$ that minimizes risk:

$$h^* = \arg\min_{h \in \mathcal{H}} R(h) \tag{2.2}$$

Since $P(x, y)$ is not known, however, one cannot compute $R(h)$ explicitly. Instead, the expected risk has to be estimated empirically, i.e by finding the arithmetic average of the risk associated with each prediction by the hypothesis over the training set:

$$R_{emp}(h) = \frac{1}{n} \sum_{i=1}^{n} L(h(x_i), y_i) \tag{2.3}$$

This risk can in turn be minimized with respect to the hypothesis class. This is called empirical risk minimization (ERM):

$$\hat{h} = \arg\min_{h \in \mathcal{H}} R_{emp}(h) \tag{2.4}$$

To reiterate, the central idea with this approach to machine learning is that the training data can be considered a finite iid sampling of the underlying distribution. As such, by the central limit theorem, the hold-out performance of the computed hypothesis will approach iid-optimal performance given a sufficient amount of training data and some sufficiently capable and regularized training procedure. This should in theory allow deep learning systems to be able to generalize, since the empirical risk in theory can approximate the true risk arbitrarily well given sufficient training data support.

2.3.2 A taxonomy of Generalisation Failure Modes

As the analysis in 2.2 shows, ERM nonetheless readily fails to generate generalisable predictors with respect to out-of-distribution data). Understanding exactly why this is the case is a subject of ongoing study, and the literature around the matter is highly fragmented. Naturally, generalisation is a complex and highly multifaceted phenomenon, with roots in any number of different factors, so there does not typically exist one unique property that sufficiently fully characterizes every instance of generalisation failure. To conduct a proper analysis thereof, it is as such beneficial to construct a taxonomy over the various forms of generalisation failure, the properties that induce them, and the how these properties emerge with respect to empirical risk minimization. First, consider the assumptions upon which ERM is based, namely that:

1. The empirical risk is a good approximation of the true risk $R(h)$
2. f exists in $\mathcal{H}$
3. $\{x_i, y_i\}$ is an IID sampling of $P(x, y)$. This is the aforementioned iid assumption.

4. $P(x, y)$ (and, given that 3 is true, $\{x_i, y_i\}$) is independently and identically distributed to full space of input-output pairs one might expect in deployment, henceforth denoted by $P_\infty(x, y)$.

5. $\hat{h}$ is unique in in $\mathcal{H}$

Violations of any one of these assumptions induces a corresponding generalisation failure mode. The behavior that violations of assumptions 2 and 1 correspond is well understood and fairly easy to detect, and is referred to as underfitting and overfitting respectively, but violations of the remaining assumptions, result in more subtle forms of failure, namely internal misalignment, external misalignment, and underspecification respectively for assumptions 3, 4 and 5.

Underspecification

Overfitting

Underfitting

Structural misalignment

2.3.3 A Bayesian perspective of generalisation

2.4 Mitigating generalisation failure

2.4.1 Adversarial Training

2.4.2 Adversarial attacks and defences

2.4.3 Improved Risk estimation

Data augmentation

Distributional modelling

2.4.4 Bayesian Learning

Chapter 3

Methodology

As described in earlier sections, good generalizability can only be achieved if the pipeline can reliably produce predictors that infer the right inductive biases. Naturally, the set of correct inductive biases are not known, so any such pipeline instead has to learn to not infer the wrong inductive biases. To achieve this, a model of natural variance is constructed, which aims to encapsulate all the variability one might expect to see in the domain. This model can then be leveraged to force the pipeline to be robust to natural variance through contrastive learning. The central idea, then, is that it is more likely that the model learns to infer generalizable inductive biases as opposed to learning to learning to simply be robust to all possible configurations of a large amount of transformations.

To evaluate this, several predictors are trained from several pipelines with and without the influence of (algorithm name). Their performance is then evaluated on both a stress-test, and two separate polyp datasets, namely Etis-larib and EndoCV2021).

3.1 (algorithm name)

3.1.1 Model of natural variability

In order to account for any natural variation one may expect to find in deployment, it is necessary to construct a model which can parameterize the variability that is encountered, in other words a model of natural variability (MNV) Naturally, there is no way of knowing the full extent thereof, but it may be sufficient to model some subset of the possible distributional shifts. This, naturally, requires some knowledge of the domain from which the dataset is collected. Similarly to how adding rotational augmentations is a bad idea for classification of hand-written numbers, certain transformations may or may not be suitable for use within a MNV.

In the case of polyp-segmentation, it is clear that it is necessary to account for variability in for instance lighting, polyp-size, polyp-shape, polyp-location, camera-quality, color-shifts, blurs, optical distortions, and affine transformations. Thus, a model is required that can (more or less)

parametrize this variability. Broadly speaking, these transformations can be categorized as follows:

- Pixel-wise variability, which affect only the image, i.e color-shifts, brightness shifts, contrast-shifts, lighting, blurs etc
- Geometric variability, which affect both the image and the segmentation mask by some parametrizable quantity, i.e affine transforms and distortions
- Manifold variablity, which affects both the image and the segmentation mask depending on a learned model of the distribution, i.e the size, shape and location of polyps

Pixel-wise variability and geometric variability can be modeled fairly trivially through the use of the same transformations typically used for data-augmentation. Manifold-variability, however, is somewhat more difficult. Similar to how [12] employs cross-dataset style-transfer, it is necessary to find some way to model the distributional properties of the data, and then apply perturbations using the resulting model. Since both the size, shape, and position of polyps can be expected to vary, a model that can change all these factors is necessary. To this end, an in-painting model can be constructed. In particular, a GAN-inpainter.

Gan-based polyp inpainting

3.1.2 Geometric and pixel-wise transformations

3.2 Baselines

Several models were tested (...)

3.3 Datasets

3.4 Metrics and evaluation

Chapter 4

Results

Chapter 5

Results

5.1 Augmentation Robustness and Consistency Loss

As the results show, the performance of the pipeline that merely used augmentations is more or less equivalent to the performance exhibited by the modified pipeline. There is a very good reason for this: Consistency loss is mathematically equivalent to data augmentation, up to the choice of hyperparemeters - i.e augmentation probability, learning rates, etc. This section presents a proof of this fact, along with a theoretical analysis of how data augmentation affects the pipeline.

5.1.1 Data augmentation

Let $Y := \{y, \hat{y} := f(x)\}$ be the set consisting of the segmentation predictions and masks for the unaugmented samples, and $A := \{a := MNV(y), \hat{a} := f(MNV(x))\}$ be the set consisting of segmentation predictions and masks for the augmented samples. Finally, let $Z := \{z, \hat{z}\} \in_R \{Y, A\}$. The loss function subject to data augmentation can then be expressed as $L(Z \in_R Y, A)$, where L is any loss function. For the sake of simplicity in remaining calculations, this will be treated as the Jaccard loss, i.e $L(y, \hat{y}) := 1 - \sum y \cap \hat{y} / \sum y \cup \hat{y}$

$$L(Z \in_R Y, A)$$

5.1.2 Consistency loss

$$L_s = \frac{1}{\sum \hat{y} \cup \hat{a}} \sum \hat{y} \ominus y \tag{5.1}$$

$$L_c = \frac{1}{\sum \hat{y} \cup \hat{a}} \sum [\hat{y} \ominus y \ominus \hat{a} \ominus a] \tag{5.2}$$

$$L_{c+s} = L_c(Y, A) + L_s(Y) \tag{5.3}$$

$$= \frac{1}{\sum \hat{y} \cup \hat{a}} \left[\sum \{\hat{y} \ominus y \ominus \hat{a} \ominus a\} + \sum \{\hat{y} \ominus y\} \right] \tag{5.4}$$

$$\begin{aligned} &= \frac{1}{\sum \hat{y} \cup \hat{a}} \Bigg[\sum \{\hat{y} \ominus y\} + \sum \{\hat{a} \ominus a\} \\ &- \sum \{\backslash y \cap \hat{y} \cap a \cap \hat{a}\} \cup \{y \cap \backslash \hat{y} \cap a \cap \hat{a}\} \cup \\ &\{y \cap \hat{y} \cap \backslash a \cap \hat{a}\} \cup \{y \cap \hat{y} \cap a \cap \backslash \hat{a}\} \\ &- \sum \{\backslash y \cap \hat{y} \cap \backslash a \cap \hat{a}\} \cup \{y \cap \backslash \hat{y} \cap \backslash a \cap \hat{a}\} - \\ &\cup \{\backslash y \cap \hat{y} \cap a \cap \backslash \hat{a}\} \cup \{y \cap \backslash \hat{y} \cap a \cap \backslash \hat{a}\} \\ &+ \sum \{\hat{y} \ominus y\} \Bigg] \end{aligned} \tag{5.5}$$

$$\begin{aligned} &= 2L_s(y, \hat{y}) + L_s(a, \hat{a}) + \frac{1}{\sum \hat{y} \cup \hat{a}} \Bigg[\\ &- \sum \{\backslash y \cap \hat{y} \cap a \cap \hat{a}\} \cup \{y \cap \backslash \hat{y} \cap a \cap \hat{a}\} \cup \\ &\{y \cap \hat{y} \cap \backslash a \cap \hat{a}\} \cup \{y \cap \hat{y} \cap a \cap \backslash \hat{a}\} \\ &- \sum \{\backslash y \cap \hat{y} \cap \backslash a \cap \hat{a}\} \cup \{y \cap \backslash \hat{y} \cap \backslash a \cap \hat{a}\} - \\ &\cup \{\backslash y \cap \hat{y} \cap a \cap \backslash \hat{a}\} \cup \{y \cap \backslash \hat{y} \cap a \cap \backslash \hat{a}\} \Bigg] \end{aligned} \tag{5.6}$$

The non-loss terms in equation 5.6 are proper subsets of the symmetric difference of the mask and segmentation across either dataset. The component of the loss that corresponds to these terms consequently grows in proportion to both $L_s(y, \hat{y})$ and $L_s(a, \hat{a})$. L_{c+s} and L_{sy+sa} are therefore monotonically correlated - i.e, when one grows, the other grows with it, and when one falls, the other one falls with it.

5.1.3 Adversarial Dice

$$L = \frac{1}{2} L(a, \hat{a}) + \frac{1}{2} L(y, \hat{y})$$

This should be asymptotically equivalent to data augmentation wit p=0.5

Chapter 6

Discussion

asdasdf

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